Mushroom Science news

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Ganoderma lucidum

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American Herbal Pharmacopoeia Publishes Therapeutic Compendium for Ganoderma lucidum (Reishi)

There are a limited number of medicinal mushrooms that both traditional medicine and contemporary scientific investigation hold in high esteem. Among the most respected is *Ganoderma lucidum* (Reishi). Because of this, it is no surprise that Reishi was the first medicinal mushroom that the *American Herbal Pharmacopoeia (AHP)* chose for comprehensive review in its series of therapeutic compendiums (published September 2000). This publication brings much needed focus and objectivity to issues of quality in commercially available products and, up to this point, is the best source of information on actions, constituents, and scientific research.

Quality Issues

There are many publications, books, and articles available to practitioners and the general public that discuss medicinal mushrooms and their uses. The AHP compendium is the first to address raw material processing and how that relates to the quality of the final product in terms of bio-availability and levels of active constituents identified in the clinical research.

The observations in regard to *Ganoderma lucidum* hold true for all medicinal mushrooms given their similar biology and morphology. Because people with serious health conditions, including cancer, use medicinal mushroom products, such a focus is long overdue and essential if medicinal mushroom compounds are to reach their full potential as safe, effective, and inexpensive options to treat the health concerns for which they have been proven effective.

The review is most critical of medicinal mushroom products consisting of "mycelium bio-mass," a product type that represents a significant portion if not a majority of the medicinal mushroom supplements sold to the general public and health practitioners in North America.

Mycelium bio-mass is created by growing the mycelium (the vegetative stage) through sterilized grain in plastic bags. The end product of this solid state fermentation process, which is still approximately 50% grain, is dried, powdered, and pressed into tablets or encapsulated.

The authors of this review not only question the bio-availability of these products, they state that "most of the studies reviewed used concentrations of isolated constituents that are magnitudes higher than what is available in crude mycelium biomass preparations." Further, they state that the constituent profile "varies greatly" from one batch of mycelium bio-mass to the next.[1]

This is important information for practitioners to consider when they choose the proper medicinal mushroom product for their patients' serious health concerns. While mycelium bio-mass products present a number of problems, a properly made hot water or hot

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Anti-herpetic activities of acidic protein bound polysaccharide isolated from Ganoderma lucidum alone and in combination with acyclovir and vidarabine. (College of Pharmacy, Chungbuk National University, Cheongju 361–763, South Korea.)

A promising new clinical application for medicinal mushroom isolates may be to combine them with existing pharmaceutical anti-viral and anti-biotic medications to enhance the pharmaceutical treatment's effectiveness. A recent study at the College of Pharmacy at Chungbuk National University in South Korea looked at the use of an isolate from Reishi (Ganoderma lucidum) to improve the effectiveness of an existing pharmaceutical treatment for herpes.

To investigate potential anti-herpetic activity, an acidic protein-bound polysaccharide (APBP) was isolated from the fruit bodies (mushroom) of *Ganoderma lucidum*. This brownish APBP was isolated from water-soluble substances of the fruit body by activity-guided isolation method. APBP was tested for its antiviral activity against herpes simplex virus type 1 (HSV-1) and type 2 (HSV-2) by plaque reduction assay in tissue culture.

APBP showed potent antiviral activity against HSV-1 and HSV-2 in Vero cells at its 50% effective concentration (EC(50)) of 300 and 440 microg/ml, respectively. APBP had no cytotoxicity on Vero cells at a concentration of 1 x 10(4) microg/ml. APBP exhibited a potent antiviral activity with selectivity index (SI) of more than 22.73. The combined anti-herpetic effects of APBP with nucleoside anti-herpetic agents, acyclovir (ACV) and vidarabine (ara-A), were examined on the multiplication of these two strains of herpes viruses in Vero cells by the combination assay. The results of combination assay were evaluated by the combination index (CI) that was calculated by the multiple drug effect analysis. CI values were ranged 0.47–0.51 for a combination of APBP with ACV, and between 1.02–1.18 for a combination of APBP with ara-A.

The combinations of APBP with ACV on HSV-1 and HSV-2 showed potent synergistic effects, and these results suggest that the possibility of developing APBP as a new anti-herpetic agent. (Oh KW, Lee CK, Kim YS, Eo SK, Han SS. J. Ethnopharmacol 2000 Oct; 72 (3): 475-81).

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water/alcohol extract does not. The quality of an extract can be assayed to confirm equivalence with the identity and concentration of isolates used in scientific investigation. Extracts guarantee bio-availability and the effective and consistent dosing of the active constituents. Ground up mushrooms and mycelium bio-mass, unless broken down by hot water extraction, should be considered food and not medicine.

Actions, Constituents, and Scientific Research

Ganoderma lucidum, also referred to as "Reishi" throughout the *AHP* review share, with other fungi, the important classification of constituents called beta-glucans, or proteoglycans. These compounds are proven to be potent human and animal immune stimulators. However, Reishi, unlike the other popular medicinal fungi, also contains an important group of chemicals called triterpenes, which leads many practitioners to make this the mushroom of choice when there are cardiovascular and cholesterol concerns.

Constituents: Carbohydrates, steroids, triterpenes (more than 100 identified), lipids, alkaloids, glycoproteins, ergosterol, a coumarin glycoside, volatile oils, and protein-bound polysaccharides (beta-1-3 and beta-1-6 D-glucans) with identified amino acids, in descending order of concentrations, of serine, alanine, glycine, threonine, aspartic acid, glutamic acid, proline, and valine.

Indications: Immuno-modulation, especially in cancer and hepatitis, liver support, detoxification, hepatitis, cholesterol regulation, cardiovascular support, diabetes.

Safety: Rare/occasional diarrhea and dermatitis. No reports of serious or permanent injury.

Contra-indications: The main concern for the use of Reishi is when its actions parallel the actions of prescriptions that a patient may already be using. The primary areas of concern would be anti-coagulation medications, and cholesterol-lowering drugs that involve the HMG-CoA reductase pathways of the liver. Whether due to its reported sedative and antidepressant actions or due to hepatic clearance pathways, Reishi has been reported to influence the actions of reserpine, chlorpromazine, and barbital medications.[2] Hypoglycemic actions warrant a careful regulation of oral and injected diabetic medicines and, as with all potent immuno-modulators careful consideration and monitoring are required for use with organ transplant recipients.

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Immuno-Modulation and Anti-Cancer Activity of Polysaccharide-Protein Complexes (The Chinese University of Hong Kong):

Three anti-tumor mushroom polysaccharides, i.e., lentinan, schizophyllan, and protein-bound polysaccharide (PSK, Krestin), isolated respectively, from *Lentinus edodes*, *Schizophyllum commune*, and *Coriolus versicolor*, have become large market items in Japan.

Lentinan and schizophyllan are pure beta-glucan, whereas PSK is protein-bound beta-glucan.

A polysaccharide peptide (PSP), isolated from a strain of *Coriolus versicolor* in China, has also been widely used as an anti-cancer and immunomodulatory agent.

Although the mechanism of their anti-tumor action is still not completely clear, these polysaccharides and polysaccharide-protein complexes are suggested to enhance cell-mediated immune responses in vivo and in vitro and act as biological response modifiers. Potentiation of the host defense system may result in the activation of many kinds of immune cells that are vitally important for the maintenance of homeostasis. Polysaccharides or polysaccharide-protein complexes are considered as multi-cytokine inducers and cytokine receptors. Some interesting studies focus on investigation of the relationship between their structure and anti-tumor activity, and elucidation of their anti-tumor mechanism at the molecular level. (VE Ooi and F Liu, Curr Med Chem.,7(7) (2000) 715-29).

Effect of Polysaccharide Krestin on Glutathione Peroxidase Gene Expression in Mouse Peritoneal Macrophages (First Military Medical University, China):

Previously, PSK was found to reduce the oxidative injury that oxidized low-density lipoprotein (Ox-LDL) produced in monocytes/macrophages, and therefore have prophylactic or therapeutic effect on atherosclerosis.

In order to find out if the effects of PSK were associated with antioxidant enzymes, researchers at China's First Military Medical University investigated its effect on glutathione peroxidase activity and messenger RNA (mRNA) expression in mouse peritoneal macrophages. Results showed that PSK enhanced SeGPx and non-SeGPx activity, and increased SeGPx and GST-P (pi class GST) mRNA in mouse peritoneal macrophages. Researchers concluded that PSK improved glutathione peroxidase activity through transcriptional induction of mRNA expression. (Z. J. Pang et al., Br.J.Biomed. Sci. 57(2) (2000) 130-6).

Reduction of the Oxidative Injury to Rabbits With Established Atherosclerosis by Protein-Bound Polysaccharide from Coriolus versicolor (The First Military Medical University, China):

Recent evidence has emerged that macrophage glutathione (GSH) content and selenium-dependent glutathione peroxidase (SeGSHPx) activity are inversely related to cell-mediated oxidation of LDL, and intervention means to enhance the macrophage GSH-SeGSHPx status may contribute to attenuation of the atherosclerotic process. Researchers' previous work showed that protein-bound polysaccharide (PSK) injected intra-peritonateally could enhance SeGSHPx activity and mRNA content of mouse macrophages. The aim of the present study is to demonstrate whether PSK can reduce the oxidative injury to the established atherosclerotic rabbits. Through the increment of SeGSHPx activity and improves the antioxidant/prooxidant imbalance in them, and thus decrease Ox-LDL, LPO and cholesterol content of plasma and tissues, and regresses lesion area of aortae in the established atherosclerotic rabbits. (M. Zhou et al., Am. J. Chin. Med. 28(2) (2000) 239-49).

PSK and OK-432-Induced Immuno-Modulation of Inducible Nitric Oxide (NO) Synthase Gene Expression in Mouse Peritoneal Polymorphonuclear Leukocytes and NO-Mediated Cytotoxicity (Kyoto Prefectural University of Medicine, Japan):

Researchers at Japan's Kyoto Prefectural University of Medicine investigated whether PSK (a polysaccharide extracted from *Coriolus versicolor*) or OK-432 (a streptococcal preparation) can up-regulate inducible nitric oxide synthase (iNOS) gene expression and nitric oxide (NO) production in mouse peritoneal polymorphonuclear leukocytes (PMNs). The results suggest that PMNs produce NO after stimulation with PSK or OK-432 in combination with IFN-gamma and may regulate the immune system in vivo, although the NO production induced by these agents is insufficient for tumor cell killing in vitro. (A. K. Kato et al. Immunopharmacol Immunotoxicol, 22 (2) (2000) 221-35).

Communications

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What are the differences between PSK®, PSP, and VPS®?

PSK, **PSP**, and **VPS** are all proteoglycans extracted and purified from the mycelia or fruit body (mushroom) of *Coriolus versicolor*. The Proton NMR spectra of these proteoglycans are nearly indentical with minor chemical differences occuring in those constituents not considered to be the active compounds, such as the amino acids and single sugars.

PSK is a protein-bound polysaccharide and was first manufactured by Kureha Chemical Co. of Japan. The PS in PSK is an abbreviation for polysaccharide and the K represents the first letter of the company name. The commercial name of this product is **Krestin**.

PSP is a polysaccharide-peptide and was invented by Shanghai Teaching University in China. As there is less branching, and consequently less mass in that portion of the molecule that consists of amino acids, it is classified as a peptide rather than a protein. The PS in PSP is an abbreviation for polysaccharide while the letter P represents the word peptide.

VPS is a protein-bound polysaccharide and is slightly less purified than the protein-bound polysaccharide PSK. The letter V is an abbreviation of the word versicolor while the PS stands for polysaccharide.

	PSK®	PSP	VPS®
Origin	Japan	China	USA
Raw Material	Mycelium or Fruit body	Mycelium or Fruit body	Wild fruit bodies
Fermentation nitrogen source	peptone yeast cake	soy bean cake powder	no fermentation
Extraction solvent	dilute alkaline solution	aqueous alcohol	hot water
Further purification	salting out with ammonia sulfate	precipitation with alcohol	membrane filtration
Polysaccharide composition	- arabinose - rhamnose + fucose	+ arabinose + rhamnose - fucose	+ arabinose + rhamnose + fucose
Legal status	prescription drug in Japan	OTCdrug in China	dietary supplement in USA

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Clinical research: Reishi is one of the most widely researched natural remedies in Asia with most of the research centering on four therapeutic actions: immune-enhancing, cardiovascular-regulating, hypoglycemic, and hepatoprotectant.

The two constituent categories researched in these studies were the triterpenes and the beta-glucans. While isolates of triterpenes have been used in diabetic studies, the majority of the research uses extracts of the fruit bodies that contain both the beta-glucans and the triterpenes. Synergism or independent actions of the other constituents are largely unknown and minimally researched.

It is also important to note that mycelium-based extracts are characteristically much lower in triterpenes levels, including many of the compounds that benefit cardiovascular health. Standard assay can identify the important constituents with reliable measurements of heavy molecular weight polysaccharides, their nitrogen content, and their linkage. Similarly, concentration and identification of individual and total triterpenes is commonly available.

Quality extracts of Reishi inhibit platelet aggregation, improve diabetic parameters, decrease cholesterol, decrease inflammation of the liver from viral and chemical aggravation and insult, boost the immunity for resistance to infection, and to combat neoplastic action within tissues.

Clinical anecdotes: I have used high-quality Reishi extracts for many years. Many of my patients with "familial hypercholesterolemia" show marked reductions in just four months with a dose of 800 mg per day. I have had many diabetic parameters including glycohemoaglobin improve with regular oral consumption of Reishi extract, and consider it to be the "poor man's (sic) hepatitis medicine," showing reduction in viral load and liver enzymes (I still consider *Coriolus versicolor* the fungi of choice for both Hep. B and C). Reishi should be considered a major player in treating cardiovascular disease, high cholesterol, hepatitis, diabetes and cancer.

To order a copy of the compendium contact the *American Herbal Pharmacopoeia* at:

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[1] *American Herbal Pharmacopoeia*, September 2000, Editor Roy Upton, Santa Cruz, California, p19.
[2] *American Herbal Pharmacopoeia*, September 2000, Editor Roy Upton, Santa Cruz, California.