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## Review

# Are mushrooms medicinal?



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### ABSTRACT

Despite the longstanding use of dried mushrooms and mushroom extracts in traditional Chinese medicine, there is no scientific evidence to support the effectiveness of these preparations in the treatment of human disease. Consumers should evaluate assertions made by companies about the miraculous properties of medicinal mushrooms very critically. The potential harm caused by these natural products is another important consideration. In a more positive vein, the presence of potent toxins and neurotropic compounds in basidiomycete fruit bodies suggests that secondary metabolites with useful pharmacological properties are widespread in these fungi. Major investment in controlled experiments and objective clinical trials is necessary to develop this natural pharmacopeia.

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Mushrooms have featured in traditional Chinese medicine for centuries and dried extracts from fruit bodies occupy a lucrative segment of the market for herbal medicines in western countries. The advertising of these natural products in North America and Europe is poorly regulated, allowing companies to make fictitious statements about the medicinal benefits of mushrooms. A number of issues must be considered objectively to assess this controversial topic. We begin with the traditional uses of mushrooms in Chinese medicine.

Medicinal use of the shiitake mushroom, *Lentinula edodes*, became widespread in the Ming Dynasty (1368–1644) after the development of methods for cultivating the fungus on logs (Jones 1995). Shiitake was adopted as a tonic that could counteract the quotidian aches, pains, and fatigue associated

with aging. More specific virtues of shiitake were supposed to include its promotion of heart health and efficacy against lung disease and intestinal worms. It also became associated with the treatment of cancer. There is little experimental support for any of these qualities. Contemporary advocates of medicinal mushrooms argue that this dissonance is rooted in a mismatch in philosophy between Chinese and Western medicine.

Traditional Chinese medicine treats symptoms of cardiovascular disease, for example, as a manifestation of an imbalance between multiple physiological processes in an individual patient. Treatments, including acupuncture and herbal medicines, are designed to restore balance to the ‘flow of energy’ in the body. (‘Flow of energy’ is placed in quotation marks because the meaning of this phrase cannot be articulated in any

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succinct manner.) Western medicine addresses some forms of heart disease very differently, by prescribing drugs that reduce blood pressure and serum cholesterol, and recommending changes in diet and exercise. The use of a combination of therapies in Chinese medicine, which is often adjusted for each patient, makes it difficult to measure the particular usefulness of shiitake mushrooms in a clinical trial.

A handful of experiments on the properties of specific chemical compounds extracted from shiitake have been promising (Memorial Sloan Kettering Cancer Center [MSKCC] MSKCC 2015a).<sup>1</sup> Lentinan is a  $\beta$ -(1 → 3)-D-glucan in the cell walls of the masses of hyphae that form the shiitake fruit body (Zhang et al. 2011). Lentinan research has demonstrated that the molecule acts as an adjuvant that stimulates the production of antibodies in mice injected with a vaccine against hepatitis B. Other experiments on tissue cultures show that lentinan stimulates cells of the immune system to attack cancer cells and cells infected with viruses. In a rare instance of a clinical trial using a mushroom extract, Japanese researchers found that patients receiving chemotherapy for advanced stomach cancer survived longer if lentinan was added to their drug cocktail (Ina et al. 2013). These results fall short of proving that shiitake is useful in cancer therapy, but they certainly encourage further study.

The lentinan research appears, at first glance, to buttress the historical case for using mushrooms, but there are some important caveats. One of the problems is that the results of studies on single chemical compounds are unlikely to apply to the consumption of whole fruit bodies or concoctions made from dried mushroom powder. It is impossible, for example, to link the immunological consequences of injecting mice with cell wall polysaccharides to the expediency of drinking hot tea brewed from shiitake. Nevertheless, companies that market herbal medicines exploit references to studies on mice in their promotion of mushroom capsules and throat sprays for treating all kinds of ailments. They also base their trade on the bromide of special knowledge privileged to Asian culture. This cliché should have been retired a long time ago. It is instructive to consider that life expectancy in China increased from 35 y in the 1940s, to 75 today. Many factors contribute to this phenomenal demographic change, but the introduction of Western medicine is significant (Zhou et al. 2015). Chinese people choose Western medicine when they are diagnosed with serious illnesses today.

As the Chinese embrace modern medicine, the global appetite for herbal medicines has moved in the opposite direction. Annual sales of these products account for a big chunk of the wider market for nutritional supplements that is valued at \$50 billion and seems impervious to the economic instability that has affected other business sectors (Harrison-Dunn 2014). This profitable trade provides a powerful incentive for companies to test the credulity of their customers and

unsupported assertions have come to define the medicinal mushroom business.

The bracket fungus *Ganoderma lucidum*, called lingzhi (in China) and reishi (in Japan), is one of the most popular medicinal mushrooms and has a history of use in China that is even older than the regional enthusiasm for shiitake. Lingzhi is mentioned in a 2000-year-old poem from the Han dynasty and earlier descriptions of the ‘Mushroom of Immortality’ probably refer to this species. The fungus grows on rotting wood in the wild and modern farmers raise the fungus on sawdust pellets or straw packed into plastic bags (Fig 1). Like shiitake, lingzhi is believed to have an immense range of benefits and is used to treat cancer, seizures, cardiovascular problems, and diabetes (Wachtel-Galor et al. 2011). Comprehensive reviews of the available evidence dampen enthusiasm for lingzhi, offering no support for the use of this mushroom in treating heart disease or cancer (Jin et al. 2012; Klupp et al. 2015; MSKCC 2015b). Investigators reached identical conclusions in their evaluation of the extensive studies on the little bracket fungus, *Trametes versicolor*, called turkey tail (MSKCC 2015c).

Chaga, *Inonotus obliquus*, grows as a rock-hard excrescence from birch trees. This dense structure is a sclerotium rather than a fruit body. The powdered sclerotia of chaga have been used as a folk remedy against cancer and the fungus is mentioned in Aleksandr Solzhenitsyn’s brilliant and disturbing novel ‘Cancer Ward’ (Solzhenitsyn 1969). Reviewing experiments showing the effects of chaga extracts on cultured cells, the Memorial Sloan Kettering Cancer Center in New York concluded, ‘No clinical trials have been conducted to assess chaga’s safety and efficacy for disease prevention or for the treatment of cancer, cardiovascular disease, or diabetes’ (MSKCC 2015d). Much the same applies to maitake, *Grifola frondosa*, also known as hen of the woods, which is a polypore that grows as masses of fruit bodies at the base of oak trees (MSKCC 2015e). The only thing that we can say with confidence is that extracts from shiitake, lingzhi, turkey tail, chaga, and maitake stimulate cells in tissue culture experiments.

The ascomycete *Ophiocordyceps sinensis* is another fungus associated with a range of pharmacological properties, including its effectiveness at reversing altitude sickness and erectile dysfunction. The 2013 harvest of 50 tonnes of this wild fungus in the Tibetan Autonomous Region was valued at \$1.2 billion, but scientific evidence for its diverse medicinal applications is lacking (Anon 2015; MSKCC 2015f).

With so little critical study of the benefits of medicinal mushrooms, it is alarming that the potential harm done by these natural products has been neglected. A few studies suggest that any side effects of mushroom extracts are not serious (Klupp et al. 2015), but cases of food allergy, cheilitis (inflammation of the lips), flagellate erythema, and liver damage have been reported in the literature (Yuen et al. 2004; Mukai et al. 2006; Suehiro et al. 2007; Wanmuang et al. 2007; Goikoetxea, Fernández-Benítez, Sanz 2009; Girard & Bessis 2010). Contamination of harvested mushrooms by toxigenic fungi and bacteria is another concern for consumers (Ahmad et al. 2014).

The medicinal mushroom product range of Fungi Perfecti®, a company based in Washington State, includes a variety of capsules and bottled fluids that contain extracts from the

<sup>1</sup> The Integrative Medicine links on the website of the Memorial Sloan Kettering Cancer Center in New York provide an objective analysis of hundreds of ‘herbs, botanicals, and other products’ that have purported uses in the treatment of cancer. Each webpage dedicated to a medicinal mushroom species has an up-to-date list of references to clinical studies (<https://www.mskcc.org>).



**Fig 1 – Lingzhi or reishi, *Ganoderma lucidum*, cultivated on bags filled with sawdust. Source: Ceekchean Tan, with permission.**

cultured mycelia of the fungi described in this article ([www.fungi.com](http://www.fungi.com) 2015). The use of cultures rather than fruit bodies is interesting in itself, requiring consumers to accept that the active compounds in the mushrooms are generated in a constitutive fashion so that they also present themselves in the vegetative hyphae (Bak et al. 2014; Konno et al. 2014). Putting this complication aside, the company says that ‘Healthy respiratory support’ is furnished by a mixture of reishi and other mushrooms; chaga extract covers ‘Antioxidant and DNA support’, and maitake offers the promise of helping to ‘maintain healthy blood sugar levels.’ Another group of products targets particular parts of the body, with one dietary supplement addressing ‘breast health’, another affecting the brain (‘helps to support mental clarity’), and a third dealing with the liver. The list of ingredients in these supplements includes mushrooms that support ‘immune function’ (turkey tail) and ‘hormonal and adrenal function’ (lingzhi). An asterisk accompanies every property, referencing the following manufacturer’s disclaimer: ‘These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure or prevent any disease.’ This is like making bicycles and telling customers that they are not meant to be ridden!

Fungi Perfecti is one of many companies that market medicinal mushrooms and its product claims are quite modest compared with endorsements provided by other peddlers of naturopathic medicines. If something is sold for the purpose of improving heart health, it seems reasonable that there should be evidence for its potency and that this information should be available to the public. Unlike prescription medicines, medicinal mushrooms have escaped these requirements, which means that a fruit body extract can be sold in the United States for the stated purpose of ‘comprehensive

immune support’, or just about anything else, as long as the company provides the standard disclaimer. The laws in Europe are even looser, allowing companies in the United Kingdom to market medicinal mushrooms without employing a legal rider.

The medicinal mushroom industry is aware of growing criticism and many companies have scaled back the claims in their advertisements to protect themselves from lawsuits. Until quite recently, some catalogues listed extracts from cultures of mushroom mycelia for the treatment of cancer and other serious diseases. Few companies make these claims directly today, even under the protection of the asterisk.

The majority of prescription drugs work by affecting particular biochemical pathways. The best-selling medicines for reducing cholesterol levels and blood pressure work by inhibiting single enzymes, and antibiotics disrupt specific molecular processes in bacterial cells. None of these drugs are perfect and all of them can produce unpleasant side effects. But most of them work as advertised and the manufacturers can be held liable if their products harm consumers. Horrifying errors have been made in licensing some medicines, and the pharmaceutical industry wins few awards for altruism, but, warts and all, prescription drugs are a perfect reflection of the ethos of Western medicine. Anyone whose life has been saved by antibiotic therapy must agree that the discovery and development of the  $\beta$ -lactams and later generations of antibiotics represents one of the greatest achievements of the modern era.

Pursuing this critical exploration of medicinal mushrooms, it seems very likely that mushrooms do contain compounds with important pharmacological properties. This optimism is encouraged by the deep history of interactions between fruit bodies and potentially fungivorous animals. The ability



of fruit bodies to survive damage by insects and other pests long enough to release spores suggests that they generate a range of cryptic antifeedants that interact with molecular targets in animals. Toxins and neurotropic compounds synthesized by fruit bodies are obvious examples of mushroom products with extraordinary pharmacological activities. Disregarding the dafter ideas about medicinal mushrooms, it is possible that these fungi offer a treasure trove of uncharacterized metabolites that could prove useful in treating our illnesses.

The work on ubiquitous compounds like lentinan from shiitake may be a distraction from the work of bioprospecting. Lentinan is a version of a polysaccharide that is found in all fungi. Although it is possible that there is something special about the chemical structure of lentinan,  $\beta$ -glucans extracted from any mushroom are likely to have the same medicinal properties, or lack thereof, as lentinan. Shiitake may have been adopted in China for the simple reason that it was easy to cultivate. A better model for future research on medicinal mushrooms is provided by a pair of molecules identified in lion's mane, *Hericiium erinaceus*. This is another mushroom that has been used in China for centuries. It is cultivated on sawdust pellets like lingzhi (Fig 2). This species has become associated with the unusual characteristic of promoting neurological health, which attracts a lot of attention in our time of aging populations and the spectre of Alzheimer's disease. The active compounds extracted from lion's mane are called erinacines and hericenones. Erinacines and hericenones stimulate the release of nerve growth factor in rat brains and cultured nerve cells (Ma *et al.* 2010). This effect seems worthy of additional analysis.

The worst of the advertisements for medicinal mushrooms recall the era of medical quackery that tolerated patent medicines including 'Dr. Bonker's Celebrated Egyptian Oil', which was advertised as a cure for colic and cramps in humans and farm animals, and 'Dr. Solomon's Cordial Balm of Gilead' that was praised as a treatment for venereal disease and a plethora of other maladies (Helfand 1989). Putting aside the current fantasies about mushrooms, there are good



**Fig 2 – Lion's mane, *Hericiium erinaceus*, cultivated on bags of sawdust and wood chips. Source: Nutthawit Wiangya, with permission.**

reasons for surveying the galaxy of metabolites in these organisms. After all, other kinds of fungi are the source of antibiotics old (penicillin) and new (cephalosporins), the cholesterol-lowering drug lovastatin, and cyclosporins for supporting patients after organ transplants (Watkinson, Boddy, Money 2015). Miraculous drugs may be sitting in the least prepossessing fruit bodies. And with a choice of 16000 or more species of basidiomycetes that form mushrooms, there are lots of places to look. It is time to treat anti-aging tonics made from mushrooms as a sad phase in the history of mycology and proceed with the exploration of novel compounds with the potential to change the course of our modern plagues.

## Disclaimer

Given his role as a Senior Editor of Fungal Biology, Nicholas Money had no involvement in the peer review of this article and has no access to information regarding its peer review. Full responsibility for the editorial process for this article was delegated to Geoffrey Gadd.

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