

Mushroom Medicine: Challenges and Potential

Christopher Hobbs, Ph.D., L.Ac., RH (AHG)

Fungi are extremely ancient organisms, and tremendous diversity exists in many habitats throughout the world. Most of the scientific work performed on fungi with regard to their medicinal and healing effects can be thought of in two categories: antibiotics and immunomodulators.

A landmark discovery in human history was that various soil fungi contain powerful antibiotics, apparently to protect themselves from bacterial infections. These antibiotics have saved literally millions of lives, starting with penicillin discovered in 1928, and streptomycin in 1943. While these medicines have been mostly beneficial, many decades of their medical misuse and overuse, plus their widespread inclusion in animal and dairy products, have created a global emergency: the arrival of antibiotic-resistant superbugs that might cause pandemics that could wipe out millions.

But the relationship between fungi and humans is far older than the potent 20th-century antibiotics described above. Many other fungi have been used in healing and medicine, going back over 3,000-4,000 years, and possibly further back to the Stone Age (Peintner & Pöder 2000). Instead of soil organisms, these medicines were and are derived from “higher” fungi, the macrofungi that produce visible fruiting bodies – commonly known as mushrooms – for the

distribution of their spores.

Besides humans’ long relationship with them for use as medicine and food, mushrooms are also recognized as pathogens, perhaps as best evidenced by the body’s innate recognition of specific compounds that all fungi carry as part of their cell walls: beta-glucans (β -glucans).

Fungal β -glucans and the Immune System

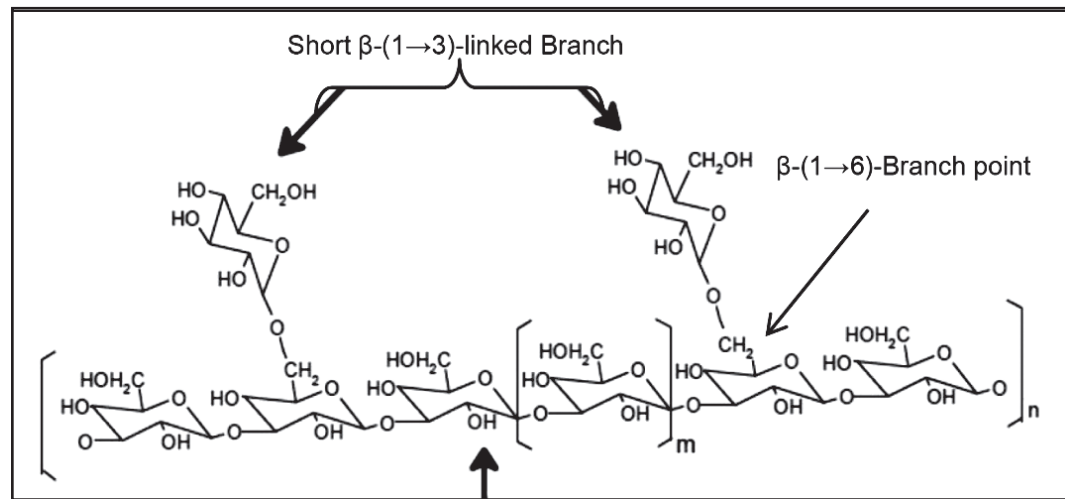
Also found in some plants and bacteria, β -glucans are glucose polymers occurring in many sizes and shapes. The major active compounds for immunomodulatory and antitumor effects are the β -D-glucans, which often occur in a triple helix conformation. Many structural variations of these bioactive mushroom cell wall carbohydrates exist in different species, but all have a main chain consisting of (1 \rightarrow 3)-linked β -D-glucopyranosyl units along which are randomly dispersed single β -D-glucopyranosyl units attached by 1 \rightarrow 6 linkages giving a comb-like structure (Bohn & BeMiller 1995).

Just as shape plays a role in β -glucans’ activity, so do size and solubility. Larger forms of the β -glucan molecules derived from the cell walls of fungi, especially in their native triple helix form (Bohn & BeMiller 1995), or particles of these, seem to be more potent than smaller molecules. Water-soluble β -glucans have also been widely studied and shown to have a variety of immunostimulatory (activate immune



Dr. Christopher Hobbs is a fourth-generation, internationally renowned herbalist, licensed acupuncturist, herbal clinician, research scientist, consultant to the dietary supplement industry, expert witness, botanist, and mycologist with over 35 years of experience. Christopher is the author or co-author of over 20 books, including the groundbreaking *Medicinal Mushrooms* (Book Publishing Co., 1987) and *Grow It, Heal It* (Rodale Press, 2013). Christopher lectures on herbal medicine worldwide. He has taught at universities and medical schools such as Stanford Medical School, Yale Medical School, Bastyr University and the National School of Naturopathic Medicine. He has taught classes for the last six years at the University of California, Berkeley as a Ph.D. graduate student in evolutionary biology, phylogenetics, plant chemistry, and ethnobotany. Visit Christopher’s website at www.christopherhobbs.com.

Figure 1: An example of the molecular structure of soluble yeast β -glucan (Waszkiewicz-Robak B 2013)



functions) or immunomodulatory (regulate immune functions) effects (Batbayar et al 2012, Rice et al 2005). An extract of a mushroom fruiting body, such as *Lentinula edodes* (shiitake)

or *Trametes versicolor* (turkey tail), might contain up to about 40-50 percent or higher β -glucans.

Once inside the human body, the primary effect of β -glucans seems to be activation of the immune response to alert the host to the presence of, and to inhibit, infectious pathogens. Is it serendipity that mushrooms that are edible and nutritious contain compounds that stimulate the immune system, but without the threat of disease?

How do fungi act as immunostimulants? The mechanisms are still not clearly defined, but β -glucans are absorbed in the gut, where they bind to gut-associated lymphatic tissue (GALT) binding sites without intestinal absorption. Additionally, β -glucans bind to macrophages associated with the gut barrier, acting on several immune receptors including Dectin-1, complement receptor 3 (CR3) and toll-like receptors (TLR-2/6), triggering a group of immune cells including macrophages, neutrophils, monocytes, natural killer cells and dendritic cells (Goodridge et al 2001). Due to these actions, both innate and adaptive immune responses can be modulated by β -glucans, and phagocytosis (the engulfment of pathogens and foreign substances to break them down or clear them) can be enhanced (Chan et al 2009).

Most β -glucans cannot be digested, and so have to be captured by macrophages, internalized and fragmented within the cells, then transported by macrophages to the marrow and endothelial reticular system. The smaller β -glucans fragments are subsequently released by the macrophages and taken up by other immune cells which leads to

Choosing Medicinal Species

Since all mushrooms contain β -glucans, and β -glucans are recognized by the human immune system through ancient cellular evolutionary interactions, it stands to reason that all mushrooms are immunomodulating and immunostimulating. Despite this, we focus on well-known medicinal species like *Trametes versicolor* (turkey tail), *Lentinula edodes* (shiitake), and *Grifola frondosa* (maitake), because these are commonly available and have a long history of use, or perhaps because of their striking appearance as in the case of *Ganoderma lucidum* (reishi). Reishi has been valued for its beautiful shape and bright varnished appearance for many centuries.

Based on my research and experience, I prefer to use turkey tail and shiitake above other species, simply because they have a larger body of clinical trials and long traditional use. Reishi has a very long history of use, but is only supported by clinical reports from China (which reported that the mushroom tea administered to people yielded better outcomes than expected), not rigorously-designed clinical trials. Human clinical trials with larger sets of volunteers taking the remedy vs. those having a placebo for at least 12 months, and following up for at least five years, are needed. These studies are ongoing in Asia and in the U.S., where preliminary evidence is promising. I do not rely upon animal studies mainly because of the wide range of differences in activity of β -glucans and other compounds as well as the way the liver metabolizes them in different species.

I do recommend use of *Inonotus obliquus* (chaga), *Auricularia polytricha* (wood ear), *Hericium erinaceus* (lion's mane), and other up-and-coming species as well, but limited scientific research and information about traditional use of these mushrooms are available.

diverse immune responses.

In summary, when specific fungal, bacterial, or other microorganismal markers are detected in the gut, a large number of immune system mechanisms, likely both humoral and cellular, are activated (Batbayar et al 2012). These processes stimulate the immune system's vigilance to attack viruses, abnormal cells, and of course, pathogenic fungi and bacteria. The terminology for pattern-recognition of fungal β -glucans by our immune system, recognition that has developed over evolutionary time, is pathogen-associated molecular pattern (PAMP) (deSmet et al 2013).

Preparation and Dosage

For maximum activity, delivery of mushroom medicine via water-based extract or micropowder is best. These methods of administration are preferable to alcoholic extract because β -glucans and proteins are not alcohol-soluble, and alcohol interferes with hydrogen bonding, altering the tertiary structures to the point where immunomodulatory activity is reduced (Bohn & BeMiller 1995). For these reasons, I do not recommend tinctures for immune disorders, cancer, or viral syndromes. On the other hand, some mushrooms contain small weight molecular compounds (e.g., reishi triterpenes) which have demonstrated sedative, anti-allergenic, hepatoprotective and other activity, and these compounds are soluble in alcohol. The tincture may be useful in these cases.

Based on a lot of clinical and personal experience, I'm convinced that a high dose is necessary where there is a need for strong immunomodulation or stimulation and one is dealing with a serious ailment such as cancer. The average dose used in many clinical trials for cancer support with chemotherapy is about 5 to 6 grams per day of enzymatically processed mycelial extract, such as the *Trametes versicolor*-derived pharmaceutical products Polysaccharide peptide (PSP) or Polysaccharide K (PSK), which are produced in liquid culture using fermentation technologies. These products are highly refined and concentrated protein-bound polysaccharides that are often characterized as drugs and are in no way comparable to crude mycelium produced on grain.



Photo by Christopher Hobbs

For prevention, about 25 grams of shredded or powdered crude mushroom fruiting body as a decoction (drink 1 strong cup, twice daily for maximum effect, and less for prevention or maintenance), or 2 to 3 grams per day of a water-based extract (a minimum of two "oo" capsules twice daily, equaling a total of 2 grams) should be sufficient for most people. This dose applies to finely-powdered fruiting body, steamed or otherwise, though steaming the powder or shredded mushrooms first, then drying and powdering may be preferable for reducing the possibility of digestive disturbance. The idea is to get the particles as fine as possible to allow for greater surface area exposure and absorption. About twice this dose is appropriate for treating more serious conditions (typically used as adjuvants with other drugs, remedies, or functional medicines like CoQ10), depending on the user's body weight and sensitivity.

Pharmacodynamically, β -glucans stay in the blood for some time (Rice et al 2005). For instance, after 24 hours, 20 percent of laminarin was still detectable in the blood serum. This

Trametes versicolor
(turkey tail).

means that some activity likely continues throughout the day with oral intake. Still, mushroom extracts act as short-acting mitogens, which means that they have to be taken frequently for full benefits. In my experience, a divided dose of half in the morning and half in the evening works best. A dosage of three times a day offers maximum effects, but this frequency seems to create a problem with compliance for most patients.

Since I wrote the first edition of my *Medicinal Mushrooms* book in 1987 (second edition in 1995, Botanica Press, published by the Book Publishing Company in Tennessee), I've been experimenting with medicinal mushrooms both inside the clinic and out, personally and with friends and family. I've been combing the research for many years as well. After all this time I still have questions: Which species make the strongest medicine? What form of extraction — water-based decoctions or steaming the powdered fruiting bodies — will be more potent? Definitive studies to help resolve these issues are still needed.

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Pleurotus ostreatus (oyster mushroom).



Photo by Jason Hollinger CC BY SA 2.0

Are the fruiting bodies stronger than the mycelial product? Based on my sense of taste and my clinical and personal experience, I always prefer the fruiting bodies for making medicine because this reduces the possibility that a significant amount of grain or other substrate such as straw will be present in the finished product, thereby reducing the amount of active ingredients and increasing levels of starch or other inactive common molecules.

Medicinal Mushrooms as a Dietary Supplement

What can one really expect from a full dose of medicinal mushrooms added to the diet daily? Mushroom medicines are widely recommended for prevention of cancer, as an adjuvant treatment for cancer with chemotherapy, or for some people perhaps by itself, as a standalone treatment (though no clinical trials here). First of all, keep in mind that chronic metabolic illnesses like cancer, liver diseases, viral syndromes, immune weakness, and especially chronic immune weakness in general, are conditions that have likely settled into the body deeply over years, and so are very difficult to treat. Medicinal mushrooms are not panaceas or magic bullets and may be of limited benefit in some cases. A total program for health is needed: diet, meditation, mindfulness and spiritual practice, exercise, handling and reducing stress as well as possible, herbs, body work, and counseling.

Medicinal mushrooms should be used as regular dietary supplements that can offer proven and decided benefits, while being exceptionally safe. It's important to take them daily and very regularly for full health benefits. I believe that anyone or nearly anyone with cancer, viral syndromes and immune weakness can obtain some benefit from medicinal mushrooms. From my experience, the regular addition of edible mushrooms (especially oyster mushrooms, shiitake, maitake, wood ear, porcini, chanterelles) can provide a significant health benefit for balancing blood lipids, blood sugar, immune function, weight, and overall nutrition.

Recently I've been focusing on the nutritional and health-giving benefits of mushrooms added to the diet regularly, and even

daily. Mushrooms are amazing dietary supplements simply for their nutritional value alone. Almost all mushrooms should be cooked before eating. That's because mushrooms contain a lot of indigestible long-chain polymers like chitin, an amino polymer found in crab shells. You can imagine how tough a crab shell is to digest. In fact, the irritating qualities of the larger molecular weight polymers in raw mushrooms can cause stomach upset readily. After cooking, mushrooms yield a lot of valuable health-giving nutrients such as trace minerals including copper, zinc, and many others. Mushrooms also contain rather high amounts of macro minerals such as potassium and phosphorus.

For food or nutritional purposes, stick to the fleshy fungi that are soft and tender like *Pleurotus ostreatus* (oyster mushrooms), shiitake, various *Agaricus* species, or *Auricularia polytricha* (wood ear). I believe that the many varieties of oyster mushrooms are the most digestible of all. These mushrooms yield valuable soluble fiber and some insoluble fiber; in fact they are one of nature's foods highest in fiber. Fiber helps move the bowels, removes toxic waste products, regulates blood cholesterol levels, and interacts with the immune system and gut microflora in beneficial ways. Some mushrooms also contain an amazing amount of protein. For instance, shiitake and oyster mushrooms contain up to one quarter usable protein (Khan et al 2008). This protein is quite high quality, and in some cases rivals egg protein. Many mushrooms are also very tasty, especially *Boletus edulis* (king bolete), *Cantharellus cibarius* (chanterelle), oyster mushrooms, maitake, and many others. Considering their high-fiber, low-carbohydrate and high-protein content, plus other nutritional properties and their delicious flavor, mushrooms are really the ideal diet food. Eaten regularly, mushrooms will provide all of these nutritional and health-giving benefits, along with the medicinal actions.

Most medicinal polypores like reishi or *Ganoderma applanatum* (artist's conk) are hard as a piece of wood. You can cook them all you want and pound them too, but they just will not tenderize. Fortunately, the medicinal qualities of these fruiting bodies can be liberated by boiling or other methods of extraction.

A Note about Foraging

Wild mushroom hunters must bear in mind that some species are quite toxic, or even lethal. As the old saying goes, "There are old mushroom hunters, and bold mushroom hunters, but there are no old and bold mushroom hunters." I have eaten over 50 wild species and have lived to tell the tale. This is because I make sure of the identity of the mushroom I'm about to eat and take few chances. Special attention should be paid to the world's most poisonous mushrooms, such as *Amanita phalloides*. Anyone daring to forage mushrooms in the wild should be able to recognize these deadly species without doubt, paying attention to all their subtle characteristics such as spore color, stem shape and texture, and whether the gills (if present) connect to the stem or are free. Considering all wild mushrooms, very few are lethal, but all it takes is one. Take a class, get some good books with lots of pictures, and for medicinal mushroom identification you can check out my book by the same name, or others. ■

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