Turkey Tail or Yun zhi (Trametes versicolor, syn. Coriolus versicolor) fruiting from a downed tree in the Olympic Peninsula rainforest of the Pacific Northwest. Photo © 2001 P. Stamets

Novel Antimicrobials from mushrooms

by Paul Stamets
Although most healthcare professionals skilled in the art of botanical medicine are aware of the immune enhancing properties of certain mushrooms and other fungi, few may realize that mushrooms are rich sources of natural antibiotics. In these, the cell wall glucans are well-known for their immunomodulatory properties, but few medical practitioners are aware that many of the externalized secondary metabolites — extracellular secretions by the mycelium — combat bacteria and viruses. Additionally, the exudates from mushroom mycelia are active against protozoa such as the parasite that causes malaria, *Plasmodium falciparum,* and other microorganisms.

Fungi and animals are more closely related to one another than either is to plants, diverging from plants more than 460 million years ago. Diseases of plants typically do not afflict humans whereas diseases of fungi do. Since humans (animals) and fungi share common microbial antagonists such as *Escherichia coli, Staphylococcus aureus,* and *Pseudomonas aeruginosa,* humans can benefit from the natural defensive strategies of fungi that produce antibiotics to fight infection from microorganisms. Hence, it is not surprising our most significant anti-bacterial antibiotics have been derived from fungi.

Interestingly, some mushrooms and their components are target-specific in their antibiotic properties, whereas others have broader effects. With an increasing number of bacteria developing resistance to commercial antibiotics, such as MSRA (methicillin-resistant *S. aureus*) and *Pseudomonas* species, extracts from mushrooms hold great promise for novel medicines in modern times. The hypothesis, increasingly substantiated, is that mushrooms, especially polypores, provide a protective immunological shield against a variety of infectious diseases.

Two thousand years have passed since the first century Greek physician Dioscorides included the larch polypore (*Fomitopsis officinalis* (Villars:Fr.) Bond. & Singer, Polyporaceae; syn. *Laricifomes officinalis* (Villars:Fr.) Kotlaba & Pouzar) in his *De Materia Medica* published approximately 65 C.E. Known then as *agaricus* or *agarikon,* and later as the quinine conk, it was used as a treatment for “consumption,” a disease now known as tuberculosis. The pharmaceutical industry has been slow to explore mushrooms for antibiotic activity, in part because basidiomycetous fungi are slower growing in fermentation and less yielding compared to the mold fungi, such as the well known *Penicillium notatum,* the fungus from which Alexander Fleming discovered penicillin in 1928.

For hundreds of years, the Haida of the Queen Charlotte Islands of British Columbia and other Northwest Coast First Peoples have used shelf polypore fungi medicinally. The Haida gave *F. officinalis* a name that translates into “ghost bread” or “tree biscuit.” Shelf fungi were also used spiritually, and were found in shaman graves. Additionally, the Haida personified bracket fungus as “Fungus Man,” who, because of his ritual strength, was conscripted by Yaahl, or Raven, as a steersman for his canoe when he went to obtain female genitalia in the Haida narrative on the origin of women. The strong association of this fungus with women, in particular, and their similarity in form, suggests an underlying female archetype.

In a recent *in vitro* study, extracts of more than 75 percent of polypore mushroom species surveyed showed antimicrobial activity and...
45 percent of 204 mushroom species (polypores and gilled mushrooms alike) inhibited growth of a wide variety of microorganisms. In particular, this study showed that species in the polypore genus *Ganoderma* such as reishi (*G. lucidum* (Curtis:Fr.) P. Karst.), *G. pfeifferi* Corner, and *G. resinaceum* Boud., all of the family *Ganodermataceae*, were specifically effective against bacillus (*Bacillus subtilis*). They were not, however, effective against other bacteria, including *P. aeruginosa*, *Serratia marcescens*, *S. aureus*, *Enterococcus faecium*, and *Mycobacterium smegmatis*. Another study showed that the artist conk (*Ganoderma applanatum* (Pers.) Pat.) demonstrated antimicrobial activity against Gram-positive *Bacillus cereus*, *S. aureus*, and less activity against the Gram-negative *E. coli*, and *P. aeruginosa*. In contrast, gilled mushrooms such as *Psilocybe semilanceata* ((Fr.) Quél., *Strophariaceae*), *Pleurotus eryngii* ((De Candolle: Fr.) Quél., *Pleurotaceae*) and *Lactarius delicious* ((Fr.) S.F. Gray, *Russulaceae*) all strongly inhibited the growth of *S. aureus* bacteria.

Two other mushrooms from the family *Polyporaceae* are notable — the tinder fungus (*Fomes fomentarius* (L.:Fr.) J. Kickx.) and the birch polypore (*Piptoporus betulinus* (Fr.) P. Karst.) — both of which the famous 5,300 year old Otzi, or Ice Man, had with him when his body was discovered in the high alpine mountains on the border of Italy and Austria. Scientists believe his use of these mushrooms was likely for their antimicrobial properties and/or for tinder. The woody tinder fungus has been shown to inhibit the growth of *P. aeruginosa* and *S. marcescens*, while the birch fungus was effective against these two bacteria, and, further, exhibited strong inhibitory activity against *S. aureus*, *B. subtilis*, and *M. smegmatis*, a cousin to the pathogenic *Mycobacterium tuberculosis*. In vitro studies of 26 proprietary cultures of basidiomycetous mushrooms provided by the author found that four species “completely” inhibited *E. coli*, stopping bacterial growth well in advance of the encroaching mycelia, suggesting an extracellular antibiotic. Of these four species totally inhibiting *E. coli*, three were polypores cloned by the author from the Old Growth forests of the Pacific Northwest of North America: *Ganoderma oregonense* Murr., artist conk (*G. applanatum*), and the tinder fungus (*F. fomentarius*). A fourth polypore, turkey tail (*Trametes versicolor* (L.:Fr.) Pilát, *Polyporaceae*), did not stifle the *E. coli* remotely, but its mycelium consumed the *E. coli* upon contact. *F. fomentarius*, as well as other polypores, have anti-

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*Fomes fomentarius* is called the tinder fungus for its utility in keeping embers alive for days on end. The mushroom is dried, hollowed out, then stuffed with hot embers, and repacked. The embers continue to burn, slowly, for days. To re-ignite, the tinder fungus is uncorked, and the embers are fanned into flame. Alternately, the dried mushroom can be pounded, with the skeletal hyphae dissociating, and becoming a wooly-like mass.
antiviral properties. A highly water soluble, low cytotoxic polysaccharopeptide (PSP) isolated from *T. versicolor* has been proposed as an anti-viral agent inhibiting HIV replication. The fact that mushrooms can have both anti-viral and anti-bacterial properties, with low cytotoxicity to animalian hosts, underscores their usefulness as natural sources of medicines.

That the Ice Man had these polypore fungi as components of his mobile pharmacopoeia strongly suggests that these mushrooms provided medicine for Paleolithic Europeans, as well as a method to transport and start fire. Since autopsies of the Ice Man showed he was suffering from intestinal pathogens, as well as an arrowhead imbedded in his shoulder, his presumed use of these mushrooms appears well-warranted.

Higher concentrations of effective antibacterial agents from polypore fungi validates that this barely explored group, in particular those with a long history of folkloric use by indigenous peoples, should be carefully surveyed. The brilliantly colored chicken-of-the-woods (*Laetiporus sulphureus* (Bull.:Fr.) Murr., Polyporaceae syn. *Polyporus sulphureus* Bull.:Fr.) produces antibiotics strongly antagonistic to *S. aureus* and has been noted to consume *E. coli* upon contact. Extracts of cultures of this mushroom are currently the subject of *in vitro* scan investigations for antibacterial properties based, in part, upon a long history of folkloric use in the Russian Far East. Extracts of shiitake (*Lentinula edodes* (Berk.) Pegler, Polyporaceae) were recently reported to inhibit growth of *S. aureus* and *E. coli*, due in part to the formation of oxalic acid, a common crystal on the cellular surfaces of the mycelia of many mushroom species.

The Suay *et al.* study, by far the most extensive to date, also determined that gilled mushrooms (order Agaricales) had more species with antifungal activities than did the polypores. The submerged fermentation of the mycelium of the gilled oyster mushroom (*Pleurotus ostreatus* (Jacq.:Fr.) Kumm., Pleurotaceae) has shown effectiveness against *Aspergillus niger*, one of the most aggressive of all molds and one of the fungi causing aspergillosis lung disease, a malady that can pose a serious threat to persons with compromised immune systems. Yamabushitake (*Hericium erinaceus* (Bull.:Fr.) Pers., Hydnaceae) has also shown anti-fungal

### Cross-Index of Mushrooms and Targeted Therapeutic Effects

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### Key Codes to Medicinal Mushroom Species

- **Ab**: *Agaricus blazei* (Royal Sun Agaricus)
- **Cs**: *Cordyceps sinensis* (Cordyceps)
- **Ff**: *Fomes fomentarius* (Tinder fungus)
- **Fv**: *Flammulina velutipes* (Enoki)
- **Ga**: *Ganoderma applanatum* (Artist Conk)
- **Gf**: *Gribo frondosa* (Maitake)
- **Gl**: *Ganoderma lucidum* (Reishi)
- **Go**: *Ganoderma oregonense* (Oregon ganoderma)
- **He**: *Hericium erinaceus* (Yamabushitake)
- **Io**: *Inonotus obliquus* (Chaga)
- **Le**: *Lentinula edodes* (Shiitake)
- **Ls**: *Laetiporus sulphureus* (Chicken-of-the-Woods or Sulphur Tuft)
- **Pl**: *Phellinus linteus* (Meshimakobu)
- **Po**: *Pleurotus ostreatus* (Oyster)
- **Pu**: *Polyporus umbellatus* (Zhu ling)
- **Sc**: *Schizophyllum commune* (Split-gill Polypore or Suehirotake)
- **Tv**: *Trametes versicolor* (Turkey Tail or Yun Zhi)
activity against the mold *A. niger* and the yeast *Saccharomyces cerevisiae*. Additionally, this mushroom is effective against aggressive HeLa cells.33

Not only do the extracellular metabolites inhibit microbes, but so do the heavy molecular weight cell-wall polysaccharides. This dual source of anti-microbials enhances the effectiveness of mushrooms for medicinal purposes. The polysaccharide lentinan from shiitake and schizophyllan from the split-gill polypore (*Schizophyllum commune* (L.) Fr., *Schizophyllum*ae) inhibit *Candida albicans* and *S. aureus*.34 Lentinan is also effective in retarding *Mycobacterium tuberculosis* and *Listeria monocytogenes*35 while an extract of the mycelium was active against herpes simplex virus type 1 (HSV-1).35 Mushroom polysaccharides such as lentinan can enhance the immune system, potentiating a host-mediated response, and indirectly, but effectively, may be antimicrobial.36-38

The well-studied polysaccharide PSK from turkey tail (*T. versicolor*) also inhibits the growth of *C. albicans*.39-41 Simple hot-water extracts of the blewitt (*Lepista nuda* (Bull.) Cooke, *Tricholomataceae*), presumably rich with polysaccharides, retarded *C. albicans*.42 A small study reported that the symptoms of 12 of 13 women with chronic yeast infections were substantially alleviated after a daily consumption of maitake (*Grifola frondosa* (Dicks.:Fr.) S.F. Gray, *Polyporaceae*).43 These studies substantiate that various, novel antibiotics from many mushroom species are at play, diverse and often microbially specific.

Medicinal mushrooms have a long and rich history of use. More than 2,000 years ago, Dioscorides knew that *E. officinalis* fought “consumption;” the Ice Man had *F. fomentarius* and *P. betulinus* with him; and the healers — even shamans of Paleolithic peoples — knew and used mushrooms as powerful medicines to fight illnesses. In the world of the pre-modern shaman, spirits caused diseases, and medicinal compounds were administered to appease or treat them. Although science now knows that pathogenic microorganisms cause many diseases, it is not known whether Paleolithic peoples had an intuitive or specific knowledge of the nature of infection from microbes. Whether disease is caused by “spirits” or invisible microbes, both views hold in common an underlying cause of the unseen universe.44 In the future that shared vision may extend to using the same tools as a practical treatment for microbial infection.

The mushroom genome stands out as a virtually untapped resource for novel anti-microbials. The declining ancestral forests of the Pacific Northwest harbor novel mushroom species and strains that occur nowhere else in the world. Focusing on these fungi may lead to novel myco-medicines, hopefully before the opportunity is forever lost as old growth temperate rainforests are converted into tree plantations. A rich fungal genome is an essential component of the ecosystem, potentiating a host-mediated response, and indirectly, but effectively, may be antimicrobial.45-48

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Paul Stamets is the author of five books, including Growing Gourmet & Medicinal Mushrooms, a mushroom cultivation textbook used worldwide. On the editorial boards of the International Journal of Medicinal Mushrooms and Mushroom, the Journal, he also serves as an advisor to the Program for Integrative Medicine, University of Arizona. His company, Fungi Perfecti, purveys Certified Organic materials to grow gourmet and medicinal mushrooms for personal use or professional cultivation. He may be reached by email at <mycomedia@aol.com>, or at <www.fungi.com>.

**References**