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 mus and the second second

A lthough 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<sup>1,2</sup> and viruses.<sup>3-6</sup> Additionally, the exudates from mushroom mycelia are active against protozoa such as the parasite that causes malaria, *Plasmodium falciparum*,<sup>7,8</sup> and other microorganisms.<sup>9</sup>

Fungi and animals are more closely related to one another than either is to plants, diverging from plants more than 460 million years ago.<sup>10</sup> Diseases of plants typically do not afflict humans whereas diseases of fungi do.<sup>11</sup> 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.<sup>12</sup>

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, extracts and derivatives 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.<sup>13-15</sup>

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 *agaricum* 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,<sup>9</sup> such as the well known *Penicillium notatum*, the fungus from which Alexander Fleming discovered penicillin in 1928.<sup>16</sup>

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."<sup>17</sup> 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.<sup>17</sup> 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.<sup>18</sup> 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.<sup>19</sup> In contrast, gilled mushrooms such as Psilocybe semilanceata ((Fr.) Quél., Strophariaceae), Pleurotus eryngii ((De Candolle: Fr.) Quél., Pleurotaceae) and Lactarius delicious ((Fr.) S.F. Grav. 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.<sup>20</sup> Scientists believe his use of these mushrooms was

likely for their antimicrobial properties<sup>21</sup> and/or for tinder.<sup>22</sup> 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*.<sup>18</sup>

*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.<sup>23</sup>

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, Polypo-

elf Drawing of an argillite plate, carved by Charles Edenshaw in approx. 1890, depicting the Haida myth of the origin of women. Fungus Man (*Fomitopsis officinalis*) is paddling the canoe with Raven in the bow in search of female genitalia. Diameter = 35 cm. Redrawn from a photograph, courtesy of the Field Museum of Natural History, Chicago.



A spectacular Chicken-of-the-Woods or Sulphur Tuft (*Laetiporus sulphureus*, syn. *Polyporus sulphureus*) specimen collected from the Soleduck River drainage of the Olympic Peninsula, Washington State. Photo © 2001 by P. Stamets

raceae), 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-viral properties.<sup>6,24,25</sup> A highly water soluble, low cytotoxic polysaccharopeptide (PSP) isolated from *T. versicolor* has been proposed as an anti-viral agent inhibiting HIV replica-

tion.<sup>4</sup> The fact that mushrooms can have both anti-viral and antibacterial 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.<sup>27,28</sup> The brilliantly colored chicken-of-the-woods (*Laetiporus sulphureus* (Bull.:Fr.) Murr., Polyporaceae syn. *Polyporus sulphureus* Bull.:Fr.) produces antibiotics strongly



Dusty Yao with a 30+ year old *Fomitopsis officinalis* known to the Greeks as *agarikon*, a species now nearly extinct in western Europe. Found in an old growth forest of Washington State, this mushroom grew downward from a fallen Hemlock tree traversing a wilderness stream. Photo © 2001 P. Stamets

antagonistic to S. aureus<sup>18</sup> and has been noted to consume E. coli upon contact.23 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.<sup>29</sup> 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.30

The Suay *et al.* study,<sup>18</sup> 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*,<sup>31</sup> 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. Yamabushi-

<sup>\*</sup> *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.<sup>26</sup>

take (*Hericium erinaceus* (Bull.:Fr.) Pers., Hydnaceae) has also shown anti-fungal activity against the mold *A. niger* and the yeast *Saccharomyces cervesiae*.<sup>32</sup> Additionally, this mushroom is effective against aggressive HeLa cells.<sup>33</sup>

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., Schizophylaceae) inhibit *Candida albicans* and *S. aureus.*<sup>34</sup> Lentinan is also effective in retarding *Mycobacterium tuberculosis* and *Listeria monocytogenes*<sup>43</sup> while an extract of the mycelium was active against herpes simplex virus type 1 (HSV-1).<sup>35</sup> Mushroom polysaccharides such as lentinan can enhance the immune system, potentiating a host-mediated response, and indirectly, but effectively, may be antimicrobial.<sup>36-38</sup>

The well-studied polysaccharide PSK from turkey tail (*T. versi-color*) also inhibits the growth of *C. albicans*<sup>39-41</sup> Simple hot-water extracts of the blewitt (*Lepista nuda* (Bull.) Cooke, Tricholomat-

aceae), presumably rich with polysaccharides, retarded *C. albicans*<sup>18</sup> 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).<sup>42</sup> 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 *F. 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.<sup>17</sup> In the future that shared vision may extend to

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Ff -	Fomes fomentarius (Tind				He	Hericium erinaceus (Yamabushitake)						Pu		5					
Fv Flammulina velutipes (Enoki)					lo	1 ( 5)						Sc		Schizophyllum commune					
Ga Ganoderma applanatum (Artist			Conk)		Le	Lentinula edodes (Shiitake)							(Split-gill Polypore or Suehirotake)						
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Gl	Ganoderma lucidum (Reishi)					Woods or Sulphur Tuft) or Yun Zhi) hets, all rights reserved. Do not duplicate without permission.													

Source: Supporting reference information at <http://www.fungi.com/mycomed.html> (Below Table of Contents, select "Information about medicinal mushrooms")

using the same tools as a practical treatment for microbial infection.

The mushroom genome stands out as a virtually untapped resource for novel antimicrobials. 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 our natural heritage and may be society's greatest protection against microbial diseases. The intelligent use of these fungi can potentiate the host defenses of both people and planet. A

Acknowledgments: The author thanks Andrew Weil, M.D.; Donald Abrams, M.D.; Reinhold Poder, Ph.D.; Christopher Hobbs, L.Ac., AHG; Dusty Yao; Frank Pirano, Ph.D.; Solomon Wasser, Ph.D.; and the peer reviewers of HerbalGram.

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>.

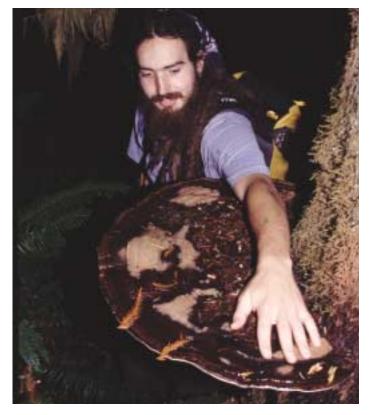
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Once thought by anthropologists to be made from wood, this "Grave Guardian," was carved from *Fomitopsis officinalis*, and "placed upon graves to protect the shaman during his long death sleep." Dims: 16cm L x 11cm W x 19cm H. Collected from Augoon, Alaska, by Emmons in 1902; now located at the American Museum of Natural History, New York (E/1044). Photo courtesy of R. Blanchette.

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Steve Cividanes with a 35-year-old Artist Conk or Kofukisaruno Koshikake (*Ganoderma applanatum*) growing from an Old Growth conifer tree in the Duckabush River drainage of the Olympic Peninsula. Photo © 2001 P. Stamets

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## Ice Man's Medicine Kit



Otzi or the Ice Man, who used mushrooms more than 5,000 years ago.

The discovery of the mummified human body known as the "Ice Man" in a glacier in the Italian Alps in September 1991 caused great excitement in the scientific world. Luigi Capasso, an anthropologist at the National Archeological Museum in Chieti, Italy, reported in *The Lancet* that the two walnut-sized lumps carried by this individual have been identified as the woody fruit of Piptoporus betulinus, a bracket fungus common in alpine and other cold environments. *P*. betulinus contains toxic resins

and an active compound, agaric acid, which are powerful purgatives and result in bouts of diarrhea. The fungus also contains oils that are toxic to metazoans and have antibiotic properties, acting against mycobacteria.

Says Dr. Capasso, "An analysis of the content of the Ice Man's rectum revealed Trichuris michiura eggs, which cause a condition that might have progressed without symptoms. more resulted abdominal pain and cyclic anemia.'



but<br/>likelyThe "wooly mass" in possession of the Ice Man.likely<br/>in<br/>in<br/>in a l<br/>cyclicMade from Fomes fomentarius, the hardened<br/>wood conk is first moistened, and then pounded<br/>until the hyphae separate. This material is highly<br/>flammable, and can be woven into garments.

Ice Man may have been aware of his intestinal parasites and fought them with possibly the only remedy then



The Birch Polypore (*Piptoporus betulinus*) is thought by many to have been used as an anti-microbial agent. Photos above © 1998 R. Poder

available in Europe measured doses of *P*. *betulinus*.

> — Barbara A. Johnston

[Wilford JN. Lessons in Iceman's Prehistoric Medicine Kit. *New York Times Science.* December 8, 1998.

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