Medicinal Lichens: The Final Frontier

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Herbalists of myriad traditions have explored the healing properties of life-forms from at least five kingdoms: Monera (bacteria)*, Protista (algae), Fungi, Plantae, and Animalia (the latter being primarily the domain of TCM practitioners, who use gecko, snake, oyster shell, various insects, and other animal-derived substances). Nevertheless, with few exceptions, herbalists have neglected an important life-form in our medicines: the symbiotic intersection of algae and fungi with a history of over 600 million years on our wayward planet —the lichens.

How little we know of this symbiotic life-form, the pioneer community on bare rock that begins the process of soil creation, creating an environment for deep-rooted organisms! Beatrix Potter attempted to introduce her research on lichens, suggesting algae's symbiotic relationship with fungi, to the Linnaean Society over 100 years ago; they wouldn't entertain the then-radical notion of symbiosis, and certainly would never allow a woman to present a technical paper before this solidly male organization. The Linnaean Society posthumously apologized to Ms. Potter about 10 years ago. (Rejected but thankfully not dejected, Beatrix gave us Peter Rabbit and friends.)

As we learn more about the medicinal properties of the lichens, I believe this oft-overlooked life-form will achieve greater prominence in our herbal pharmacopoeia. This article discusses recent scientific research indicating important uses for well-known lichens (*Cetraria islandica* and *Usnea spp.*) as well as less familiar species (*Flavoparmelia caperata* and *Lobaria pulmonaria*).

**Recall the ancient Nubians' crafting of medicinal beers, rich in tetracycline from the soil-borne Streptomyces bacteria found on the brewers' grain (Nelson et al 2010). This medicine was given to children as well as adults.*

Cetraria islandica, C. spp. **The Iceland Mosses**

Any discussion of edible and medicinal lichens must begin with *Cetraria islandica* and allied *Cetraria* species, better known as the Iceland mosses. These include *Cetraria chlorophylla* and *Cetraria platyphylla*, growing here on the northern California coast at low altitude. The common name throws us a curve ball, as these are not mosses at all. Mosses are true plants, albeit primitive, without vascular tissue, bearing spores but no seeds. Nor are these lichens necessarily from Iceland or points north in the Arctic. Rather, these are temperate and arctic lichens, with various species growing throughout the Northern Hemisphere. *C. islandica* itself can be found throughout northern Canada and Alaska, into the southern Rockies, New England, and south into Appalachia; and on to Great Britain, Ireland, Scandinavia, and of course, Iceland. This is the primary winter forage of caribou, and is a staple in

Iceland moss, "C*etraria islandica* 290808" by Bernd Haynold, CC BY SA 3.0

northern latitudes, being mixed with flour to bake bread or make porridge.

As medicine, *Cetraria* fills an important niche. It's a wonderful pectoral, allaying cough, and soothing sore throat and bronchial irritation. Its polysaccharides provide a strong anti-microbial, anti-inflammatory, and immune-stimulating/immune-modulating remedy (Freysdottir et al 2008; Kramer et al 1995).

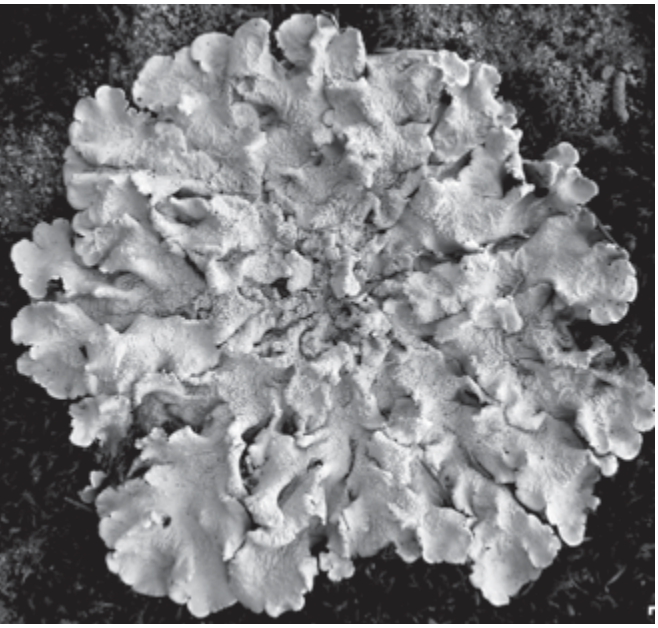
Cetraria is a great Yin tonic, replenishing fluids and vital substance for those recuperating from chronic or serious illness, yet addresses chronic diarrhea via an atypical astringency. It improves digestion, stimulates appetite, and allays dyspepsia. Its bitter antibiotic principle makes it well suited to inclusion in formulae treating *Helicobactor pylori* (Ingolfsdottir et al 1997).

Cetraria was an important ingredient in HIV+/AIDS formulas I created in the early 1980s. It was one of the herbs that showed promise as an antiviral in laboratory and clinical studies, and had demonstrated efficacy in reducing replication of the AIDS virus (Pengsuparp et al 1995). Protocetraric, cetraric, lichenostearic, and other organic acids are the bitter components responsible for the Damp Heat-clearing, anti-microbial activity of this lichen (Igoli et al 2014). *Cetraria* was also a component of formulae I made for AIDS patients with MAI (*Mycobacterium avium intracellulare* complex, also known as MAC), an antibiotic-resistant close relative of *Mycobacterium tuberculosis*. That MAI, an opportunistic infection once most commonly seen in patients with severe immune deficiencies, is now seen in patients without HIV or cancer, may mean that either MAI is becoming more virulent, or people are becoming more immuno-compromised. MAI has been found lurking in the majority of shower heads tested (Feazel et al 2009)! I'm treating patients experiencing this condition with increasing frequency. As with many herbs, concern over such

Lichens: Paving the Way for Life on Earth

The first life-forms of planet Earth evolved in the sea. Formation of landmasses challenged these primitive oceanic organisms to adapt to this dry new environment. First came the fungi, emerging from their marine environment to take up residence at the terrestrial edge of fresh and salt water, utilizing dead material as a food source. Next came the algae, developing thickened cell walls as a vital adaptation to avoid dessication on dry land. Then something remarkable happened: the two life-forms teamed up to create a composite organism. Fungi, able to secrete acid to dissolve bare rock and initiate soil formation, needed a partner to provide energy; photosynthetic algae provided that sustenance. In return, fungi gave algae protection, as well as a continuous source of water via fungal water storage during dry spells, and a constant supply of minerals. The product of this symbiosis is the organism we commonly know as "lichen."

And oh how they do thrive together! Over 25,000 free living fungal species have allied with algae and cyanobacteria to form lichen. Elaborating colorful terpenoids as anti-oxidants, the fungus protects itself and the algae or bacteria so well that this partnership ages slowly; lichens can attain an age of 9,000 years living in harsh environments (Liebes et al 1998). Over time, lichens dissolve rock, and in concert with rain, freeze and thaw, sunlight, and oxygen, begin to render that which makes our lives possible: the soil. So when we think of "be fruitful and multiply," we can thank this ancient pioneer community from two divergent kingdoms of life.



"*Flavoparmelia caperata* 240112" (left) by Jason Hollinger, CC BY-SA 3.0.

pharmacodynamic and pharmacokinetic interactions as induction and suppression of cytochrome P450 (CYP) hepatic enzymes, P-Glycoprotein (P-gp), and organic anion-transporting polypeptides (OATPs), and receptor binding, led to discontinuation of these formulae with the advent of the pharmaceutical "triple cocktail."

Flavoparmelia caperata The Common Green Shield Lichen (Parmeliaceae family)

Despite the word "common" being part of its name, this is a lesser known, perhaps even downright obscure lichen, likely one few botanists or herbalists would recognize in the field. (Depending upon its habitat, *Flavoparmelia* can vary from pale yellow-green, to blue-gray-green, to bright lime green. For a botanical description of this lichen, visit http://eol.org/data_objects/10547609.) Despite its low profile, it is a remarkable medicine, with great potential for incorporation into our herbal repertoire.

Flavoparmelia caperata brings the best of *Cetraria* and *Usnea/Lobaria*, containing both protocetraric acid and usnic acid, the two predominant phenolic compounds of their respective genera. Additional active compounds include atranorin and caperatic acid. These powerful antioxidant compounds scavenge free radicals and superoxide anions, and have anticancer activity against melanoma and colon carcinoma, and antimicrobial activity (Manojlović et al 2012).

Usnea spp.: Pharmacognosy, Clinical Uses, and Toxicology

A global perspective of the genus *Usnea* requires taking a step back, and observing the order Lecanorales, suborder Lecanorineae, families Lecanoriaceae and Parmeliaceae (the latter including the genera *Usnea* and *Cetraria*). Humans have a long history of economic usage of lichens in this suborder. *Lecanora esculenta* is believed to be the Biblical "manna from heaven" (Exodus 16) as biblical quantities of this edible lichen can blow upon the wind, depositing thick mats in Middle Eastern deserts. In times of famine, *Lecanora* provides sustenance by way of carbohydrate calories and some mineral and amino-acid nutrients until a source of protein can be secured. Among genera in the suborder Lecanorineae, families Parmeliaceae, Ramalinaceae, and Lecanoriaceae, we find that many species of *Cladonia, Lecanora, Ramalina, Evernia, Parmelia*,

Usnea longissima (left) has been categorized as rare and endangered in some localities of northern California, Oregon, and Washington state. Unless you know this species is locally common and widespread in your area, do not harvest! It's best to walk with a lichenologist to get an overview of lichen ecology, morphology, and taxonomy. Note that all *Usnea spp*. have a tri-layer structure: an axis which is elastic (critical for keying out), and a cortex and medulla. If the lichen has a lacy, doily-like structure, it's likely a *Ramalina* or allied genus, and while some of these do contain usnic acid and have the yellow coloration, they have no history of medicinal use, and would be suspect as medicine. *Photo by Brian Weissbuch.*

and *Alectoria* contain usnic acid.

Of these, *Usnea spp*. (and also *Lobaria pulmonaria*, of the order Peltigerales, family Lobariaceae, discussed below) are uniquely suited to medicinal use, as all *Usnea* species contain usnic acid. Many *Usnea spp.* also contain structurally similar diffractaic and barbatic acids, and these two genera are relatively non-toxic, compared to other usnic acid-containing lichen genera. All three organic acids have a similar potent antibiotic effect against Gram-positive bacteria, including *Mycobacterium tuberculosis*, *Mycobacterium avium-intracellulare* complex (MAI, MAC), *Staphylococcus* (including Methicillin-resistant *S. aureus*), *Streptococcus*, and Vancomycin-resistant *Enterococcus* (Honda et al 2010; Gupta et al 2012; Srivastava et al 2013; Cansaran et al 2006; Elo, Matikainen and Pelttari 2007) . They also exhibit antiviral (Sokolov et al 2012), antiprotozoal (Lauinger et al 2013, De Carvalho et al 2005), anti-mitotic (Einarsdottir et al 2010, Brisdelli et al 2013), and anti-inflammatory activity (Su et al 2014).

The most common traditional medicinal application for *Usnea spp*. is in compound herbal formulae for treatment of cystitis, an infection of the urinary bladder. Over 80 percent of urinary tract infections are caused by *E. coli*, with *Staphylococcus* responsible for most of the remainder (Nicolle 2008). Bladder infections are a notable problem for women due to their shorter urethra located more closely to the anus, relative to men. Also, catheterized patients are at high risk for urethritis and cystitis. Antibiotics used to treat catheters lose effectiveness rapidly, and are incapable of penetrating biofilms.

What are "biofilms"? Many pathogenic bacteria, including those above, congregate and secrete an extra-cellular matrix of polysaccharide polymers, engulfing these communities of bacteria in a biofilm that renders enclosed bacteria impervious to attack by our immune system and pharmaceutical antibiotics. Pathogenic bacteria encapsulated in biofilms cause diverse infections, including sinusitis, cystitis, endocarditis, otitis media, and gingivitis, as well as blood-borne spirochetal infections such as *Borrelia* (Lyme disease).

Chinese and Western herbal formulae utilizing *Usnea spp.* (*Sung Luo* in Mandarin) are noted to treat cystitis rapidly and effectively. Indeed, under the Scanning Tunneling Microscope, usnic acid is seen dissolving these biofilms and killing the pathogenic bacteria therein, validating an empirical usage dating back over 3,000 years (Francolini et al 2004).

Venous catheters also present serious risk of systemic infection. The Centers for Disease Control and Prevention has estimated that approximately 80,000 central venous catheter-associated bloodstream infections occur in intensive care units each year in the United States (CDC 2001). Recent studies have shown that a wide range of persistent catheter-related infections may be related to the ability of infectious bacteria and fungi to form biofilms (Nicolle 2014; Ye et al 2014).

Pharmaceutical companies are actively researching potential medications that attack bacterial biofilms. To date, they have been unsuccessful. Usnic acid itself, taken out of its natural matrix of constituents in *Usnea spp.* and *Lobaria pulmonaria*, is too toxic for human use, causing acute liver injury (chemical-induced hepatitis) (U.S. National Libarary of Medicine 2013, Moreira et al 2013, Sahu et al 2012). Because U.S. pharmaceutical companies cannot patent a whole "herb," they will not develop a whole *Usnea* extract. In Europe and Asia, many *Usnea spp.*-based herbal formulae are used within the medical system. For example, in Germany, an M.D. would likely prescribe an *Usnea*-based herb formula for cystitis or other infections.

However, this is not to say that "more is better" when it comes to this powerful medicinal. I strongly advise patients against self-medication with *Usnea spp.*, especially for serious and/or chronic infections. In traditional medicine, *Usnea* is always prescribed within the context of an herbal formula utilizing other herbs with complementary, synergistic, and protective functions. Taken as a single herb, the quantity of *Usnea* required to adequately treat an infection would be a toxic dosage. I generally include *Usnea* as only 8 to 10 percent of a formula by volume. *Usnea* assists with antibacterial function, but its primary use is to destroy the polysaccharide biofilm polymers. Also, usnic acid and related compounds are relatively

Lichen Morphology

Lichens are characterized by their gross morphological characteristics, and most are placed in one of three broad categories:

Crustose lichens adhere tightly to rock, bark, leaves, and other surfaces, and are frequently very thin, hard, dry, and inflexible.

Foliose lichens, of which *Flavoparmelia*, *Cetraria*, and *Lobaria* are examples, have "leaf-like" thalli, and are more loosely attached to their substrate.

Fruticose lichens, of which *Usnea* is an example, have branching thalli that frequently hang loosely from their substrate.

Lichen morphology engenders a vocabulary unique to this group, with its diverse reproductive and adaptive structures.

insoluble in boiling water, so alcoholic mentstruum-based fluid extracts are the only effective delivery system for this herb.

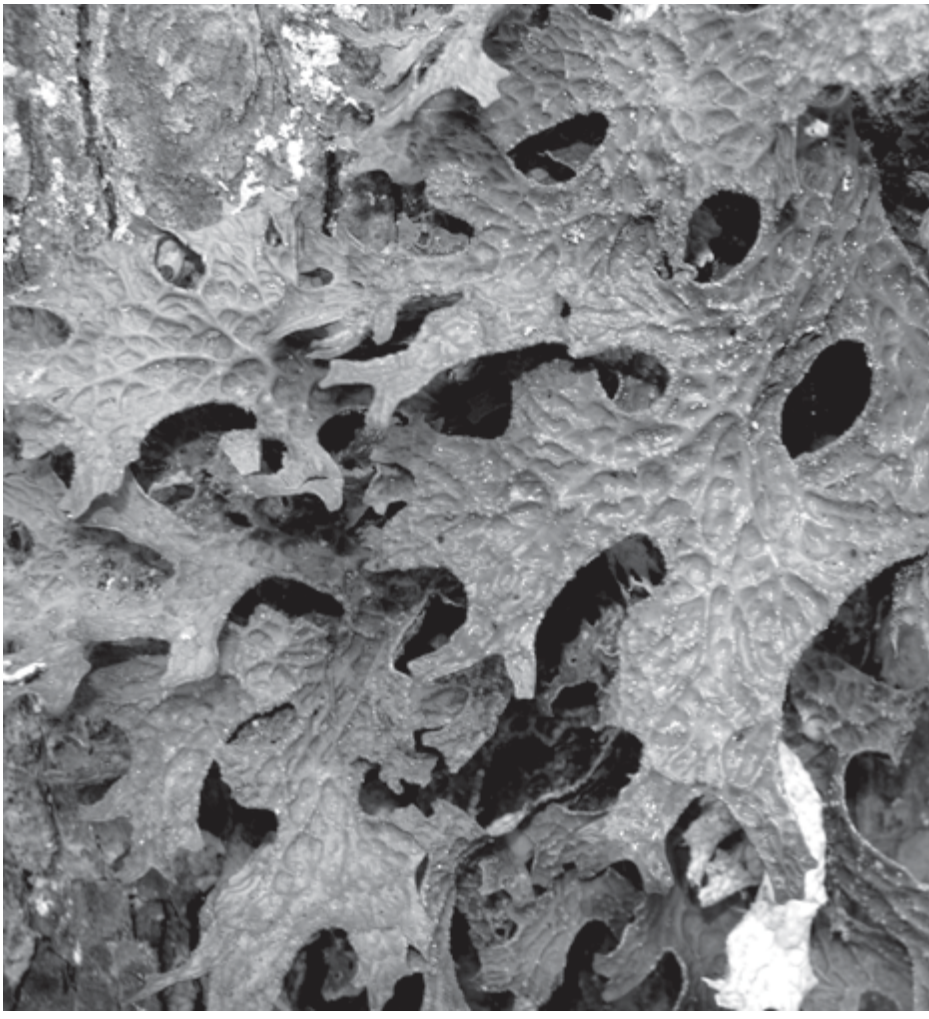
Additionally, the keen eye of a biologist or naturalist versed in lichen taxonomy is required for identification of this genus. The closely related *Letharia vulpina* (wolf lichen) and other yellow fruticose species in the Parmeliaceae family containing the very toxic compound vulpinic acid were once used in Europe to poison wolves. As both usnic and vulpinic acids are bitter yellow compounds, knowledge of macroscopic lichen morphology is required for unambiguous identification. After examining the two side by side, accurate identification is easy.

Lobaria pulmonaria
Lungwort Lichen (Order-Peltigerales, Family-Lobariaceae)

Of all the herbs with doctrine of signature coherences, *Lobaria* is surely the empress. Its affinity for the lungs is as legendary as its resemblance to lung tissue. I've used it confidently in formulae for treating simple bacterial infections to the extremes of "walking pneumonia" and valley fever. Like *Usnea*, it is taken in relatively low doses with herbs to nourish and protect the Yin (e.g., *Cetraria islandica*). However, recent research has brought renewed attention to this amazing herb.

Neurodegenerative disease-associated prion protein is the probable etiological agent of transmissible spongiform encephalopathies (TSEs), better known as mad cow disease, Creutzfeldt-Jacob disease, or PrP(TSE). This "misfolded isoform" protein is extremely resistant to degradation by autoclaving and disinfectants, and is persistent in the environment (Johnson et al 2011). Three lichen extracts, including *Lobaria pulmonaria*, are the first substances found to inactivate TSE proteins via lichen protease enzymes (Rodriguez, Bennett and Johnson 2012). Tests performed upon infected hamsters, mice, and deer demonstrated clinical efficacy for *Lobaria* extracts (Johnson et al 2011). Given the extreme danger posed by TSEs in surgical settings (even autoclaved surgical instruments have been implicated as infective agents!), this discovery provides a possible life-saving remedy.

Further studies indicate that it is the mycobiont (fungal portion of the lichen) that provides this prionicidal actitivity, rather than the photobionts. *Dictyochloropsis reticulata* is the algal photobiont, and *Nostoc spp.* is the cyanobacterial photobiont. (Johnson et al 2011). This comes as no surprise to biologists familiar with the origin of fungi. When I was in grad school, mycology (the study of fungi) was a unit within the botany department. We now know that fungi are not at all related to plants. Animals and fungi share a common ancestor, and we humans share 70 percent of the same DNA with our fungal friends. Fungi are vulnerable to many of the same infective and pro-inflammatory agents that we are, and have, over the last 600 million years or so, elaborated a formidable defense structure to prevent microbial and inflammatory/oxidative attack. Due to our similar vulnerabilities, we benefit by utilizing the substances that various



Lobaria pulmonaria by Bernd Haynold, CC BY SA 3.0

fungi have created for their own defense.

The astute biologist will realize that from the beginning of this article, I have neglected a most important kingdom or domain of life: the Archaea. These are the pre-bacterial organisms known as thermophiles and extremophiles, living at undersea volcanic vents and in geysers, as well as glacial ice, and utilizing atypical energetic pathways (e.g., methane) for nourishment. In fact, we now know that in addition to our intestinal bacteria, we have symbiotic intestinal archaea (methanogens) that utilize the methane produced during fermentative digestion. Archaea also live in our belly buttons, likely there since the cord was cut at birth. Researchers now believe that going back even further than our divergence from the fungi, we share the common ancestor of Archaea, as we have chemical pathways in our cells that resemble this ancient lineage rather than the more modern bacterial lineage. Of course, with horizontal gene transfer, all bets are off...

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