Medicinal Mushrooms and Cancer

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Immune Modulation From Five Major Mushrooms: Application to Integrative Oncology

Alena G. Guggenheim, ND; Kirsten M. Wright, BS; Heather L. Zwickey, PhD

Abstract

This review discusses the immunological roles of 5 major mushrooms in oncology: *Agaricus blazei*, *Cordyceps sinensis*, *Grifola frondosa*, *Ganoderma lucidum*, and *Trametes versicolor*. These mushrooms were selected based on the body of research performed on mushroom immunology in an oncology model. First, this article focuses on how mushrooms modify cytokines within specific cancer models and on how those cytokines affect the disease process. Second, this article examines the direct effect of mushrooms on cancer. Finally, this article presents an analysis of how mushrooms interact with chemotherapeutic agents, including their effects on its efficacy and on the myelosuppression that results from it. For these 5 mushrooms, an abundance of in vitro evidence exists that elucidates the anticancer immunological mechanisms. Preliminary research in humans is also available and is promising for treatment.

Scientific Name	Common Name	Specific Constituent	Type of Constituent
Agaricus blazei	Agaricus	β-D-glucan	Polysaccharide
Ganoderma lucidum	Reishi, lingzhi	Ganoderic acid Danoderiol Danderenic acid Lucidenic acid GLPS	Protein Protein Protein Protein Polysaccharide
Cordyceps sinensis	Cordyceps, caterpillar mushroom	Adenosine Cordycepin	Nucleotide Nucleotide
Trametes versicolor (formerly *Coriolus*)	Turkey tail	PSP PSK	Polysaccharide peptide Polysaccharide peptide
Grifolia frondosa	Maitake	Grifolan D-fraction MD-fraction	Polysaccharide Polysaccharide Polysaccharide
Lentinula edodes	Shitake	Active Hexose Correlated	Polysaccharide

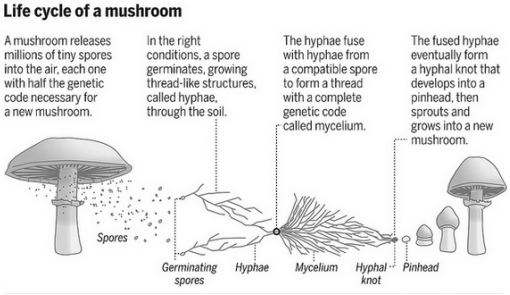
Adapted from Guggenheim

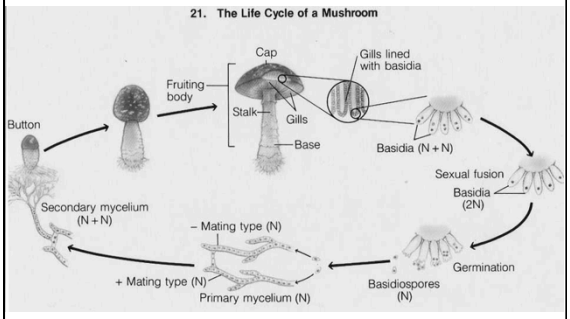
Medicinal Mushrooms: Overview

- Properties: immunostimulating, antimicrobial, anti-inflammatory, cardio-protective, anti-diabetic, hepato-protective and anti-cancer
- Immunomodulating effects on Natural Killer cells, dendritic cells, T lymphocytes, macrophages and hematopoietic stem cells

Medicinal Mushrooms and Cancer

- *Trametes versicolor (Coriolus)*
- *Ganoderma lucidum* (Reishi)
- *Grifolia frondosa (*Maitake)
- *Lentinula edodes* (Shitake)
- *Inonotus obliquus (*Chaga)
- *Cordyceps sinensis*
- *Hericeum erinaeus* (Lion's Mane)
- *Agaricus blazei, sylvaticus, bisporus (Button mushrooms)*
- *Psilocybe cyanescens (*Psilocybin)





Mushrooms & Cancer

- Research has demonstrated potent:
  - Antineoplastic properties
  - Regulation of tumor genes
  - Decrease in tumor angiogenesis
  - Increase in malignant-cell phagocytosis
  - Chemo-sensitizing
  - Protection against chemo-induced bone marrow suppression

β-glucans

- Mushroom polysaccharides are primarily responsible for the potent immunomodulating effects
- Glucans can be extracted from cell walls of yeast, oat, barley, seaweeds, algae and bacteria, as well as fungi
- Fungal polysaccharides include chitin, cellulose, β-glucans (eg lentinan, grifolan, krestin [PSK]) and α-glucans (eg glycogen), or polysaccharide-protein complexes
- Specific receptors for glucans on immune cells
- Vannucci L et al. Immunostimulatory properties and antitumor activities of glucans (Review). Int J Onc 2013. 43: 357-364, 2013

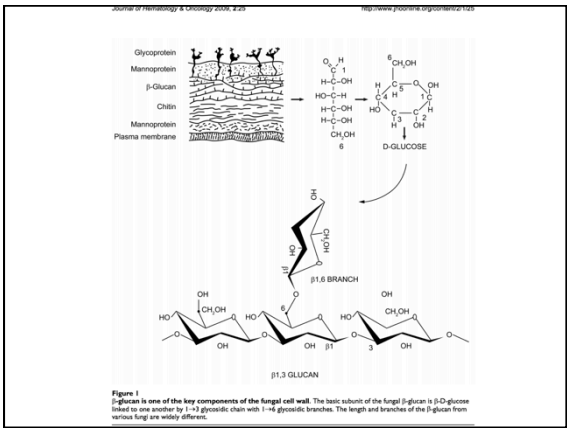
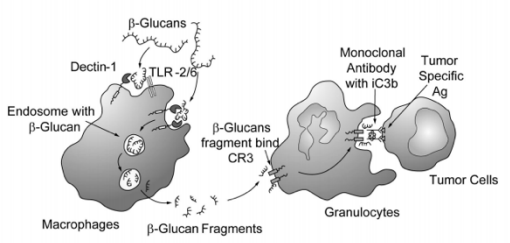
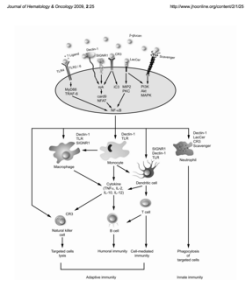


Figure 1
β-glucan is one of the key components of the fungal cell wall. The basic subunit of the fungal β-glucan is β-D-glucose linked to one another by 1→3 glycosidic chain with 1→6 glycosidic branches. The length and branches of the β-glucan from various fungi are widely different.

β-D-glucan receptors on immune cell



Immune Activation Induced by Beta-glucans



Specific effects of β-D-glucans on the immune system:

- Increased number of circulating NK cells and increased NK cell activity
- Increased antimicrobial activity of monocytes and neutrophils
- Enhanced functional activity of macrophages (inducing NO production)
- Stimulating proliferation of monocytes and macrophages
- Stimulating production of pro-inflammatory molecules such as complement components, TNF-alfa, IL-2, IFN-gamma
- Enhanced phagocytosis of neutrophils
- Increased number of leukocytes
- Induction of activation of NFkB-like nuclear transcription factor

Limitations of Current Beta-glucans Research

Chan GC, et al. The effects of beta-glucan on human immune and cancer cells. J Hem Onc 2009, 2:25

- No Beta-glucan standard with specific molecular weight and branches are available.
- Most of the Beta-glucan publications used zymosan, which is a mixture of chitoxan, Beta-glucans and cell wall particles.
- Most of the Beta-glucan containing herbal research are based on extracts rather than purified Beta-glucans
- No well-characterized methods either qualitatively or quantitatively are currently available for assessing and comparing Beta-glucans from different sources
- Lack of translational approach to apply knowledge of receptor and signal pathways of Beta-glucans to animal or clinical trials.
- The exact immunological actions and signaling pathway induced by Beta-glucan are still unclear and have to be further defined.

Dietary mushroom intake and cancer risk

Nutr Cancer. 2010;62(4):476-83. doi: 10.1080/01635580903441212.

Dietary mushroom intake and the risk of breast cancer based on hormone receptor status.

Shin A[1], Kim J, Lim SY, Kim G, Sung MK, Lee ES, Ro J.

Author information

Abstract

Although many studies have documented the antitumor activities of mushrooms, the association between mushroom intake and breast cancer, defined by hormone receptor status, has received minimal empirical investigation. This study evaluated the association between mushroom intake and the risk of breast cancer according to hormone receptor status among Korean women. Mushroom intake and breast cancer risk were examined among 358 breast cancer patients and 360 cancer-free controls. Intake of mushrooms was assessed using a quantitative food frequency questionnaire. Greater mushroom intake was related to lower risk of breast cancers among premenopausal women (odds ratio [OR] = 0.35, 95% confidence interval [CI] = 0.13-0.91 for the highest vs. the lowest quartile intake). The association was stronger for premenopausal women with estrogen receptor (ER)+/progesterone receptor (PR) + tumors (OR = 0.30, 95% CI = 0.11-0.79 for the highest vs. the lowest quartile intake) than those with ER-/PR- tumors. Our results suggest that high consumption of mushrooms might be related to lower risks for breast cancers among premenopausal women; this association may be more robust among women with hormone receptor positive tumors.

PMID: 20432168 [PubMed - indexed for MEDLINE]

Int J Cancer. 2009 Mar 15;124(6):1404-8. doi: 10.1002/ijc.24047.

Dietary intakes of mushrooms and green tea combine to reduce the risk of breast cancer in Chinese women.

Zhang M[1], Huang J, Xie X, Holman CD.

Author information

Abstract

To investigate effects of dietary mushrooms and joint effects of mushrooms and green tea on breast cancer, a case-control study was conducted in southeast China in 2004-2005. The incident cases were 1,009 female patients aged 20-87 years with histologically confirmed breast cancer. The 1,009 age-matched controls were healthy women randomly recruited from outpatient breast clinics. Information on frequency and quantity of dietary intake of mushrooms and tea consumption, usual diet, and lifestyle were collected by face-to-face interview using a validated and reliable questionnaire. Compared with nonconsumers, the Odds ratios (Ors) were 0.36 (95% CI = 0.25-0.51) and 0.53 (0.38-0.73) for daily intake of >or=10 g fresh mushrooms and >or=4 g dried mushrooms, based on multivariate logistic regression analysis adjusting for established and potential confounders. There were dose-response relationships with significant tests for trend ($p < 0.001$). The inverse association was found in both pre- and postmenopausal women. Compared with those who consumed neither mushrooms nor green tea, the ORs were 0.11 (0.06-0.20) and 0.18 (0.11-0.29) for daily high intake of fresh and dried mushrooms combined with consuming beverages made from >or=1.05 g dried green tea leaves per day. The corresponding linear trends were statistically significant for joint effect ($p < 0.001$). We conclude that higher dietary intake of mushrooms decreased breast cancer risk in pre- and postmenopausal Chinese women and an additional decreased risk of breast cancer from joint effect of mushrooms and green tea was observed. More research is warranted to examine the effects of dietary mushrooms and mechanism of joint effects of phytochemicals on breast cancer.

Comment in

Vitamin D2 could be one of the protective phytochemicals. [Int J Cancer. 2009]

PMID: 19048616 [PubMed - indexed for MEDLINE]

TABLE III – ASSOCIATIONS BETWEEN BREAST CANCER AND DIETARY INTAKES OF MUSHROOMS

	No. cases/controls	OR (95% CI)[1]	OR (95% CI)[2]
Fresh mushrooms (g/day)			
All women			
0	231/200	1.0 (referent)	1.0 (referent)
<2	191/187	0.86 (0.65–1.15)	0.88 (0.66–1.19)
2–<10	185/190	0.78 (0.58–1.06)	0.81 (0.59–1.10)
≥10	84/192	0.34 (0.24–0.48)	0.36 (0.25–0.51)
P_{trend}[3]		<0.001	<0.001
Premenopausal women			
0	151/114	1.0 (referent)	1.0 (referent)
<2	139/129	0.82 (0.58–1.16)	0.86 (0.59–1.23)
2–<10	126/136	0.69 (0.47–0.99)	0.71 (0.48–1.01)
≥10	63/140	0.33 (0.22–0.50)	0.34 (0.22–0.52)
P_{trend}[3]		<0.001	<0.001
Postmenopausal women			
0	80/86	1.0 (referent)	1.0 (referent)
<2	52/58	1.00 (0.60–1.67)	0.97 (0.57–1.65)
2–<10	59/54	0.98 (0.57–1.69)	0.99 (0.56–1.75)
≥10	21/52	0.34 (0.17–0.67)	0.35 (0.17–0.70)
P_{trend}[3]		0.01	<0.01
Dried mushrooms (g/day)			
All women			
0	231/200	1.0 (referent)	1.0 (referent)
<1	358/283	1.10 (0.85–1.42)	1.15 (0.88–1.49)
1–<4	220/221	0.87 (0.65–1.15)	0.90 (0.67–1.21)
≥4	140/217	0.50 (0.37–0.68)	0.53 (0.38–0.73)
P_{trend}[3]		<0.001	<0.001
Premenopausal women			
0	151/114	1.0 (referent)	1.0 (referent)
<1	242/194	0.99 (0.72–1.35)	1.03 (0.74–1.45)
1–<4	139/151	0.75 (0.53–1.08)	0.76 (0.53–1.11)
≥4	95/142	0.47 (0.32–0.69)	0.51 (0.34–0.75)
P_{trend}[3]		<0.001	<0.001
Postmenopausal women			
0	80/86	1.0 (referent)	1.0 (referent)
<1	116/89	1.30 (0.85–1.99)	1.35 (0.87–2.10)
1–<4	81/70	1.10 (0.68–1.77)	1.17 (0.71–1.93)
≥4	45/75	0.53 (0.31–0.92)	0.53 (0.30–0.93)
P_{trend}[3]		<0.01	<0.01

MUSHROOMS, GREEN TEA AND BREAST CANCER RISK

TABLE IV – COMBINED EFFECT OF DIETARY MUSHROOMS AND GREEN TEA ON BREAST CANCER RIS

Dietary mushrooms (g/day)	Green tea leaves (g/day)	No. cases/controls	OR (95% CI)[1]	p^2
Fresh mushrooms				
None	None	141/67	1.0 (referent)	<0.0
	Low <1.05	180/106	0.75 (0.50–1.13)	
	High ≥1.05	65/84	0.32 (0.20–0.51)	
Low <7	None	49/55	0.43 (0.25–0.71)	
	Low <1.05	88/90	0.43 (0.28–0.68)	
	High ≥1.05	27/79	0.13 (0.07–0.24)	
High ≥7	None	29/60	0.22 (0.13–0.39)	
	Low <1.05	53/98	0.22 (0.14–0.36)	
	High ≥1.05	21/76	0.11 (0.06–0.20)	
Dried mushrooms				
None	None	141/67	1.0 (referent)	<0.0
	Low <1.05	210/117	0.88 (0.59–1.30)	
	High ≥1.05	174/128	0.62 (0.42–0.93)	
Low <2	None	49/55	0.43 (0.26–0.72)	
	Low <1.05	98/81	0.57 (0.37–0.89)	
	High ≥1.05	90/133	0.31 (0.20–0.48)	
High ≥2	None	29/60	0.22 (0.13–0.39)	
	Low <1.05	58/100	0.28 (0.18–0.45)	
	High ≥1.05	47/116	0.18 (0.11–0.29)	

[1]Estimates from separate unconditional logistic regression models included terms for age at inter (yr, continuous), residential area (urban, rural), education (none, primary, secondary, tertiary), BMI (tinuous, 5-yr ago), age at menarche (continuous), oral contraceptive use (never/ever), hormone rep ment therapy (never/ever), breast cancer in first degree relatives (no/yes), total energy intake (kcal, tinuous), menopausal status (no/yes), alcohol consumption (no/yes), tobacco smoking (no/yes), pa smoking (no/yes), and physical activity (weekly MET-hour, continuous).–p value for the interac using the women who consumed neither green tea nor dietary mushrooms as a reference category.

Trametes (Coriolus) versicolor
Turkey tail

Recent Pat Inflamm Allergy Drug Discov. 2012 Jan;6(1):76-87.

Efficacy of Yun Zhi (Coriolus versicolor) on survival in cancer patients: systematic review and meta-analysis.

Eliza WL, Fai CK, Chung LP.

Author information

Abstract

AIM: Patients with cancer frequently use herbs along with the conventional medical treatment, hoping to enhance recovery. Mushrooms have an established history of use in traditional oriental therapies. In Asian cultures, mushrooms are combined with herbal mixtures to treat cancer. This systematic review and meta-analysis draw from randomized, placebo-controlled, double-blind trials to assess the efficacy of Yun Zhi (YZ) for survival in cancer patients.

MATERIAL & METHODS: Systematic review and meta-analysis technique were used to aggregate and analyze the efficacy of Yun Zhi on survival in cancer patients from 13 clinical trials using computerized database and manual search.

RESULTS: The findings show that Yun Zhi results in a significant survival advantage compared with standard conventional anti-cancer treatment alone. Of patient randomized to Yun Zhi, there was a 9% absolute reduction in 5-year mortality, resulting in one additional patient alive for every 11 patients treated. In patients with breast cancer, gastric cancer, or colorectal cancer treated with chemotherapy, the effects of the combination of Yun Zhi preparation on the overall 5-year survival rate was more evident, but not in esophageal cancer and nasophayngeal carcinoma. However, subgroup analysis could not conclude which type of anti-cancer treatment may maximize the benefit from Yun Zhi.

CONCLUSION: This meta-analysis has provided strong evidence that Yun Zhi would have survival benefit in cancer patients, particularly in carcinoma of breast, gastric and colorectal. Nevertheless, the findings highlight the need for further evidence from prospective studies of outcome to guide future potential modifications of treatment regimes. Recent patents on the use of mushrooms for the treatment of cancer are also summarized in this review.

PMID: 22185453 [PubMed - indexed for MEDLINE]

Trametes and Lung Cancer

- Fritz H[1], Kennedy DA[2], Ishii M[1], Fergusson D[3], Fernandes R[2], Cooley K[2], Seely D[4]. **Polysaccharide K and Coriolus versicolor extracts for lung cancer: a systematic review.** Integr Cancer Ther. 2015 May;14(3):201-11

- 28 studies included in analysis: 6 RCTs, 5 non-randomized CTs, 17 preclinical
- 15 of 17 preclinical studies supported anticancer effects for PSK through immunomodulation and potentiation of immune surveillance, and direct tumor inhibiting actions in vivo that resulted in reduced tumor growth and antimetastatic effects.
- Nonrandomized controlled trials showed improvement of various survival measures including median survival and 1-, 2-, and 5-year survival.
- Randomized controlled trials showed benefits on immune parameters and hematological function, performance status and body weight, fatigue and anorexia, and survival.
- Overall most randomized controlled trials supported a positive impact for PSK on these endpoints

ISRN Oncol. 2012;2012:251632. doi: 10.5402/2012/251632. Epub 2012 May 30.

Phase 1 Clinical Trial of Trametes versicolor in Women with Breast Cancer.

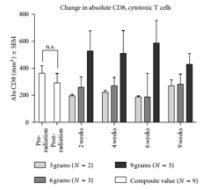
Torkelson CJ[1], Sweet E, Martzen MR, Sasagawa M, Wenner CA, Gay J, Putiri A, Standish LJ.

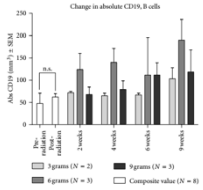
Author information

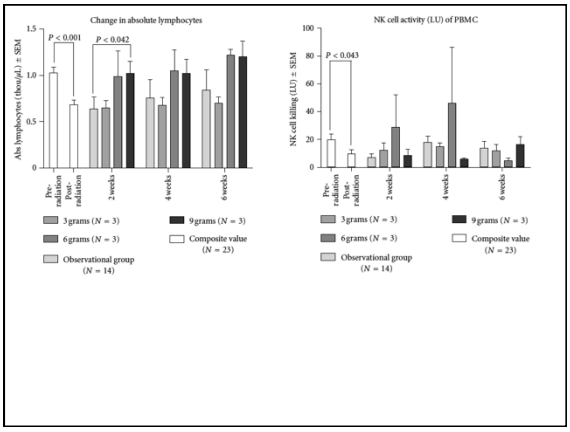
Abstract

Introduction. Orally administered preparations from the Trametes versicolor (Tv) mushroom have been hypothesized to improve immune response in women with breast cancer after standard chemotherapy and radiotherapy. Methods. A phase I, two-center, dose escalation study was done to determine the maximum tolerated dose of a Tv preparation when taken daily in divided doses for 6 weeks after recent completion of radiotherapy. Eleven participants were recruited and nine women completed the study. Each cohort was comprised of three participants given one of three doses of Tv (3, 6, or 9 grams). Immune data was collected pre- and postradiation, at 3 on-treatment time points and after a 3-week washout. Results. Nine adverse events were reported (7 mild, 1 moderate, and 1 severe), suggesting that Tv was well tolerated. Immunological results indicated trends in (1) increased lymphocyte counts at 6 and 9 grams/day; (2) increased natural killer cell functional activity at 6 grams/day; (3) dose-related increases in CD8(+) T cells and CD19(+) B cells , but not CD4(+) T cells or CD16(+)56(+) NK cells. Conclusion. These findings show that up to 9 grams/day of a Tv preparation is safe and tolerable in women with breast cancer in the postprimary treatment setting. This Tv preparation may improve immune status in immunocompromised breast cancer patients following standard primary oncologic treatment.

PMID: 22701186 [PubMed] PMCID: PMC3369477 **Free PMC Article**







Clin Cancer Res. 2011 Nov 1;17(21):6742-53. doi: 10.1158/1078-0432.CCR-11-1142. Epub 2011 Sep 14.

TLR2 agonist PSK activates human NK cells and enhances the antitumor effect of HER2-targeted monoclonal antibody therapy.

Lu H[1], Yang Y, Gad E, Inatsuka C, Wenner CA, Disis ML, Standish LJ.

Author information

Abstract

PURPOSE: The therapeutic effect of trastuzumab monoclonal antibody (mAb) therapy has been shown to be partially dependent on functional natural killer (NK) cells. Novel agents that enhance NK cell function could potentially improve the antitumor effect of trastuzumab. We recently identified polysaccharide krestin (PSK), a natural product extracted from medicinal mushroom Trametes versicolor, as a potent toll-like receptor 2 (TLR2) agonist. This study was undertaken to evaluate the effect of PSK on human NK cells and the potential of using PSK to enhance HER2-targeted mAb therapy.

EXPERIMENTAL DESIGN: Human peripheral blood mononuclear cells were stimulated with PSK to evaluate the effect of PSK on NK cell activation, IFN-γ production, cytotoxicity, and trastuzumab-mediated antibody-dependent cell-mediated cytotoxicity (ADCC). Whether the effect of PSK on NK cells is direct or indirect was also investigated. Then, in vivo experiment in neu transgenic (neu-T) mice was carried out to determine the potential of using PSK to augment the antitumor effect of HER2-targeted mAb therapy.

RESULTS: PSK activated human NK cells to produce IFN-γ and to lyse K562 target cells. PSK also enhanced trastuzumab-mediated ADCC against SKBR3 and MDA-MB-231 breast cancer cells. Both direct and interleukin-12-dependent indirect effects seem to be involved in the effect of PSK on NK cells. Oral administration of PSK significantly potentiated the antitumor effect of anti-HER2/neu mAb therapy in neu-T mice.

CONCLUSION: These results showed that PSK activates human NK cells and potentiates trastuzumab-mediated ADCC. Concurrent treatment with PSK and trastuzumab may be a novel way to augment the antitumor effect of trastuzumab.

PMID: 21918170 [PubMed - indexed for MEDLINE] PMCID: PMC3206987 **Free PMC Article**

Oncol Rep. 2006 Apr;15(4):861-8.

Beneficial effects of protein-bound polysaccharide K plus tegafur/uracil in patients with stage II or III colorectal cancer: analysis of immunological parameters.

Ohwada S[1], Ogawa T, Makita F, Tanahashi Y, Ohya T, Tomizawa N, Satoh Y, Kobayashi I, Izumi M, Takeyoshi I, Hamada K, Minaguchi S, Togo Y, Toshihiko T, Koyama T, Kamio M

Author information

Abstract

Protein-bound polysaccharide K (PSK) increased the 5-year disease-free survival rate and reduced the risk of recurrence in a randomised, controlled study for stage II and III colorectal cancer. In order to elucidate the disease-free survival benefits with PSK and what immunological markers could indicate a PSK responder, serial changes in immunological parameters were monitored in the study. PSK decreased the mean serum immunosuppressive acidic protein (IAP) level, and increased the mean population of natural killer (NK) cells compared with the controls. The 5-year disease-free and overall survival rate for patients with serum IAP values <or=500 microg ml(-1), which represents the normal value, were 75.5% (95% CI: 66.8-84.2%; p=0.016) and 85.1% (95% CI: 77.9-92.3%; p=0.032), respectively, in the PSK group compared with 57.5% (95% CI: 43.3-71.6%) and 70.2% (95% CI: 57.1-83.3%) in the control group. In patients with NK cell population >or=8% at 3 months after surgery, PSK conferred a significantly better (p=0.038) 5-year disease-free survival (86.7%; 95% CI: 74.5-98.8%) compared to the control group (60.0%; 95% CI: 29.6-90.4%). In the proportional hazards model, the presence of regional metastases (relative risk, 3.595; 95% CI: 1.518 to 8.518; p=0.004) and omission of PSK treatment (relative risk, 3.099; 95% CI: 1.202 to 7.990; p=0.019) were significant indicators of recurrence. PSK acts as an immunomodulatory activity and biochemical modulator in stage II or III colorectal cancer. Pre-operative serum IAP values <or=500 microg ml(-1) and an NK cell population >or=8% at 3 months after surgery are possible PSK response predictors.

PMID: 16525672 [PubMed - indexed for MEDLINE]

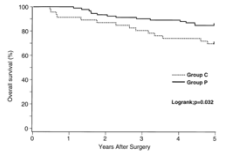


Figure 5. The 5-year overall survival rates of patients with serum IAP values ≤500 μg ml^{-1}. The 5-year overall survival rate for patients with serum IAP values ≤500 μg ml^{-1} was 85.1% (95% CI: 77.9-92.3%) in the PSK group compared with 70.2% (95% CI: 57.1-83.3%) in the control group (p=0.032).

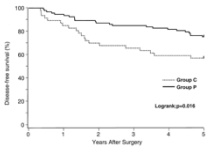


Figure 4. The 5-year disease-free survival rates of patients with serum IAP values ≤300 μg ml^{-1}. The 5-year disease-free survival rate of patients with serum IAP values ≤500 μg ml^{-1} was 75.5% (95% CI: 66.8-84.2%) in the PSK group and 57.5% (95% CI: 43.3-71.6%) in the control group (p=0.016).

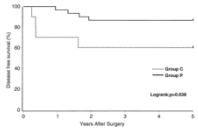


Figure 6. The 5-year disease-free survival rates of patients with NK cell population ≥8% at 3 months after surgery. PSK conferred a significantly better (p=0.038) 5-year disease-free survival rate (86.7%; 95% CI: 74.5-98.8%) compared with the control group (60.0%; 95% CI: 29.6-90.4%).

Int J Oncol. 2012 Apr;40(4):905-13. doi: 10.3892/ijo.2011.1292. Epub 2011 Dec 12.

Polysaccharide-K augments docetaxel-induced tumor suppression and antitumor immune response in an immunocompetent murine model of human prostate cancer.

Wenner CA[1], Martzen MR, Lu H, Verneris MR, Wang H, Slaton JW.

Author information

Abstract

Advanced castration-resistant prostate cancer has high mortality rates and limited treatment options. Novel therapies are needed to better contend with this disease. Polysaccharide-K® (PSK), an extract of the mushroom Trametes versicolor, has immunomodulatory and tumor suppressive activities. PSK is used in Asia as a cancer immunotherapy. However, its benefit in combination with taxanes for prostate cancer is unknown. We examined whether PSK would enhance docetaxel-induced apoptosis and augment anti-tumor immune responses in orthotopic tumors using transgenic adenocarcinoma of the mouse prostate (TRAMP)-C2-bearing mice. Combining PSK with docetaxel induced significantly higher tumor suppression than either treatment alone ($p<0.05$), including a reduction in tumor proliferation and enhanced apoptosis. Combined PSK and docetaxel treatment led to a lower decrease in number of white blood cells than docetaxel alone, an effect accompanied by increased numbers of tumor-infiltrating CD4+ and CD8+ T cells. PSK with or without docetaxel significantly enhanced mRNA expression of IFN-γ compared to control, but did not significantly alter T-regulatory FoxP3 mRNA expression in tumors. PSK also augmented docetaxel-induced splenic natural killer cell cytolytic activity against YAC-1 target cells ($p=0.045$). This study is the first to show that PSK enhances docetaxel-induced prostate cancer tumor suppression, apoptosis and antitumor responses.

PMID: 22159900 [PubMed - indexed for MEDLINE] PMCID: PMC3584555 **Free PMC Article**

Meta-analysis of 3 large trials of PSK and CRC

- n=578
- All had surgery and chemo with and w/o PSK
- Hot water extract of Trametes versicolor 3 gms/day
- Increased survival and disease-free survival for treated patients (p=0.006)

  Sakamoto J et al. Ca Immunol Immunother 2006 55:404-411

Ganoderma lucidum
Reishi

Cochrane Database Syst Rev. 2012 Jun 13;6:CD007731. doi: 10.1002/14651858.CD007731.pub2.

Ganoderma lucidum (Reishi mushroom) for cancer treatment.

Jin X, Ruiz Beguerie J, Sze DM, Chan GC.

Author information

Abstract

BACKGROUND: Ganoderma lucidum is a natural medicine that is widely used and recommended by Asian physicians and naturopaths for its supporting effects on immune system. Laboratory research and a handful of preclinical trials have suggested that G. lucidum carries promising anticancer and immunomodulatory properties. The popularity of taking G. lucidum as an alternative medicine has been increasing in cancer patients. However, there is no systematic review that has been conducted to evaluate the actual benefits of G. lucidum in cancer treatment.

OBJECTIVES: To evaluate the clinical effects of G. lucidum on long-term survival, tumour response, host immune functions and quality of life in cancer patients, as well as adverse events associated with its use.

SEARCH METHODS: The authors ran an extensive set of databases including the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE, NIH, AMED, CBM, CNKI, CMCC and VIP Information/Chinese Scientific Journals Database was searched for randomised controlled trials (RCTs) in October 2011. Other strategies used were scanning the references of articles retrieved, handsearching of the International Journal of Medicinal Mushrooms and contact with herbal medicine experts and manufacturers of G. lucidum.

SELECTION CRITERIA: To be eligible for being included in this review, studies had to be RCTs comparing the efficacy of G. lucidum medications to active or placebo control in patients with cancer that had been diagnosed by pathology. All types and stages of cancer were eligible for inclusion. Trials were not restricted on the basis of language.

DATA COLLECTION AND ANALYSIS: Five RCTs met the inclusion criteria and were included in this review. Two independent review authors were assigned to assess the methodological quality of individual trials. Common primary outcomes were tumour response evaluated according to the World Health Organization (WHO) criteria, immune function parameters such as natural killer (NK)-cell activity and T-lymphocyte co-receptor subsets, and quality of life measured by the Karnofsky scale score. No trial had recorded long-term survival rates. Associated adverse events were reported in one study. A meta-analysis was performed to pool available data from the primary trials. Results were gauged using relative risks (RR) and standard mean differences (SMD) for dichotomous and continuous data respectively, with a 95% confidence interval (CI).

Ganoderma and Advanced Cancer

- 30 advanced-stage cancer patients treated with 1800 mg Ganoderma extract, TID before meals for 12 weeks.
- Immune parameters (cytokines, T cell subsets, mitotic response to phytohemagglutinin (PHA) and natural killer activity) were compared between baseline and after 12-week treatment
- Significant increase in IL-2, IL-6, IFN-gamma, CD56+ cells
- IL-1 and TNF-alpha significantly decreased
- CD4:CD8 T cell ratios unchanged.
- PHA significantly enhanced in most patients compared to baseline
- **Significant increase (P < 0.05) in mean NK activity compared to baselines (34.5 +/- 11.8% vs 26.6 +/- 8.3%)**

- Gao Y, et al. **Effects of ganopoly (a Ganoderma lucidum polysaccharide extract) on the immune functions in advanced-stage cancer patients.** Immunol Invest. 2003 Aug;32(3):201-15.

Nutr Cancer. 2005;53(1):11-7.

Anticancer effects of Ganoderma lucidum: a review of scientific evidence.

Yuen JW[1], Gohel MD.

Author information

Abstract

"Lingzhi" (Ganoderma lucidum), a popular medicinal mushroom, has been used in China for longevity and health promotion since ancient times. Investigations into the anticancer activity of lingzhi have been performed in both in vitro and in vivo studies, supporting its application for cancer treatment and prevention. The proposed anticancer activity of lingzhi has prompted its usage by cancer patients. It remains debatable as to whether lingzhi is a food supplement for health maintenance or actually a therapeutic "drug" for medical proposes. Thus far there has been no report of human trials using lingzhi as a direct anticancer agent, despite some evidence showing the usage of lingzhi as a potential supplement to cancer patients. Cellular immune responses and mitogenic reactivity of cancer patients have been enhanced by lingzhi, as reported in two randomized and one nonrandomized trials, and the quality of life of 65% of lung cancer patients improved in one study. The direct cytotoxic and anti-angiogenesis mechanisms of lingzhi have been established by in vitro studies; however, clinical studies should not be neglected to define the applicable dosage in vivo. At present, lingzhi is a health food supplement to support cancer patients, yet the evidence supporting the potential of direct in vivo anticancer effects should not be underestimated. Lingzhi or its products can be classified as an anticancer agent when current and more direct scientific evidence becomes available.

PMID: 16351502 [PubMed - indexed for MEDLINE]

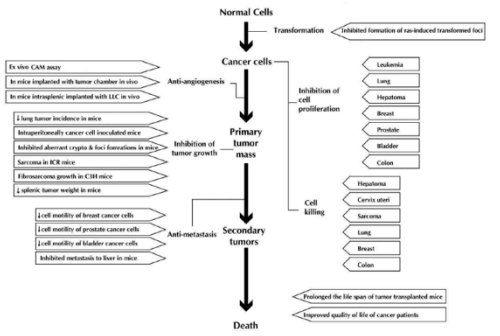


Figure 1. Anticancer activities of lingzhi corresponding to the stages of carcinogenesis.

Hiroshima J Med Sci. 2010 Mar;59(1):1-8.

A water-soluble extract from culture medium of Ganoderma lucidum mycelia suppresses the development of colorectal adenomas.

Oka S, Tanaka S, Yoshida S, Hiyama T, Ueno Y, Ito M, Kitadai Y, Yoshihara M, Chayama K.

Author information

Abstract

A water-soluble extract from a cultured medium of Ganoderma lucidum mycelia (MAK) is one of the G. lucidum extracts that has been reported to show have exhibit cancer-preventive effects in the animal studies. To confirm cancer-preventive effects of MAK, we performed a no-treatment concurrent controlled trial on patients with colorectal adenomas. Patients who were determined to be carrying colorectal adenomas by colonoscopy were enrolled in this study. Patients in the MAK group took MAK (1.5 g/day) for 12 months. Follow-up colonoscopy was performed after 12 months, and the colonoscopists recorded the size, site and macroscopic type of all adenomas. Among 123 patients who enrolled in the MAK group, 96 eligible patients completed the trial. The 102 eligible patients in the no-treatment control group were selected randomly from our department's patients. The changes in the number of adenomas up to 12 months increased to 0.66 +/- 0.10 (mean +/- SE) in the control group, while decreasing in the MAK group to -0.42 +/- 0.10 ($p < 0.01$). The total size of adenomas increased to 1.73 +/- 0.28 mm in the control group and decreased to -1.40 +/- 0.64 mm in the MAK group ($p < 0.01$). The resultssuggest that MAK suppresses the development of colorectal adenomas - precancerous lesions of the large bowel.

PMID: 20518254 [PubMed - indexed for MEDLINE]

Int Immunopharmacol. 2006 Mar;6(3):499-508. Epub 2005 Sep 15.

Monitoring of immune responses to a herbal immuno-modulator in patients with advanced colorectal cancer.

Chen X, Hu ZP, Yang XX, Huang M, Gao Y, Tang W, Chan SY, Dai X, Ye J, Ho PC, Duan W, Yang HY, Zhu YZ, Zhou SF.

Author information

Abstract

Many herbal medicines are widely used as immuno-modulators in Asian countries. Ganoderma lucidum (Lingzhi) is one of the most commonly used herbs in Asia and preclinical studies have established that the polysaccharide fractions of G. lucidum have potent immuno-modulating effects. However, clinical evidence for this is scanty. The present open-labeled study aimed to evaluate the effects of G. lucidum polysaccharides on selected immune functions in patients with advanced colorectal cancer. Forty-seven patients were enrolled and treated with oral G. lucidum at 5.4 g/day for 12 weeks. Selected immune parameters were monitored using various immunological methods throughout the study. In 41 assessable cancer patients, treatment with G. lucidum tended to increase mitogenic reactivity to phytohemagglutinin, counts of CD3, CD4, CD8 and CD56 lymphocytes, plasma concentrations of interleukin (IL)-2, IL-6 and interferon (IFN)-gamma, and NK activity, whereas plasma concentrations of IL-1 and tumor necrosis factor (TNF)-alpha were decreased. For all of these parameters, no statistical significance was observed when a comparison was conducted between baseline and those values after a 12-week treatment with G. lucidum. The changes of IL-1 were correlated with those for IL-6, IFN-gamma, CD3, CD4, CD8 and NK activity ($p<0.05$) and IL-2 changes were correlated with those for IL-6, CD8 and NK activity. The results indicate that G. lucidum may have potential immuno-modulating effect in patients with advanced colorectal cancer. Further studies are needed to explore the benefits and safety of G. lucidum in cancer patients.

PMID: 16420086 [PubMed - indexed for MEDLINE]

Ganoderma and Radioprotection

Mutat Res. 2013 Mar 18;751(2):109-15. doi: 10.1016/j.mrgentox.2012.12.005. Epub 2012 Dec 28.

Mushroom beta glucan: potential candidate for post irradiation protection.

Pillai TG[1], Uma Devi P.

Author information

Abstract

The in vivo radioprotective effect of a beta-glucan (BG) isolated from the mushroom Ganoderma lucidum, against radiation (RT) induced damage was investigated taking mouse survival, hematology, liver GSH (Reduced glutathione), liver Malondialdehyde (MDA) and bone marrow chromosomal aberrations as end points. Young adult swiss albino mice were whole body exposed to gamma radiation. For mouse survival study, BG was administered orally (250μg/kg body wt or 500μg/kg body wt) 15min before or 5min after 8Gy exposure. For other parameters BG was given orally 5min after 4Gy exposure. The radioprotective effect of BG was compared with that of clinically used radioprotective drug amifostine (WR-2721), at 300mg/kg body wt administered intraperitoneally, 30min before irradiation. BG (500μg/kg body wt) produced (66%) mouse survival at 30 days given post irradiation, and 83% survived at 30 days with 300mg/kg body wt of amifostine administered before RT while RT alone produced 100% mortality. BG is not toxic at the radioprotective dose. Significant reduction in number of aberrant cells and different types of aberration was observed in both BG and amifostine administered groups compared to radiation alone treated group. BG seems to have potential for use in protection against unplanned radiation exposures.

PMID: 23277319 [PubMed - indexed for MEDLINE]

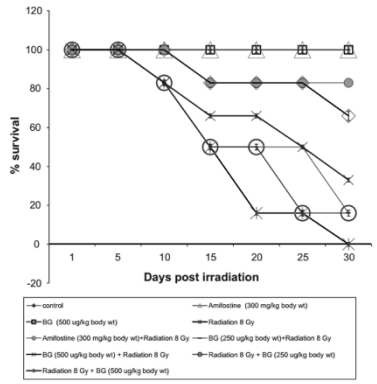


Fig. 1. Effect of BG on 30 days survival of mice exposed to 8 Gy gamma radiation.

Grifolia frondosa
Maitake

Grifola frondosa (Maitake)
King of Mushrooms

Grifolia frondosa for MDS

- Stimulates hematopoietic progenitor cell differentiation, granulocyte colony-stimulating factor production, and recovery of peripheral blood leukocytes after bone marrow injury
- In 18 patients with myelodysplastic syndrome, Grifolia enhanced *in vitro* neutrophil and monocyte function
- Wesa KM et al. Maitake mushroom extract in myelodysplastic syndromes (MDS): a phase II study. Cancer Immunol Immunother. 2015 Feb;64(2):237-47

J Cancer Res Clin Oncol. 2009 Sep;135(9):1215-21. doi: 10.1007/s00432-009-0562-z. Epub 2009 Mar 1.

A phase I/II trial of a polysaccharide extract from Grifola frondosa (Maitake mushroom) in breast cancer patients: immunological effects.

Deng G, Lin H, Seidman A, Fornier M, D'Andrea G, Wesa K, Yeung S, Cunningham-Rundles S, Vickers AJ, Cassileth B.

Author information

Abstract

BACKGROUND: Cancer patients commonly use dietary supplements to "boost immune function". A polysaccharide extract from Grifola frondosa (Maitake extract) showed immunomodulatory effects in preclinical studies and therefore the potential for clinical use. Whether oral administration in human produces measurable immunologic effects, however, is unknown.

METHODS: In a phase I/II dose escalation trial, 34 postmenopausal breast cancer patients, free of disease after initial treatment, were enrolled sequentially in five cohorts. Maitake liquid extract was taken orally at 0.1, 0.5, 1.5, 3, or 5 mg/kg twice daily for 3 weeks. Peripheral blood was collected at days -7, 0 (prior to the first dosing), 7, 14, and 21 for ex vivo analyses. The primary endpoints were safety and tolerability.

RESULTS: No dose-limiting toxicity was encountered. Two patients withdrew prior to completion of the study due to grade I possibly related side effects: nausea and joint swelling in one patient; rash and pruritus in the second. There was a statistically significant association between Maitake and immunologic function ($p < 0.0005$). Increasing doses of Maitake increased some immunologic parameters and depressed others; the dose-response curves for many endpoints were non-monotonic with intermediate doses having either immune enhancing or immune suppressant effects compared with both high and low doses.

CONCLUSIONS: Oral administration of a polysaccharide extract from Maitake mushroom is associated with both immunologically stimulatory and inhibitory measurable effects in peripheral blood. Cancer patients should be made aware of the fact that botanical agents produce more complex effects than assumed, and may depress as well as enhance immune function.

PMID: 19253021 [PubMed - indexed for MEDLINE] PMCID: PMC3751581 Free PMC Article

Grifola in Prevention of Recurrent Bladder Cancer

- 313 bladder cancer patients after TURBT or partial cystectomy were followed for avg 7.6 yrs.
- Recurrence rates for patients divided into 1 of 6 groups were:
- Afterloading brachytherapy: 24%
- Grifola: 34.9%
- BCG: 35.1%
- Mitomycin C: 41.7%
- Thiotepa: 52.6%
- Control: 64.7%
- Yang D et al. Prevention of postoperative recurrence of bladder cancer: a clinical study. Zhonghua Wai Ke Za Zhi. 1999 Aug;37(8):464-5

Int Immunopharmacol. 2009 May;9(5):620-6. doi: 10.1016/j.intimp.2009.02.005. Epub 2009 Feb 26.

Maitake beta-glucan enhances therapeutic effect and reduces myelosupression and nephrotoxicity of cisplatin in mice.

Masuda Y[1], Inoue M, Miyata A, Mizuno S, Nanba H.

Author information

Abstract

Cisplatin is broadly used clinically as an anticancer drug. Despite its significant anticancer activity, cisplatin-induced nephrotoxicity and myelosuppression limit its use. MD-Fraction is glucan purified from maitake (Grifola frondosa), which has beta-1, 6-main chain with beta-1, 3-branches, has been reported to exhibit antitumor and antimetastatic activities by enhancing the immune system. In this study, we demonstrate that MD-Fraction in combination with cisplatin significantly enhanced antitumor and antimetastatic activity compared to cisplatin alone. MD-Fraction reduced decreases in body weight, spleen weight and the number of immunocompetent cells such as macrophages, DCs and NK cells in cisplatin-treated mice. MD-Fraction also induced IL-12p70 production by splenocytes, resulting in increased NK cell activity in cisplatin-treated mice. MD-Fraction significantly increased the mRNA expression of GM-CSF, G-CSF, M-CSF, IFN-gamma, IL-12 p40 in splenocytes and reduced the decrease in the number of CFU-GM colonies in cisplatin-treated bone marrow. These facts suggest that MD-Fraction can reduce cisplatin-induced myelosuppression. Moreover, treatment with MD-Fraction significantly reduced cisplatin-induced nephrotoxicity accompanied by increases in serum creatinine level, necrosis and apoptosis of renal tubular cells. These results suggest that MD-Fraction in combination with cisplatin cannot only enhance antitumor and antimentastatic acitivity, but also reduce cisplatin-induced myelotoxicity and nephrotoxicity.

PMID: 19249389 [PubMed - indexed for MEDLINE]

Lentinula edodes

Shiitake

Am J Chin Med. 2011;39(3):451-9.

Efficacy and safety of orally administered Lentinula edodes mycelia extract for patients undergoing cancer chemotherapy: a pilot study.

Yamaguchi Y, Miyahara E, Hihara J.

Author information

Abstract

Lentinula edodes mycelia extract (L.E.M.) is extensively utilized as an herbal medicine. However, its safety and effectiveness have not yet been scientifically verified. In this study, we investigated its safety and its influence on quality of life (QOL) and the immune response in patients undergoing cancer chemotherapy. Seven patients were studied in total. The patients were undergoing postoperative adjuvant chemotherapy for breast cancer (n = 3) or gastrointestinal cancer (n = 2), or were receiving chemotherapy to prevent recurrence of gastrointestinal cancer (n = 2). The first course of treatment was chemotherapy alone and the second was chemotherapy plus concomitant administration of L.E.M. Adverse events and changes in the QOL score, lymphocyte subpopulations, lymphocyte activity and serum immune indices were evaluated during the study period. No adverse events attributable to L.E.M. were observed. Compared to the pre-chemotherapy state, no changes in QOL or immune parameters were noted after the first chemotherapy course. In contrast, following the second course of combined therapy, improvements were noted in QOL ($p < 0.05$), NK cell activity ($p < 0.05$) and immunosuppressive acidic protein (IAP) ($p < 0.01$) levels. Although a future large-scale investigation is necessary to confirm these results, these data suggest that the concomitant of L.E.M. with chemotherapy is safe and improves the QOL and immune function of patients undergoing chemotherapy.

PMID: 21590414 [PubMed - indexed for MEDLINE]

Table 1. Characteristics of Subjects

Case Number	Age	Sex	Chemotherapy	Primary	TNM Classification	Type
1	72	Female	EC	Breast	T2N1M0	Post-operative adjuvant chemotherapy
2	59	Female	EC	Breast	T2NXM0	Post-operative adjuvant chemotherapy
3	49	Female	EC	Breast	T1N0M0	Post-operative adjuvant chemotherapy
4	69	Female	TS-1	Gastric	T4N2M0	Post-operative adjuvant chemotherapy
5	56	Male	UFT	Colorectal	T3N0M0	Post-operative adjuvant chemotherapy
6	79	Male	TS-1	Esophageal	T4N0M0	Chemotherapy for recurrent cancer
7	54	Female	FOLFIRI	Colorectal	M1	Chemotherapy for recurrent cancer

Note: EC, epirubicine+cyclophosphamide; FOLFIRI, folate+5-fruolouracil+irinotecan.

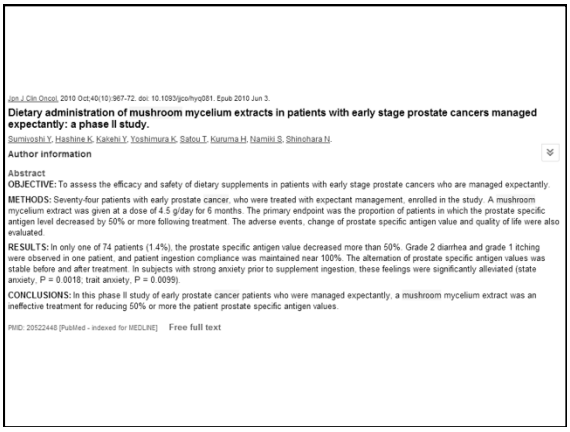
AHCC – mycelium extract of Lentinula

- Active hexose correlated compound (AHCC)]
- Generic term to describe a plant polysaccharide extracted from a liquid culture of basidiomycetous mycelia of lentinula edodes
- AHCC has immunostimulating activity, anticancer activity, cancer-preventive actions and can prevent side effects during cancer chemotherapy
- Shigama K et al. *Alleviating effect of active hexose correlated compound (AHCC) for anticancer drug-induced side effects in non-tumor-bearing mice. J Exp Ther Oncol 2009;8:43-51*

Prospective Consecutive Case Series of Hepatocellular Carcinoma

- ***Background/Aims***: We seek to determine whether AHCC can improve the prognosis of hepatocellular carcinoma (HCC) patients following surgical treatment.
- ***Methods***: A prospective cohort study was performed from February 1, 1992 to December 31, 2001. A total of 269 consecutive patients with histologically confirmed HCC were studied. All of the patients underwent resection of a liver tumor. Time to treatment failure (disease recurrence or death) and ten parameters related to liver function after surgery were examined.
- ***Results***: Of the 269 patients, 113 received AHCC orally after undergoing curative surgery (AHCC group). The AHCC group had a significantly longer no recurrence period (hazard ratio (HR), 0.639; 95% confidence interval (CI), 0.429–0.952; *P*=0.0277) and an increased overall survival rate (HR, 0.421; 95% CI, 0.253–0.701; *P*=0.0009) when compared to the control group by Cox's multivariate analysis.
- ***Conclusions***: This study suggests that AHCC intake can improve the prognosis of postoperative HCC patients.

- Matsui K et al. *Improved prognosis of postoperative hepatocellular carcinoma patients when treated with functional foods: a prospective cohort study. J Hepatol 2002;37:78-86.*



Jpn J Clin Oncol. 2010 Oct;40(10):967-72. doi: 10.1093/jjco/hyq081. Epub 2010 Jun 3.

Dietary administration of mushroom mycelium extracts in patients with early stage prostate cancers managed expectantly: a phase II study.

Sumiyoshi Y, Hashine K, Kakehi Y, Yoshimura K, Satou T, Kuruma H, Namiki S, Shinohara N.

Author information

Abstract

OBJECTIVE: To assess the efficacy and safety of dietary supplements in patients with early stage prostate cancers who are managed expectantly.

METHODS: Seventy-four patients with early prostate cancer, who were treated with expectant management, enrolled in the study. A mushroom mycelium extract was given at a dose of 4.5 g/day for 6 months. The primary endpoint was the proportion of patients in which the prostate specific antigen level decreased by 50% or more following treatment. The adverse events, change of prostate specific antigen value and quality of life were also evaluated.

RESULTS: In only one of 74 patients (1.4%), the prostate specific antigen value decreased more than 50%. Grade 2 diarrhea and grade 1 itching were observed in one patient, and patient ingestion compliance was maintained near 100%. The alternation of prostate specific antigen values was stable before and after treatment. In subjects with strong anxiety prior to supplement ingestion, these feelings were significantly alleviated (state anxiety, P = 0.0018; trait anxiety, P = 0.0099).

CONCLUSIONS: In this phase II study of early prostate cancer patients who were managed expectantly, a mushroom mycelium extract was an ineffective treatment for reducing 50% or more the patient prostate specific antigen values.

PMID: 20522448 [PubMed - indexed for MEDLINE] Free full text

Inonotus obliquus (Chaga)

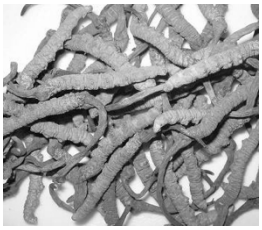

Inonotus obliquus (Chaga)

- No published human trials
- Cell studies:
  - Colorectal: Kang JH. July 2015, Lee HS. April 2015
  - Neurogliocytoma: Ning X. 2014
  - Breast and lung cancer: Nagaiyothi PC. 2014
  - Lung, colon, glioma: Lemieszek MK. 2011
  - Melanoma: Youn MJ. 2009
  - Hepatoma: Youn MJ. 2009
- Mouse model
  - Sarcoma, lung, stomach, breast, cervical cancer. Chung MJ. 2010

Inonotus obliquus (Chaga)

- Contain extremely high oxalate concentration
- Case report of oxalate nephropathy from Chaga mushroom powder (4 – 5 tsp/day) x 6 months for liver cancer
- Kikuchi Y et al. Chaga mushroom-induced oxalate nephropathy. Clin Nephrol. 2014 Jun;81(6):440-4.

Ophiocordyceps sinensis (*Cordyceps*)



Integr Cancer Ther. 2013 Jan;12(1):50-68. doi: 10.1177/1534735412441704. Epub 2012 Apr 26.

Evidence that naturopathic therapy including Cordyceps sinensis prolongs survival of patients with hepatocellular carcinoma.

Niwa Y[1], Matsuura H, Murakami M, Sato J, Hirai K, Sumi H.

Author information

Abstract

HYPOTHESIS: Naturopathic treatment will benefit patients with hepatocellular carcinoma (HCC).

STUDY DESIGN: Retrospective analysis of case series of HCC patients treated with naturopathic agents.

METHODS: HCC was diagnosed by dynamic computed tomography (CT) imaging and α-fetoprotein (AFP) or PIVKA II, or by histology. Tumor staging was determined by CT. A modified Childs-Pugh scoring was used to assess liver disease. Patients were treated with orally administered combinations of 12 naturopathic agents. Patients were monitored clinically and by CT tumor imaging, serial tumor markers, and liver function tests.

RESULTS: Patient characteristics: 101 patients with HCC (67 men and 34 women, age 67.2 ± 8.8 years) were treated for a median of 13.4 months (range 0.8–100.8). Of these 84% had cirrhosis, 63% had hepatitis C virus, 18% had hepatitis B virus, 1% had both, and 9% had metastatic disease. Median modified Childs-Pugh score was 6 (range 3–13). Barcelona Clinic Liver Cancer tumor stages of 0, A, B, C, and D were found in 36%, 25%, 20%, 14%, and 6%, respectively. Median AFP was 40 (range 0-311,000). Median PIVKA II was 59 (0-378,000). Previous treatment was included none (27%), resection with relapse (20%), transarterial chemoembolization (50%), radiofrequency ablation (28%), percutaneous ethanol injection therapy (15%), chemotherapy (14%). Outcomes: Initial treatment was with 2.6 ± 0.8 agents (range 2–4). Overall, patients were treated with 3.7 ± 1.2 agents (range 2–7). There was a significant correlation between number of agents administered and survival ($P < .0001$). Patients treated with ≥4 agents survived significantly longer than patients treated with ≤3 agents (40.2 vs 6.4 months, $P < .0001$). This difference could not be attributed to statistically significant differences in severity of liver disease or tumor stage, delay in treatment, previous treatment, concurrent nondrug treatment, or censoring effects. The greatest effect was seen in patients treated with at least 4 agents that included Cordyceps sinensis. This prolonged survival was without toxic side effects and appeared to potentiate the survival benefit of conventional therapy.

CONCLUSION: Treatment of HCC with a regimen of ≥4 agents prepared from natural products was associated with prolonged survival in a substantial portion of patients. The data provide level II evidence for the efficacy of naturopathic therapy in HCC.

PMID: 22544231 [PubMed - indexed for MEDLINE]

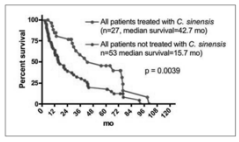


Figure 5. Comparison of patients surviving >3 months on therapy treated or not treated with *Cordyceps sinensis*
Significantly longer survival after the onset of treatment in 27 patients treated with *C sinensis* (median survival = 42.7 months), compared with 53 patients surviving >3 months of therapy and not treated with this agent (median survival = 15.7 months); $P = .0039$.

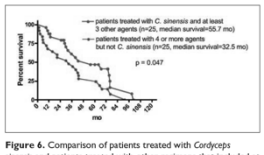


Figure 6. Comparison of patients treated with *Cordyceps sinensis* and patients treated with other regimens that included at least 4 agents

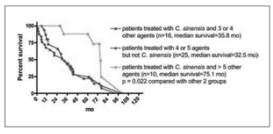


Figure 7. Apparent advantage of *Cordyceps sinensis* is seen only in combination with at least 5 other agents
The extra effect of *C sinensis* compared with other 4-agent regimens is not seen when comparable numbers of agents are used.

Hericium erinaeus (Lion's Mane)

- Anti-cancer, immunostimulating, neuroregenerative, cardio-hepato-nephroprotective, antibiotic, etc.
- Friedman M. J Agric Food Chem 2015 Aug 19;63(32):7108-23

Hericium erinaceus (Lion's Mane; Yamabushitake)

- active against liver, colon and gastric cancer cells in vitro and tumor xenografts in mice in vivo
- more effective and less toxic compared to 5-FU in all four *in vivo* tumor models.
- Li G et al. **Anticancer potential of Hericium erinaceus extracts against human gastrointestinal cancers.** J Ethnopharmacol. 2014 Apr 28;153(2):521-30

Hericium erinaceus - Neuroregeneration

- Study of daily oral Hericium erinaceus in recovery following crush injury to the peroneal nerve in rats
- Activities of H. erinaceus were compared to methylcobalamin, widely used in the treatment of peripheral nerve disorders.
- Analysis of walking track indicated that return of hind limb function and normal toe spreading occurred earlier in treated groups than in MeB12 group.
- Regeneration of axons and re-innervation of motor endplates/neuromuscular junction in extensor digitorum longus muscle of rats in treated groups developed better than in the control group.
- imImunofluorescence studies showed that dorsal root ganglia neurons ipsilateral to the crush injury in rats of treated groups expressed higher immunoreactivities for Akt and MAPK signaling pathways compared to control group. Akt cascade plays a major role in mediating neurotrophin-promoted cell survival, while MAPK cascade is involved in mediating neurite outgrowth.
- Wong KH1, Naidu M, David RP, Bakar R, Sabaratnam V. Neuroregenerative potential of lion's mane mushroom, Hericium erinaceus (Bull.: Fr.) Pers. (higher Basidiomycetes), in the treatment of peripheral nerve injury (review). Int J Med Mushrooms. 2012;14(5):427-46.

Hericium erinaceus for mild cognitive impairment

- Double-blind, parallel-group, placebo-controlled trial
- 50- to 80-year-old Japanese men and women with mild cognitive impairment
- 30 subjects were randomized into two 15-person groups, one of which was given Yamabushitake and the other placebo.
- Yamabushitake group took four 250 mg tablets dry powder TID x 16 wk
- At weeks 8, 12 and 16, the Yamabushitake group showed significantly increased scores on the cognitive function scale compared with the placebo group.
- The Yamabushitake group's scores increased with the duration of intake, but at week 4 after the termination of the 16 weeks intake, the scores decreased significantly
- Mori K, et al. **Improving effects of the mushroom Yamabushitake (Hericium erinaceus) on mild cognitive impairment: a double-blind placebo-controlled clinical trial.** Phytother Res. 2009 Mar;23(3):367-72.

Hericium ramosum (H. coralloides) Comb Tooth

- Oral administration of Hericium ramosum mycelia significantly increased concentrations of NGF in the hippocampus of intact mice.
- Suruga K et al. Effects of Comb Tooth Cap Medicinal Mushroom, Hericium ramosum (Higher Basidiomycetes) Mycelia on DPPH Radical Scavenging Activity and Nerve Growth Factor Synthesis. Int J Med Mushrooms. 2015;17(4):331-8.

Agaricus blazei

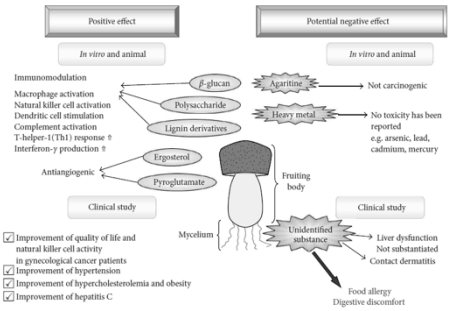


FIGURE 2: The opposite reaction of *Agaricus blazei* Murill derivatives. Our study of safety clinical trail showed that food allergy and digestive discomfort, associated with *Agaricus blazei* Murill product, were noted as new findings.

Hepatoxicity of Agaricus blazei

- An Alternative Medicine, Agaricus blazei, May Have Induced Severe Hepatic Dysfunction in Cancer Patients. Japan J Clinical Oncology. 2006. 36:808-810.
- Hisamochi A, Kage M, Arinaga T et al. Case Report: Drug-induced liver injury associated with Agaricus blazei Murill which is very similar to autoimmune hepatitis. Clinical Journal of Gastroenterology. 2013. 6: 139-144

On the other hand….

- Agaricus blazei Murill (ABM) acts as an enhancer to sensitize doxorubicin (Dox)-mediated apoptotic signaling via inhibition of NFκB activity
- ABM, when combined with low doses of Dox, has the potential to provide more efficient therapeutic effects against drug-resistant human hepatocellular carcinoma.
- Lee JS1, Hong EK. Agaricus blazei Murill enhances doxorubicin-induced apoptosis in human hepatocellular carcinoma cells by NFκB-mediated increase of intracellular doxorubicin accumulation. Int J Oncol. 2011 Feb;38(2):401-8.

Int J Gynecol Cancer. 2004 Jul-Aug;14(4):589-94.

Natural killer cell activity and quality of life were improved by consumption of a mushroom extract, Agaricus blazei Murill Kyowa, in gynecological cancer patients undergoing chemotherapy.

Ahn WS, Kim DJ, Chae GT, Lee JM, Bae SM, Sin JI, Kim YW, Namkoong SE, Lee IP.

Author information

Abstract

A mushroom extract, Agaricus blazei Murill Kyowa (ABMK), has been reported to possess antimutagenic and antitumor effects. Here, we investigate the beneficial effects of ABMK consumption on immunological status and qualities of life in cancer patients undergoing chemotherapy. One hundred cervical, ovarian, and endometrial cancer patients were treated either with carboplatin (300 mg / m(2)) plus VP16 (etoposide, 100 mg / m(2)) or with carboplatin (300 mg / m(2)) plus taxol (175 mg / m(2)) every 3 weeks for at least three cycles with or without oral consumption of ABMK. We observed that natural killer cell activity was significantly higher in ABMK-treated group (ANOVA, n = 39, P < 0.002) as compared with nontreated placebo group (n = 61). However, no significant difference in lymphokine-activated killer and monocyte activities was observed in a manner similar to the count of specific immune cell populations between ABMK-treated and nontreated groups. However, chemotherapy-associated side effects such as appetite, alopecia, emotional stability, and general weakness were all improved by ABMK treatment. Taken together, this suggests that ABMK treatment might be beneficial for gynecological cancer patients undergoing chemotherapy.

PMID: 15304151 [PubMed - indexed for MEDLINE]

Agaricus sylvaticus
The Pinewood Mushroom

Indian J Pharmacol. 2013 May-Jun;45(3):217-22. doi: 10.4103/0253-7613.111894.

Effect of Agaricus sylvaticus supplementation on nutritional status and adverse events of chemotherapy of breast cancer: a randomized, placebo-controlled, double-blind clinical trial.

Valadares F, Garbi Novaes MR, Cañete R.

Author information

Abstract

BACKGROUND: Breast cancer (BC) represents the highest incidence of malignancy in women throughout the world. Medicinal fungi can stimulate the body, reduce side-effects associated with chemotherapy and improve the quality of life in patients with cancer.

AIM: To evaluate the effects of dietary supplementation of Agaricus sylvaticus on clinical and nutritional parameters in BC patients undergoing chemotherapy.

MATERIALS AND METHODS: A randomized, placebo-controlled, double-blind, clinical trial was carried out at the Oncology Clinic, Hospital of the Federal District-Brazil from September 2007 to July 2009. Forty six patients with BC, Stage II and III, were randomly assigned to receive either nutritional supplement with A. sylvaticus (2.1 g/day) or placebo. Patients were evaluated during treatment period.

RESULTS: Patient supplemented with A. sylvaticus improved in clinical parameters and gastrointestinal functions. Poor appetite decreased by 20% with no changes in bowel functions (92.8%), nausea and vomiting (80%).

CONCLUSION: Dietary supplementation with A. sylvaticus improved nutritional status and reduced abnormal bowel functions, nausea, vomiting, and anorexia in patients with BC receiving chemotherapy.

KEYWORDS: Agaricus sylvaticus, chemotherapy side effects, nutritional status

PMID: 23833361 [PubMed - indexed for MEDLINE] PMCID: PMC3696289 **Free PMC Article**

Table 4: Clinical and gastrointestinal symptoms of patients with breast cancer who received six chemotherapy cycles

Symptoms	Groups											
	Placebo (n=10)						*Agaricus sylvaticus* (n=10)					
	Beginning		3 months		6 months		Beginning		3 months		6 months	
	n	*Fp %*	*n*	*Fp*	*n*	*Fp*	*n*	*Fp*	*n*	*Fp*	*n*	*Fp*
Appetite												
Raised	1	10	-	-	-	-	2	20	-	-	2	20
Lowered	3	30	6	60%	8	80%	3	30%	3	30%	1	10%
No change	6	60	4	40	2	20	5	50%	7	70%	7	70%
Bowel function												
No change	1	10	4	40	2	20	1	10%	7	70%	9	90%
Diarrhea	3	30	1	10%	2	20	6	60%	1	10%	-	-
Constipation	6	60	5	50%	6	60%	3	30%	2	20	1	10%
Nausea												
Yes	3	30	8	80%	10	100%	3	30%	4	40	2	20
No	7	70	2	20	-	-	7	70%	6	60%	8	80%
Vomiting												
Yes	3	30	7	70%	7	70%	2	20	2	20	1	10%
No	7	70	3	30%	3	30	8	80%	8	80%	9	90%
Fever												
Yes	1	10	2	20	7	70%	1	10%	2	20	-	-
No	9	90	8	80%	3	30%	9	90%	8	80%	10	100%

Data collected from questionnaire and clinical chart

Nutr Hosp. 2010 Jul-Aug;25(4):586-96.

Life quality of postsurgical patients with colorectal cancer after supplemented diet with agaricus sylvaticus fungus.

Costa Fortes R, Lacorte Recôva V, Lima Melo A, Carvalho Garbi Novaes MR.

Author information

Abstract

INTRODUCTION: Therapeutical alternatives, directed to improve life quality and reduce adverse effects of cancer treatment, have been the purpose of studies that try to prove the immunomodulator efficacy of medicinal fungi as coadjuvant for conventional therapies.

OBJECTIVE: The objective of this study was to evaluate the impact on the life quality of post-surgical patients with colorectal cancer after supplemented diet with Agaricus sylvaticus fungus cultivated in Brazil.

METHODS: Randomized, double-blind, placebo-controlled clinical trial carried out at the Federal District Base Hospital-Brazil, for six months. Samples of 56 enrolled patients (24 men and 32 women), stadium phases I, II and III, separated as placebo and Agaricus sylvaticus (30 mg/kg/day) supplemented groups. Form-standard and direct anamnesis-standard were used to evaluate indicators for life quality. The method of analysis was qualitative and descriptive, processed with Microsoft Excel 2003 and Epi Info 2004 programs. The protocol was approved by the Ethics Research Committee-Health Department-Federal District.

RESULTS: After six months of treatment, the supplemented group had increased adhesion to physical activity; improved disposition and good mood; reduced complaints of pains and alterations of sleep such as insomnia and restless sleep; presenting more appetite, reduced constipation, diarrhea, alternate diarrhea/constipation, flatulence, flatus retention, pyrosis, postprandial fullness, nausea, abdominal distention and abdominal pain, facts not observed in the placebo group.

CONCLUSIONS: The results suggest that a dietary supplement with Agaricus sylvaticus fungus is capable of improving the life quality of patients with colorectal cancer in post-surgical phase.

PMID: 20694295 [PubMed - indexed for MEDLINE] Free full text

Clinics (Sao Paulo). 2011;66(12):2133-9.

The effects of dietary supplementation with Agaricales mushrooms and other medicinal fungi on breast cancer: evidence-based medicine.

Novaes MR[1], Valadares F, Reis MC, Gonçalves DR, Menezes Mda C.

Author information

Abstract

Breast cancer is the most prevalent cancer in women. The most frequent therapeutic approaches for the treatment of this disease are chemotherapy, radiotherapy, hormone therapy, and surgery. Conventional pharmacological treatments cause many harmful side effects in patients. To improve the quality of life of breast cancer patients, researchers have sought alternative adjuvant treatment strategies. To assess the effects of fungi and other basidiomycetes Agaricales on the co-adjuvant treatment of breast cancer, we conducted a literary review of the available scientific evidence. We selected articles published in refereed journals from 1990 to 2011 in Medline, Lilacs, CAPES, Scielo, and Pubmed. Articles written in English, Spanish, and Portuguese were reviewed. We used the following descriptors: Agaricales, medicinal mushroom/fungus, breast cancer, dietary supplementation, synonyms, and related terms. The pharmacological effects of nutritional and medicinal mushrooms have been reported in several experimental clinical studies and have shown promising results in the adjuvant treatment of breast cancer. Adjuvant treatment with mushrooms is associated with improvements in the immunological and hematologic parameters of breast cancer, as well as in the quality of life of these patients. Randomized clinical studies are needed to elucidate the possible mechanisms of action and clinical benefits of these fungi with respect to survival time, disease progression, and metastasis in breast cancer.

PMID: 22189741 [PubMed - indexed for MEDLINE] PMCID: PMC3226811 Free PMC Article

Table 3 - The results of clinical studies using *Agaricales* and other medicinal fungi for dietary supplementation and adjuvant treatment in patients with breast cancer.

References	Mushroom Species	Active Principle	Target Group	Results
Gennari *et al.* (2002)[48]	*Agaricus sylvaticus*	Mushroom Capsule	1 patient with breast cancer and lung metastasis	↑ the number of NK cells and CD 56 total remission of lung metastasis 1.6g qid
See *et al.* (2002)[49]	*Agaricus blazei*	Mushroom tea	5 stage VI breast cancer patients	↑ the number of NK cells stimulate macrophages and other immunomodulatory effects 10mg qd

Table 2 - The effects of *Agaricales* mushrooms and other medicinal fungi on breast cancer: experimental studies in animals, *in vivo* and *in vitro*.

References	Mushroom Species	Target Group/Tumor	Results
Grube *et al.* (2001)[57]	*Agaricus bisporus*	Breast cancer cells	↓ aromatase enzyme activity, tumor cell proliferation and estrogen production
Zhao *et al.* (2003)[58]		Breast cancer cells (MCF-7)	↓ proliferation of tumor cells (via DNase)
Chen *et al.* (2006)[59]		Breast cancer cells (MCF-7) inoculated in mice	↓ tumor cell proliferation and tumor growth
Talorete *et al.* (2002)[60]	*Agaricus blazei*	Breast cancer cells (MCF-7)	↓ cell proliferation
Takimoto *et al.* (2004)[61]		Nalve BALB/c and meth A-bearing BALB/c mice	↑ natural killer activity of spleen cells in nalve BALB/c mice Potentiated cytotoxic activity in innate and adaptive immunity in meth A-bearing BALB/c mice

Agaricus bisporus
White Button Mushrooms

Aromatase Inhibition

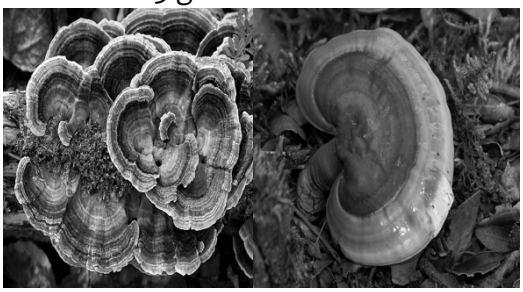
- Chen S, et al.
  Anti-aromatase activity of phytochemicals in **white button mushrooms** (Agaricus bisporus).
- **Cancer** Res. 2006 Dec 15;66(24):12026-34.
- **White button** mushroom phytochemicals inhibit aromatase activity and breast **cancer** cell proliferation.
- Grube BJ, Eng ET, Kao YC, Kwon A, **Chen S.**
- J Nutr. 2001 Dec;131(12):3288-93.

Agaricus bisporus
White Button Mushrooms

- Jeong SC et al. **Macrophage immunomodulating and antitumor activities of polysaccharides isolated from Agaricus bisporus white button mushrooms.** J Med Food. 2012 Jan;15(1):58-65

1+1 > 2

3 grams x 2 > 6?



Synergy with Mushroom Combinations

- Extract of Trametes and Ganoderma (I'm-Yunity-Too) combined is more active in inducing apoptosis of leukemia cells compared to Trametes (I'm-Yunity) alone, based on expression of caspase 3 and Bax
- ***Ethanolic*** extracts of the combination were more anti-proliferative and induced apoptosis more, compared to ***aqueous*** extracts: more down-regulation of phosphorylation of Rb and increased poly(ADP-ribose) polymerase (PARP)
- Hsieh TC, Wu JM. Regulation of cell cycle transition and induction of apoptosis in HL-60 leukemia cells by the combination of Coriolus versicolor and Ganoderma lucidum. Int J Mol Med. 2013 32(1):251-7.

Maitake and Shiitake

- Beta glucans of both were compared to either mushroom alone
- Measures of phagocytosis, NK cell activity, IL-6, IL-12, IFN-gamma and CRP
- Combination was strongest, followed by shiitake on its own
- Vetvicka, V. and Vetvickova, J. Immune-enhancing effects of Maitake (*Grifola frondosa*) and Shiitake (*Lentinula edodes*) extracts. *Annals of Translational Medicine* Vol. 2, No. 2 (2014): 14.

Dosage

- Most human trials found effectiveness with 6gm orally/day, taken either as 2 gm tid or 3 gm bid
- Pioneering studies of IV injection of soluble or particulate glucan have documented significant regression of *in vivo* models of mammary cancer and melanoma in mice
  - Di Luzio et al.

Fruiting body or mycelial extracts?

- Simultaneous presence of different products may elicit multiple stimulatory activities and enhanced immunomodulatory effects. (Vannucci et al. 2013)
- Some producers are using mycelial extracts rather than or in addition to fruiting body extracts
- Most clinical research has focused on fruiting body extracts

Fruiting Body vs. Mycelial Extracts

- active constituents in mushrooms principally beta-D-glucans, secondarily triterpenoids and ergosterol.
- Starch is utilized as an indicator of adulteration.
- Analytical methods that quantify active compounds demonstrate mushrooms fruiting bodies are high in beta-D-glucans and very low in starch.
- Mycelium produced on cereal grains is low in beta-D-glucans and high in starch.
- Ergosterol analysis shows the actual amount of fungal material in the products.
- www.nammex.com 2014:1-27

Ergosterol

- Ergosterol has antitumor and antioxidant properties, and is a precursor to vitamin D2
  - Exp Biol Med. 2004 229:393-406
- When exposed to sunlight (UVB), mushrooms as well as human skin convert ergosterol to ergocalciferol (provitamin D2).
  - DermatoEndocr. 2013 5;1:165-176

Triterpenoids

- Mushrooms grown on natural substrates contain precursors that yield secondary metabolites such as triterpenoids whereas mycelium produced on cereal grains lack such precursors.
- In addition to playing complementary role with beta-glucans in immune system activation, triterpenoid actions are hepatoprotective, lipid lowering, antioxidant, inhibition of histamine release and anti-inflammatory.
- Triterpenoids are lipids, e.g. ganoderic acids, responsible for the bitter taste of reishi and this bitterness can be used as a quick method of determining the quality of a reishi product.
- Int Immunopharm. 2009 9:1272-1280

Beta-D-glucans

- Beta-D-glucans are polysaccharide structural component of the cell walls of mushrooms, mycelium, yeast, certain bacteria, and cereal grains.
- Unique structural differences of beta-D-glucans determine medicinal activity and explain why fungal beta-glucans are more active than cereal beta-glucans.
- J Hem Onc. 2009 2:25

Beta-D-glucans

- Beta-glucans activate or potentiate both innate and adaptive immune responses and have been described as "biological response modifiers" and "host defense" potentiators.
- Beta-glucans increase the number and functional activity of macrophages, Natural Killer cells, and other subclasses of T-cells.
- Beta-glucans are not degraded by digestive enzymes and pass intact into the small intestine where they activate specific beta-glucan receptor sites.
- The immunological potentiation is not only anti-cancer but also increases protection against viral, bacterial, fungal and parasitic infections.
- Exp Biol Med. 2004 229: 393-406
- Int J Med Mushrooms. 1999 1:69-80

Beta glucans

- Beta glucans and protein-bound beta glucans are responsible for the medicinal properties of mushrooms and mycelia.
- Lentinan, a pure (1→3)beta- D-glucan [e], is extracted from shiitake mushroom *Lentinus edodes* .
- PSK and PSP are protein-bound beta-glucans derived from the fermentation of *Trametes* mycelium.

Mushrooms have few quality control standards

- The natural product market contains many fraudulent mushroom products, particularly spiked polysaccharides that manufacturers blend in.
- DNA identification is not an accurate or appropriate method for finished products
- Companies need to work with suppliers to test the raw liquid material to determine what the excipient/carrier content will be at the spray powder stage.
- Unfortunately, excipient starches test the same as polysaccharides. Most of the industry does not realize this and purchases inferior raw materials.

Mushrooms for Specific Cancers

Cancers	Indicated Mushrooms	Reference
Breast	Trametes, Ganoderma, Agaricus sylvaticus, Grifolia	Torkelson et al, 2012 Gonul et al, 2015
Colorectal	Trametes, Ganoderma, Grifolia	Ohwada, et al, 2006
Gastric	Trametes	Eliza et al, 2012
GYN Hepatocellular Leukemia Lymphoma	Ganoderma Agaricus, Ganoderma,Len Agaricus, Gano,Trametes Cordyceps	Suprasert, et al, 2014 Li et al, 2015, Matsui2002 Hsieh et al, 2013
Lung Prostate Advanced cancer	Trametes, Gano, Cordyceps Trametes Ganoderma	Fritz, et al, 2015 Wenner et al, 2012 Gao, et al, 2003

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Mushrooms and Specific Cancers

Mushroom	Cancers	Reference
Ganoderma	Breast, colon, hepatocellular, leukemia (+Trametes), prostate, sarcoma	Hsieh TC and Wu JM, 2013 Chen et al, 2006 Gonul et al, 2015 Loganathan et al, 2014 Liu et al, 2009
Trametes	Breast, colon, gastric, prostate, leukemia (+Ganoderma)	Wenner et al, 2012 Eliza et al, 2012
Grifolia	Breast, colon	Deng et al, 2009 Masuda et al, 2010
Agaricus blazei	Hepatocellular, leukemia	Lee and Hong, 2011 (in vitro) Li et al, 2014 (mice)
Cordyceps Lentinula	Lung, lymphoma Hepatocellular	Matsui et al, 2002

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Mushrooms and Chemotherapeutic Agents

Chemotherapeutic agent	Indicated Mushroom	References (mostly *in vitro*)
Trastuzumab	Trametes	Lu et al, 2011 (also in mice)
Cyclophosphamide	Ganoderma	Zhu et al, 2007
Cisplatin	Ganoderma, Cordyceps, Grifolia	Masuda et al, 2009 Yao et al, 2012
Docetaxel	Trametes	Kinoshita et al, 2009 (human) Wenner et al, 2012 (animal)
Doxorubicin	Agaricus	Lee and Hond, 2011

Mushrooms and Vitamin D2

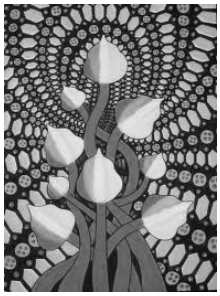
- Mushrooms as well as human skin create vitamin D when exposed to sunlight
- Mushrooms are rich in vit D precursor ergosterol, which UVB converts to ergocalciferols, aka provitamin D2
- Keegan, RH, Lu Z, Bogusz JM, Williams JE, Holick MF, Photobiology of vitamin D in mushrooms and its bioavailability in humans. 2013. Dermato-Endocrinology 5:1, 165–176;

Here's How to Do It

- 1) Obtain fresh organic shiitake, maitake, button, oyster, shimeji or other mushrooms.
- 2) On a sunny day in June, July or August, slice the fresh mushrooms. Place them evenly on a tray exposed directly to the sun from 10 am to 4 pm.
- 3) Before nightfall, cover the mushrooms with a layer of cardboard to block moisture from dewfall.
- 4) The next clear day repeat exposure to the sun from 10 am to 4 pm.
- 5) Remove the mushrooms and finish drying (if necessary in a food dehydrator until they are crispy).
- 6) When thoroughly dry, store in a glass jar or sealed container. Adding a tablespoon of uncooked rice as a moisture absorber will help keep the mushrooms dry. The mushrooms should be good for a year or more, depending upon conditions.
- 7) Take 10 grams daily per person, about a small handful. Rehydrate in water for one hour. The mushrooms will swell. Then cook as desired.
- - See more at: http://www.fungi.com/blog/items/place-mushrooms-in-sunlight-to-get-your-vitamin-d.html#sthash.u5GyOnHU.dpuf

Psilocybe cyanescens: Magic mushrooms

Psychedelic medicine: a re-emerging therapeutic paradigm. CMAJ Sept 8, 2015



Arch Gen Psychiatry. 2011 Jan;68(1):71-8. doi: 10.1001/archgenpsychiatry.2010.116. Epub 2010 Sep 6.

Pilot study of psilocybin treatment for anxiety in patients with advanced-stage cancer.

Grob CS, Danforth AL, Chopra GS, Hagerty M, McKay CR, Halberstadt AL, Greer GR.

Author information

Abstract

CONTEXT: Researchers conducted extensive investigations of hallucinogens in the 1950s and 1960s. By the early 1970s, however, political and cultural pressures forced the cessation of all projects. This investigation reexamines a potentially promising clinical application of hallucinogens in the treatment of anxiety reactive to advanced-stage cancer.

OBJECTIVE: To explore the safety and efficacy of psilocybin in patients with advanced-stage cancer and reactive anxiety.

DESIGN: A double-blind, placebo-controlled study of patients with advanced-stage cancer and anxiety, with subjects acting as their own control, using a moderate dose (0.2 mg/kg) of psilocybin.

SETTING: A clinical research unit within a large public sector academic medical center.

PARTICIPANTS: Twelve adults with advanced-stage cancer and anxiety.

MAIN OUTCOME MEASURES: In addition to monitoring safety and subjective experience before and during experimental treatment sessions, follow-up data including results from the Beck Depression Inventory, Profile of Mood States, and State-Trait Anxiety Inventory were collected unblinded for 6 months after treatment.

RESULTS: Safe physiological and psychological responses were documented during treatment sessions. There were no clinically significant adverse events with psilocybin. The State-Trait Anxiety Inventory trait anxiety subscale demonstrated a significant reduction in anxiety at 1 and 3 months after treatment. The Beck Depression Inventory revealed an improvement of mood that reached significance at 6 months; the Profile of Mood States identified mood improvement after treatment with psilocybin that approached but did not reach significance.

CONCLUSIONS: This study established the feasibility and safety of administering moderate doses of psilocybin to patients with advanced-stage cancer and anxiety. Some of the data revealed a positive trend toward improved mood and anxiety. These results support the need for more research in this long-neglected field.

TRIAL REGISTRATION: clinicaltrials.gov Identifier: NCT00302744.

PMID: 20819978 [PubMed - indexed for MEDLINE]

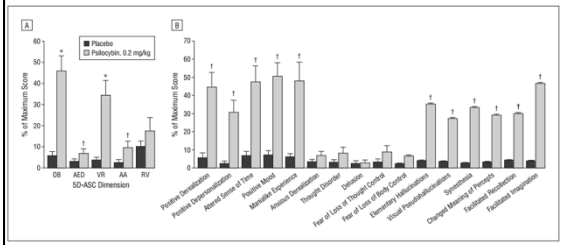


Figure 2. Subjective effects of psilocybin as measured by the 5-Dimension Altered States of Consciousness profile (5D-ASC). A, Five main 5D-ASC dimensions are shown: oceanic boundlessness (OB), anxious ego dissolution (AED), visionary restructuralization (VR), auditory alterations (AA), and reduced vigilance (RV). B, Item clusters comprising the OB, AED, and VR dimensions are shown. Values are the mean (SEM) percentages of the total possible score. *P<.01, †P<.05 for psilocybin vs niacin placebo control (1-way analyses of variance were used to compare niacin and psilocybin effects on individual 5D-ASC dimensions and 5D-ASC item clusters).

Psychopharmacologist Roland Griffiths


Johns Hopkins Study of Psilocybin in Cancer Patients
Investigators: Roland Griffiths PhD, William Richards PhD, Matthew Johnson, Ph.D., Una McCann, M.D.
Sponsor: Heffter Research Institute, Riverstyx Foundation
Contact: Roland Griffiths, PhD
This study is being done to find out if psilocybin can produce personally and spiritually meaningful experiences in cancer patients, thereby extending findings from an earlier study in our laboratory with healthy volunteers. This could be important because spirituality has been associated with increased psychological coping and decreased depression in serious illness. The study will enroll about 44 people, who will receive careful preparation and 2 sessions in which they will receive psilocybin. Structured guidance will be provided during the session and afterward to facilitate integration of the experiences.

To learn more about this study, visit the study website: http://www.cancer-insight.org

New York University Psilocybin and Cancer Study

Investigators: Stephen Ross MD; Anthony Bossis PhD; Jeffrey Guss MD

Sponsor: Heffter Research Institute
Contact: Gabrielle Agin-Liebes or Tara Malone at (646) 641-2000
This is a double-blind, placebo-controlled pilot study that will assess the efficacy of psilocybin on psychosocial distress, with the specific primary outcome variable being anxiety associated with cancer. Secondary outcome measures will look at the effect of psilocybin on symptoms of pain perception, depression, existential/psychospiritual distress, attitudes toward disease progression, quality of life, and spiritual/mystical states of consciousness.

For more information about this study, go to http://www.nyucanceranxiety.org/

Research Challenges in Cancer Mycotherapy

- Need for more well-designed randomized, placebo-controlled trials
- Varying delivery methods and types of mushroom extracts used
- Animal studies often use intra-peritoneal injection of purified mushroom extract making it difficult to translate dosage and form into human studies