CHAPTER 2-1

MEDICAL USES: MEDICAL CONDITIONS

TABLE OF CONTENTS

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Figure 1. Bryophytes and other herbs on sale in a Yunnan, China, market. The newspaper has the contents of a prescription that is under preparation, including ***Rhodobryum***. Photo courtesy of Eric Harris.

New Medical Sources

One of the reasons for exploring biological compounds in bryophytes is the potential for medical use. It's a scary thought, but substances we know as pesticides and fungicides that discourage insect feeding and bacterial or fungal attack are likely to have antibiotic properties that could prove useful in treating human disease. We know bryophytes contain numerous potentially useful compounds, including oligosaccharides, polysaccharides, sugar alcohols, amino acids, fatty acids, aliphatic compounds, phenylquinones, and aromatic and phenolic substances, but much work remains to link medical effects with specific bryophyte species or compounds (Pant & Tewari 1990). For this reason, traditional uses named here should be viewed with caution because we don't know the dosage needed, side effects, or other precautions that need to be taken. We do know that traditional medicines that may be safe for one race of people may not be for others. After all, those alive today are descendents of survivors. And diet may affect the ways that some of these compounds work, causing geographic differences.

Hansen (1994) suggested that fatty acids produced by members of **Hypnaceae** (Figure 70) and **Brachytheciaceae** (Figure 2) produce high levels of arachidonic acid and EPA and might be used for "producing unique and highly priced compounds for pharmaceutical industry." Mosses contain both n-3 (EPA, 18:3) and n-6 (arachidonic acid, DHGLA, 18:2) fatty acids. Gellerman *et al*. found that ***Mnium*** (Figure 3), ***Polytrichum*** (Figure 4), and ***Marchantia*** (Figure 5) have highly unsaturated lipids. Thus, the potential is real – we need to explore it.

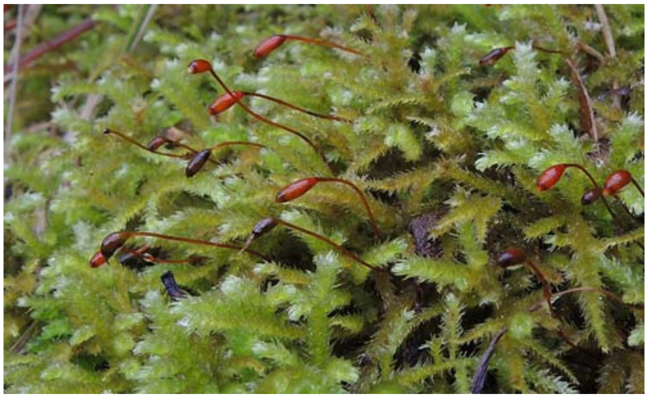

Figure 2. ***Eurhynchium striatum***, a member of the **Brachytheciaceae** with a high content of arachidonic acid. Photo by Michael Lüth, with permission.

Figure 3. ***Mnium stellare***. The genus ***Mnium*** is known to have highly unsaturated lipids. Photo by Michael Lüth, with permission.

Figure 4. ***Polytrichum commune*** is used in China to reduce inflammation and fever, as well as to treat the common cold and kidney and gallstones. Photo by Michael Lüth, with permission.

Asakawa has spent his career studying the secondary compounds of liverworts. In this time he has found that some of them produce a number of terpenoids, aromatic compounds, and acetogenins, several of which show interesting biological activity (Asakawa 2008; Asakawa *et al*. 2013). Among these are agents that cause allergenic contact dermatitis, insecticides, insect antifeedants, cytotoxins, piscicides, muscle relaxants, plant growth regulators, anti-HIV agents, DNA polymerase β inhibitory compounds, anti-obesity compounds, neurotrophic agents, NO production inhibitors, antimicrobial agents, and antifungal agents. However, few of these have reached application by the medical practitioners.

Figure 5. ***Marchantia polymorpha*** thallus illustrating the surface that the Chinese considered to resemble the cross section of the liver. Photo by Michael Lüth, with permission.

Bryophytes can be cultured to produce medical compounds. Using knockout genes, we cannot only sequence the genome of bryophytes, but also determine the function of individual genes. It is also easier to transplant genes into the bryophyte genome than into tracheophytes. This is possible because the bryophyte spends an extended period of time as a leafy plant with only one set of chromosomes. The model system ***Physcomitrella patens*** (Figure 6, Figure 7) is superior to the traditional mammalian production hosts and cultures can even be stored frozen for ten years, then begin producing again when thawed and cultured (Beike *et al*. 2010).

Figure 6. ***Physcomitrella patens*** growing in the wild. Photo by Michael Lüth, with permission.

Figure 7. ***Physcomitrella patens*** growing on agar plates. Photo by Sabisteb, through Creative Commons.

Herbal Medicines

Not surprisingly, herbal medicines of China (Figure 1), India, and Native Americans include bryophytes (Harris 2008). In China, 63 species are known to have medicinal uses. In India, 22 species are known to have medicinal use, but only in the Himalayas. Ayurvedic (holistic medicine of India, over 3000 years old) texts report little or no use. Native Americans have used bryophytes for drugs, fibers, and clothing (University of Michigan, Dearborn, 2003). The mosses ***Calymperes*** (Figure 8), ***Campylopus*** (Figure 9), and ***Sphagnum*** (Figure 10) have been used for medicinal purposes in Malaysia (Burkill 1966; Tan 2003). ***Timmiella*** (Figure 11) has been used medicinally in Egypt (Harris 2008).

Figure 8. ***Calymperes erosum***, considered a medicinal plant in Malaysia. Photo by Li Zhang, with permission.

Figure 9. ***Campylopus introflexus***, considered a medicinal plant in Malaysia. Photo by Michael Lüth, with permission.

Native Americans have long traditions of using bryophytes for medical purposes. The languages of the natives of the central coast of British Columbia include words for ***Plagiomnium insigne*** (Figure 12) that mean tiny, tiny little trees in Oweekeno; this moss is important to them for medicinal use (Turner 1973; Compton 1993; Harris 2008). The users recognize two different forms of the species (Compton 1993; Harris 2008). Those that grow under Douglas fir (*Pseudotsuga menziesii*; Figure 13) are less effective medically than those that grow under spruce (*Picea*; Figure 14).

Figure 10. ***Sphagnum centrale***, considered a medicinal plant in Malaysia. Photo courtesy of Betsy St. Pierre.

Figure 11. ***Timmiella barbuloides*** with capsules. A species of ***Timmiella*** is used for medicine in Egypt. Photo by Michael Lüth, with permission.

Figure 12. ***Plagiomnium insigne*** with capsules, a species used by natives in British Columbia, Canada. Photo from Botany Website, UBC, with permission.

Figure 13. ***Pseudotsuga menziesii*** forest in snow, habitat for ***Plagiomnium insigne***. Photo by Dave Powell, USDA, through Creative Commons.

Figure 14. ***Picea sitchensis*** forest floor. ***Plagiomnium insigne*** produces more potent medicine in western spruce forests compared to those of Douglas fir. Photo by Henry Hartley, through Creative Commons.

The Doctrine of Signatures (based on the concept that God provided visual cues through the characteristics of the plants), highly developed during the European Renaissance, has dictated the use of a variety of bryophytes, especially liverworts, in herbal medicine. For example, liverworts resemble the liver, so they have been used to treat liver ailments.

Asakawa (2015) names ***Bryum argenteum*** (Figure 47) as an antibacterial moss.

Not only do a number of bryophytes serve as medicinal herbs, but ***Sphagnum*** (Figure 10) has been used to deliver the medicine by using it to make a suppository (Stevenson 2012).

Medicinal Teas

Johannes Enroth (Bryonet 28 January 2009) visited the Yucatan, Mexico, and discovered mosses in use there. The local guide was a "coba-maya" who was familiar with uses of plants. He reported a medical tea made from a moss growing on tree trunks. Enroth collected a bit and identified the moss as ***Sematophyllum adnatum*** (Figure 15).

Figure 15. ***Sematophyllum adnatum***, a moss used to make a medicinal tea in the Yucatan of Mexico. Photo by Bob Klips, with permission.

The moss ***Rhodobryum*** (Figure 1) is used to make a medicinal tea (Franquemont *et al.* 1990; Harris 2008), and as you will see below, it has tested medicinal properties useful for several medical conditions. ***Polytrichum commune*** (Figure 4) has been boiled to make a tea for treating colds (Gulabani 1974; Beike *et al*. 2010).

Liver Ailments

The most widely known use of bryophytes determined by its appearance is that of ***Marchantia polymorpha*** (Figure 5) to treat liver and other ailments; the surface suggests the cross section of liver (Miller & Miller 1979). In China, it is still used to treat the jaundice of hepatitis and as an external cure to reduce inflammation (Hu 1987) and has gained the reputation of cooling and cleansing the liver (Bland 1971). But it has also been used for liver problems in Europe (Thieret 1956) and South America (Garcia Barriga 1992; Roig y Mesa 1945).

Based on the Doctrine of Signatures, it is not surprising that ***Marchantia polymorpha*** (Figure 5) is not the only species in that genus to be used to treat liver ailments. In India, ***M. convoluta*** is also used (Rao 2009; Chandra *et al*. 2017). And ***Marchantia palacea*** (Figure 16) is used to treat hepatitis (Sabovljević *et al*. 2011; Chandra *et al*. 2017).

Figure 16. ***Marchantia paleacea***, a liverwort used to treat hepatitis in India. Photo by Jan-Peter Frahm, with permission.

Perhaps there is more wisdom in these ancient remedies than at first appears. Asakawa (2012) found that some of the isolated terpenoids from liverworts had anti-HIV inhibitory properties. ***Fissidens nobilis*** (Figure 48) is useful for jaundice (Asakawa 2015).

Stones

In the western Himalayans, native people use ***Wiesnerella denudata*** (Figure 17) to treat gall stones (Kumar *et al*. 2007). In China, ***Polytrichum commune*** (Figure 4) is boiled to make a tea that reputedly helps to dissolve stones of the kidney and gall bladder (Gulabani 1974; Chandra *et al*. 2017). Asakawa (2015) reported that ***Conocephalum conicum*** (Figure 18) is useful in treating gallstones.

Figure 17. ***Wiesnerella denudata***, a liverwort used to treat gall stones in the western Himalayas. Photo by Jan-Peter Frahm, with permission.

Figure 18. Thallose liverwort, ***Conocephalum conicum***, one of the thallose liverworts used to treat gallstones, bites, boils, burns, cuts, eczema, and wounds. Photo by Janice Glime.

Ringworm

Riccia spp. (Figure 19) were ground to a paste and used in the Himalayas to treat ringworm (*Tinea* spp., a fungus; Figure 20) because of the resemblance of the growth habit of those liverworts to the rings made by the fungus (Shirsat 2008; Chandra *et al*. 2017). Recent tests on ***Riccia fluitans*** (Figure 21) from Florida indicated no ability to inhibit growth of bacteria [*Pseudomonas aeruginosa* (Figure 22), *Staphylococcus aureus* (Figure 23)] or yeast (*Candida albicans*; Figure 24) (Pates & Madsen 1955). Might ***Riccia*** species do any better with ringworm?

Figure 19. Circular formations of ***Riccia*** species, such as this ***Riccia austinii***, suggested their use for curing ringworm, according to the Doctrine of Signatures. Photo by Janice Glime.

Figure 20. ***Tinea*** (ringworm) on arm. Photo by Grook Da Oger, through Creative Commons.

Figure 21. ***Riccia fluitans***, a floating aquatic liverwort that seems to lack antibiotic properties. Photo by Jan-Peter Frahm, with permission.

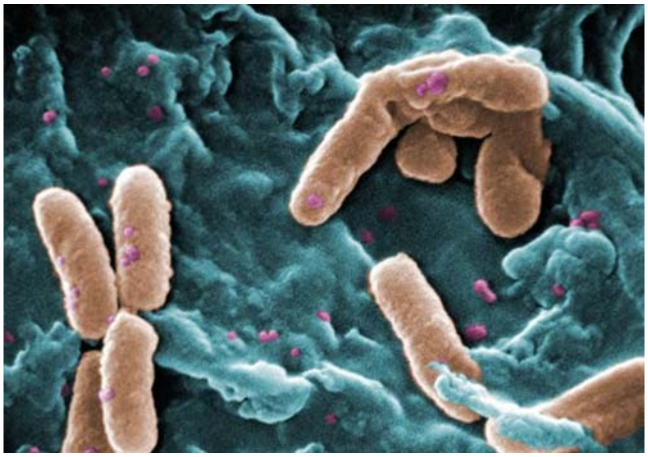

Figure 22. SEM of ***Pseudomonas aeruginosa***, a bacterial species that is not inhibited by ***Riccia fluitans***. Photo by Janice Haney Carr, through Creative Commons.

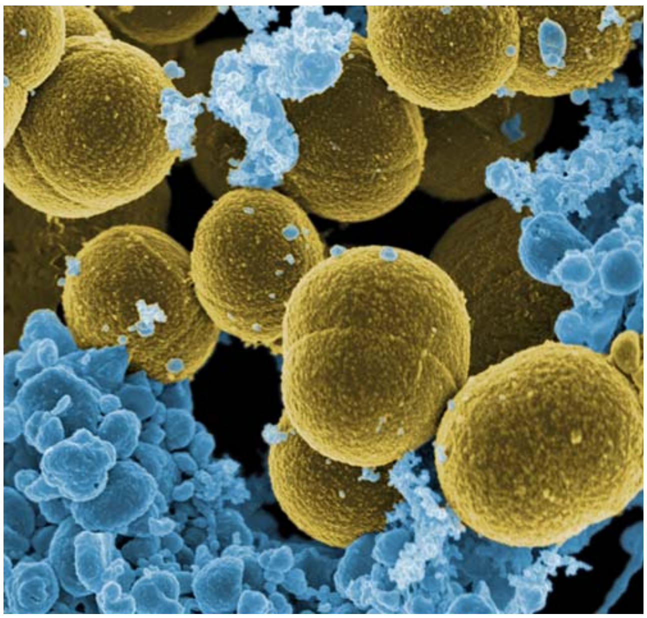

Figure 23. SEM of *Staphylococcus aureus*, a bacterium that is not inhibited by ***Riccia fluitans***. Photo by NIAID, through Creative Commons.

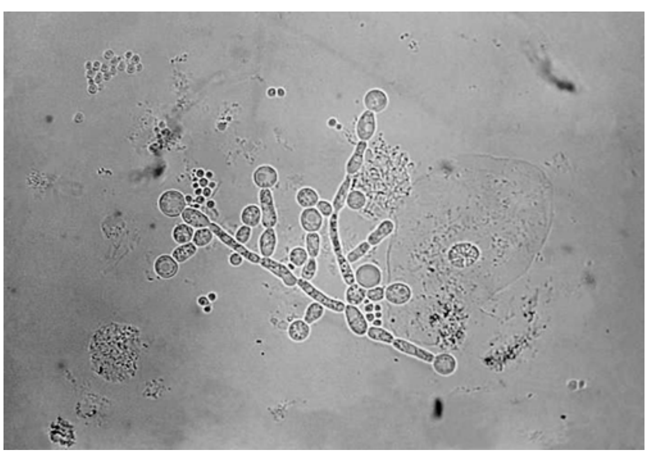

Figure 24. *Candida albicans*, a yeast species that is inhibited by extracts of the liverworts ***Conocephalum conicum***, ***Marchantia polymorpha***, and ***Plagiochasma appendiculatum***, but not ***Riccia fluitans***. Photo from Public Health Image Library, through public domain.

Heart, Blood, and Cardiovascular Medicine

In China, 30-40 species of bryophytes may be found on the shelves of the local pharmacist (Ding 1982). Among the more common ones are ***Rhodobryum giganteum*** (Figure 25, Figure 30) and ***R. roseum*** (Figure 26), used to treat nervous prostration and cardio-vascular diseases, the latter being a use that may have scientific merit (Wu 1982). Among these uses is the treatment of hypertension (high blood pressure) with ***R. giganteum*** (Wu 1977; Pant 1998; Asakawa 2007b, 2015; Chandra *et al*. 2017).

Figure 25. ***Rhodobryum giganteum***, a species widely used medicinally in Yunnan, China. Photo by David Long, with permission.

Figure 26. ***Rhodobryum roseum***, a species that is used to treat nervous prostration and cardio-vascular diseases in China. Photo by Michael Lüth, with permission.

In 1977, Wu reported the use of ***Rhodobryum giganteum*** (Figure 25, Figure 30) to cure cardiovascular disease in China. Chinese scientists have attempted to demonstrate the basis for the healing powers of some of the mosses, including ***Rhodobryum giganteum***, used in ancient treatments in China (Ding 1982). Going directly to the peasants in east Szechuan, the staff of the Laboratory of the Fourth Medical School in China learned about mosses used by the peasants (Wu 1982). Through clinical research, they successfully demonstrated that an ether extract of ***Rhodobryum giganteum***, used by these peasants to cure angina, contains volatile oils, lactones, and amino acids; when given to white mice, the extract actually reduced the oxygen resistance by increasing the rate of flow in the aorta by over 30%. Is it time to replace ACE inhibitors, calcium channel blockers, and beta blockers and their side effects?

The term *Hui Xin Cao* in Yunnan refers to the medical effect of ***Rhodobryum*** species, meaning "return-the-heart-herb" (Harris 2008). The Chinese use ***R. roseum*** (Figure 26), ***R. giganteum*** (Figure 25, Figure 30), and ***R. ontariense*** (Figure 27). Unfortunately, the term *Hui Xin Cao* refers to other plants as well (remember that the name refers to its use, not its morphology), including the moss ***Pogonatum cirratum*** (Figure 28) and the shrub *Ledum* (Figure 29). Members of the genus ***Rhodobryum*** are used in Yunnan for minor heart problems (Harris & Yang 2009). Usage depends on location, not on gender, occupation, or ethnicity. And its use also occurs in both rural areas and in traditional Chinese medicine hospitals and medical colleges.

Figure 27. ***Rhodobryum ontariense***, a species used in China to treat the heart. Photo by Janice Glime.

Figure 28. ***Pogonatum cirratum***, a species used in China to treat the heart. Photo by Li Zhang, with permission.

These reports of traditional usage were supported by a number of studies on ***Rhodobryum. giganteum*** (Figure 25, Figure 30) that demonstrated its usefulness in treating cardiovascular problems and illustrating the physiological mechanisms involved (Yu & Ma 1993; Yu *et al.* 1994, 1995; Yan *et al.* 1998; Lei *et al.* 2001a, b; Gao *et al.* 2004; Zhou *et al.* 2004; Wang *et al.* 2005; Dai *et al.* 2006; Hu *et al.* 2009). Pejin *et al.* (2011a, 2012c) reported on the antihypertensive effect of ***R. ontariense*** (Figure 27) *in vivo* and attempted to find the mechanism used by ***R. ontariense*** in controlling hypertension (Pejin *et al.* 2012e). They were able to eliminate any effect on human erythrocyte membrane fluidity, there was no reservoir of nitric oxide in the blood, and there was only low ABTS cation scavenging activity and little content of phenolic contents. The actual mechanism remains elusive.

Figure 29. ***Ledum*** sp., a shrub with the same Chinese name as ***Pogonatum cirratum*** and several species of ***Rhodobryum*** because they are all used to treat heart problems. Photo by Meggar, through Creative Commons.

Masanobu Higuchi (Bryonet, 20 November 2006) reports that when he stayed in Zhong Dian, northwestern Yunnan, China, in 1994, he saw local people selling herbal medicines by the roadside. Among these was the moss ***Rhodobryum giganteum*** (Figure 25, Figure 30) in dry condition, a traditional Tibetan medicine for heart trouble. It was selling for US $0.50 per 10g. The same species is used in the Himalayas as a neurologial and cardiac activant (Kumar *et al.* 2007).

As already noted, their use as medical plants has made ***Rhodobryum*** species the subject of a number of biochemical studies, revealing a variety of biochemical constituents in ***R. ontariense*** (Figure 27) [fatty acids 9,12,15-octadecatrien-6-ynoic and α-linolenic acid, having known heart protective activity (Pejin *et al.* 2012a); 1-kestose, a "health promoter" (Pejin *et al.* 2012b); short-chain fructooligosaccharides, well known as prebiotics (Pejin *et al.* 2012e). Thirteen essential oils have been identified in ***R. ontariense*** (Pejin *et al.* 2011b), but their roles in efficacy of Chinese medicine still remain to be determined.

But wait! Mosses are known accumulators of heavy metals, and we know that high amounts of these are dangerous to human health. Pejin *et al.* (2012d) tested ***Rhodobryum ontariense*** (Figure 27) for its heavy metal content. Fortunately, they found that the concentrations of arsenic, cadmium, chromium, copper, iron, lead, mercury, nickel, manganese, and zinc in these mosses used in tea were at safe levels for a typical daily intake of the tea. They suggested that manganese was one of the important components in treating hypertension. Nevertheless, these results do not mean that the Chinese populations and species are safe as the heavy metal concentrations vary by locations and distance from pollution source.

Lisu women in Yunnan Province, China, hike to fens in the alpine area above the Salween River Valley (Nu Jiang) to collect large amounts of ***Sphagnum*** (Figure 10), which they subsequently dry (James Shevock, Bryonet, 16 January 2007). Despite about 27 species of ***Sphagnum*** reported in Yunnan, these Lisu women (one of several minority peoples in Yunnan Province) seem able to recognize a particular species in the field; they claim that it is only this species that is used for medicinal purposes. This species of ***Sphagnum*** is used as a heart tonic, probably brewed like a tea. Once dried and packaged, the moss was to be exported to Canada! (Surely Canada has more ***Sphagnum*** than Yunnan?)

Figure 30. Dried ***Rhodobryum giganteum*** (left container) at a shop in Yunnan, China. Photo by David Long, with permission.

In India, bryophytes have also been used to treat heart disease. One such treatment is with ***Cratoneuron filicinum*** (Figure 31) (Pant 1998; Asakawa 2015; Chandra *et al*. 2017).

Figure 31. ***Cratoneuron filicinum***, a species used in India to treat the heart. Photo by Barry Stewart, with permission.

The Indians have also used several bryophytes to stop bleeding. These include the thallose liverwort ***Reboulia hemisphaerica*** (Figure 32) and the mosses ***Funaria hygrometrica*** (Figure 33), ***Plagiomnium cuspidatum*** (Figure 34), ***Polytrichum commune*** (Figure 4), ***Pogonatum cirratum*** (Figure 28), and ***Taxiphyllum taxirameum*** (Figure 35) (Gulabani 1974; Ding 1982; Pant 1998; Asakawa 2007b, 2015; Azuelo *et al*. 2011; Alam 2012; Shirsat 2008; Chandra *et al*. 2017).

Figure 32. ***Reboulia hemisphaerica***, a species used in India to stop bleeding. Photo by Jan-Peter Frahm, with permission.

Figure 33. ***Funaria hygrometrica***, a species used in India to stop bleeding. Photo by Michael Lüth, with permission.

Figure 34. ***Plagiomnium cuspidatum***, a species used in India to stop bleeding. Photo by Hermann Schachner, through Creative Commons.

Figure 35. ***Taxiphyllum taxirameum***, a species used in India to stop bleeding. Photo by Michael Lüth, with permission.

Nosebleeds

One odd choice is the use in Cambridge of ***Homalothecium sericeum*** (Figure 36) from skulls used to treat nosebleeds, with recorded records as early as 1537 (Belcher & Swale 1998). The skulls were placed in damp places to cultivate this moss. But other researchers concluded that the tale was concocted and that no medicinal value was present (Scott 1988). On the other hand, Robert Boyle used it effectively on his own nosebleeds. Perhaps it is just a good absorbent.

Figure 36. ***Homalothecium sericeum*** from skulls is used to treat nosebleeds in Cambridge. Photo by Michael Lüth, with permission.

In another context, ***Plagiomnium cuspidatum*** (Figure 34) has been used to treat nosebleeds in India (Pant 1998; Asakawa 2007a, 2015). This casts suspicion on my suggestion of absorbency as this species does not rehydrate easily. On the other hand, as already noted, Asakawa (2015) reported that the mosses ***Funaria hygrometrica*** (Figure 33), ***Oreas martiana*** (Figure 38), ***Polytrichum commune*** (Figure 4), and ***Taxiphyllum taxirameum*** (Figure 35) and the liverwort ***Reboulia hemisphaerica*** (Figure 32) stop bleeding.

Neurological Conditions

Few bryophytes seem to be used for neurological conditions. Nevertheless, in Cambridge, England, the moss ***Homalothecium sericeum*** (Figure 36) from skulls has been used in the treatment of epilepsy (Belcher & Swale 1998). In China, liverworts have been used to treat convulsions, neurasthenia (emotional disturbance typically involving lassitude, fatigue, headache, and irritability), and other nerve conditions (Asakawa 2012). ***Rhodobryum roseum*** is useful for treating neurasthenia (Asakawa 2015).

Several bryophytes have been used to treat pain. For ***Leucobryum bowringii*** (Figure 37), a paste is made of leaf tips mixed in a cup of *Phoenix sylvestris* (silver date palm) to treat pain (Lubaina *et al*. 2014; Chandra *et al*. 2017). ***Oreas martiana*** (Figure 38) is used as an anodyne for treating pain (Asakawa 2007b, 2015; Chandra *et al*. 2017). These authors also reported the use of ***Oreas martiana*** to treat nervosism and nervous exhaustion as well as epilepsy. ***Ditrichum pallidum*** (Figure 39) has been used in India to treat convulsions, especially in infants (Pant 1998; Asakawa 2007b, 2015; Chandra *et al*. 2017).

Figure 37. ***Leucobryum bowringii***, a species used to treat pain. Photo through Creative Commons.

Figure 38. ***Oreas martiana***, a species used to treat pain. Photo by Michael Lüth, with permission.

Figure 39. ***Ditrichum pallidum*** on the forest floor. This species has been used in India to treat convulsions in infants. Photo by Janice Glime.

Inflammation and Fever

Today we have freezers and use cold packs to soothe inflammation and reduce fevers, but not so long ago those conveniences were not available. Instead, ***Polytrichum commune*** (Figure 4) has been used in China to reduce inflammation and fever (Ding 1982; Chandra *et al*. 2017), and the Seminole native people in North America used the small mosses ***Barbula unguiculata*** (Figure 40) and ***Bryum capillare*** (Figure 41), as well as larger mosses like ***Octoblepharum albidum*** (Figure 42), as external applications for fever and body aches (Sturtevant 1954; Chandra *et al*. 2017). ***Barbula indica*** (Figure 43) and ***Weissia controversa*** (Figure 44) have also been used in the Western Ghats to treat intermittent fever (Lubaina *et al*. 2014). ***Taxiphyllum taxirameum*** (Figure 35) is an anti-inflammitory (Asakawa 2015).

Figure 40. ***Barbula unguiculata***, a moss used by Seminole native people in North America to treat body aches and fever. Photo by Bob Klips, with permission.

Figure 41. ***Bryum capillare*** with capsules, a moss used by Seminole native people in North America to treat body aches and fever. Photo by Michael Lüth, with permission.

Figure 42. ***Octoblepharum albidum***, a moss used by Seminole native people in North America to treat body aches and fever. Photo by Niels Klazenga, with permission.

Figure 43. ***Barbula indica***, a moss used in the Western Ghats to treat fever. Photo by Li Zhang, with permission.

Figure 44. ***Weissia controversa***, a moss used in the Western Ghats to treat fever. Photo by Michael Lüth, with permission.

Fontinalis antipyretica (Figure 45) reputedly got its specific name from its ability to work against fever, as recorded in the journal of Linnaeus (Nils Cronberg, pers. comm.). Drobnik and Stebel (2014) found that its use against fever is reported in pre-Linnaean bryophyte floras of central Europe. However, many people have interpreted the name to be derived from its use to insulate chimneys against fire, where in actuality it seems to have little value. On the other hand, it may reduce the heat penetrating into the house. But does it reduce fever? Perhaps it can serve as a cool poultice.

Figure 45. ***Fontinalis antipyretica***, reported by Linnaeus as being used to treat fever. Photo by Michael Lüth, with permission.

Sabovljević *et al*. (2011) reported the use of ***Marchantia palacea*** (Figure 16) to reduce swelling and bring down fever. ***Leptodictyum riparium*** (Figure 46), an aquatic moss, ***Philonotis fontana*** (Figure 62), a wetland moss, and the cosmopolitan moss ***Bryum argenteum*** (Figure 47) are used to treat fever in India (Pant 1998; Asakawa 2007b, 2015; Chandra *et al*. 2017). ***Octoblepharum albidum*** (Figure 42) was considered in India to have similar ability to reduce fever (Singh 2011; Chandra *et al*. 2017). The mosses ***Haplocladium capillatum*** (see Figure 52) and ***Leptodictyum riparium***, ***Polytrichum commune*** (Figure 4), ***Rhodobryum giganteum*** (Figure 25, Figure 30), and ***Weissia controversa*** (Figure 44) and the thallose liverworts ***Conocephalum conicum*** (Figure 18) and ***Marchantia polymorpha*** (Figure 5) are likewise antifever agents.

Figure 46. ***Leptodictyum riparium***, a moss used to treat fever in India. Photo by David T. Holyoak, with permission.

Figure 47. ***Bryum argenteum***, a moss used to treat fever in India. Photo by Tushar Wankhede, through Creative Commons.

Urinary and Bowel Treatments

The Chinese also use ***Polytrichum commune*** (Figure 4) as a detergent diuretic, laxative, and hemostatic agent (Ding 1982; Ando & Matsuo 1984; Hu 1987; Fan *et al*. 2004; Harris 2008). In India, ***Fissidens nobilis*** (Figure 48) and ***Dawsonia longifolia*** (Figure 49) are used as diuretics (Pant 1998; Azuelo *et al* 2011; Chandra *et al*. 2017), and Asakawa (2015) reports ***Marchantia polymorpha*** (Figure 5) for the same purpose. ***Pogonatum cirratum*** (Figure 28) has been used as a laxative in India (Azuelo *et al*. 2011; Alam 2012; Chandra *et al*. 2017). Asakawa (2015) reports ***Fissidens nobilis*** (Figure 48) as a diuretic and ***Haplocladium capillatum*** (see Figure 52) for treatig cystitis and uropathy. ***Leptodictyum riparium*** (Figure 46) and ***Rhodobryum giganteum*** (Figure 25, Figure 30) likewise are used to treat **uropathy** (restricted urine flow) (Asakawa 2015).

Figure 48. ***Fissidens nobilis***, a species that is used as a diuretic in India. Photo by Jan-Peter Frahm, with permission.

Figure 49. ***Dawsonia longifolia***, a species used as a diuretic in India. Photo by Jan-Peter Frahm, with permission.

I was surprised to find ***Polytrichum juniperinum*** (Figure 50) listed in Materia Medica as a treatment for painful urination of the elderly, obstruction or suppression, and dropsy (Available Materia Medicas 2011). The medicine is made by boiling two ounces of the moss in a liter of water until it boils down to only half that – a pint, making a "tincture." One dose (4 ozs, 113 g) should be taken every 8 hours.

Figure 50. ***Polytrichum juniperinum***, a hairy cap moss, is used in China to treat urinary and prostate problems. It can be recognized by the brown tips on the leaves and the rolled over leaf edges that cover the lamellae. Photo by Michael Lüth, with permission.

The leafy liverwort ***Herbertus*** sp. (Figure 51) is used in India as an antiseptic, antidiarrheal agent, expectorant, and astringent (Azuelo *et al.* 2011; Alam 2012; Chandra *et al.* 2017). In both China and India, **cystitis** (inflammation of the bladder) has been treated with the moss ***Haplocladium microphyllum*** (Figure 52) (Ding 1982; Pant 1998).

Figure 51. The leafy liverwort ***Herbertus sendtneri***. Some members of the genus ***Herbertus*** are used in India as a filter for smoking. Photo by Michael Lüth, with permission.

Figure 52. ***Haplocladium microphyllum***, a species that is used to treat bladder infections in China and India. Photo by Robin Bovey, with permission through Dale Vitt.

Gynecology

The absorbent properties that make ***Sphagnum*** (Figure 10) an excellent bandage also make it suitable for diapers and sanitary napkins, a product currently sold by Johnson and Johnson Company (D. H. Vitt, pers. comm.).

Figure 53. ***Sphagnum*** Sanitary napkin. Photo from National Museum of American History, with online permission.

Sphagnum (Figure 10) has also been used, along with grass, sponge, and other plant fiber, as a contraceptive to block the entry of sperm (Stanley 1995). By contrast, following successful pregnancies, the Nitinaht peoples of Vancouver Island, Canada, used ***Polytrichum commune*** (Figure 4) as a gynecological aid (Turner *et al*. 1983; Chandra *et al*. 2017). Women in labor chewed the moss to speed up the labor process.

In China, ***Polytrichum*** (Figure 4, Figure 50) has been used to stop bleeding and night sweats, presumably associated with menopause (EBCHSATCM 1999; Cheng *et al*. 2008; Fu *et al*. 2009). It has also been used to treat **uterine prolapse** (the uterus sags due to weakening of muscles or ligaments that support it).

The moss ***Oreas martiana*** (Figure 38) is used to treat **menorrhagia** (prolonged bleeding with menstrual period) (Asakawa 2007b; Chandra *et al*. 2017). ***Barbula indica*** (Figure 43) has been used in the Western Ghats to treat menstrual pain (Lubaina *et al*. 2014; Chandra *et al.* 2017).

Disinfectant and Infections

The Native American Nitinahts also used ***Sphagnum*** (Figure 10) as a disinfectant (Turner *et al*. 1983). ***Fissidens*** (Figure 54) is used in China as an antibacterial agent for swollen throats and other symptoms of bacterial infection, and in Bolivia it likewise has medicinal uses. Judith Sullivan (Bryonet, 16 January 2007) reported seeing labels on Chinese medicines that included ***Grimmia*** (Figure 55), ***Atrichum*** (Figure 56), ***Polytrichum*** (Figure 4, Figure 50), and ***Thuidium*** (Figure 57), primarily as anti-bacterial and anti-inflammatory agents. ***Polytrichum juniperinum*** (Figure 50) is used there for some prostate and urinary difficulties.

Figure 54. ***Fissidens osmundoides***, a moss in one genus used as an antibacterial agent to treat sore throats in Bolivia and several Asian countries. Photo by Michael Lüth, with permission.

Figure 55. ***Grimmia pilifera***, a Chinese species. Some members of this genus are used in medicines in China. Photo by Henk Greven, with permission.

Figure 56. ***Atrichum undulatum***. Some members of this genus are used in medicines in China. Photo by Michael Lüth, with permission.

Figure 57. ***Thuidium recognitum***. Some members of ***Thuidium*** are used as anti-bacterial and anti-inflammatory agents in China. Photo by Jan-Peter Frahm, with permission.

Dried ***Sphagnum*** (Figure 58) is sold to treat hemorrhages (Bland 1971), and ***S. teres*** (Figure 58) is used to treat eye diseases and hemorrhoids (Ding 1982). ***Haplocladium microphyllum*** (Figure 52) is sold to treat bronchitis, tonsillitis, and tympanitis, as well as cystitis (Ding 1982).

Figure 58. ***Sphagnum teres*** is used to treat eye diseases in Asia. Photo by Michael Lüth, with permission.

As noted in Chapter 1 of this volume, the soap **Sphagnol** is a ***Sphagnum*** (Figure 10; Figure 58) product used to treat skin problems such as acne, eczema, chilblains (painful inflammation of small blood vessels in the skin), dandruff, insect bites, and ringworm (a fungus) (The Science Museum 2012). This product was used during both World Wars by the British Red Cross to treat facial wounds and is believed to have antibiotic properties.

Kumar *et al*. (2007) reported on antibacterial species used in India, as discussed in Chapter 2-2 on Biologically Active Substances. ***Oreas martiana*** (Figure 38) and ***Taxiphyllum taxirameum*** (Figure 35) likewise are used to treat wounds (Asakawa 2015), perhaps having antibiotic properties. the leafy liverwort ***Frullania tamarisci*** has known antiseptic properties (Asakawa 2015).

Nose and Throat

In both India and North America, the moss ***Philonotis fontana*** (Figure 62) has been used to treat **adenopharyngitis**, an inflammation of the pharynx and tonsils (Flowers 1957; Pant 1998; Asakawa 2007b; Chandra *et al*. 2017). ***Haplocladium capillatum*** (see Figure 52) and ***Philonotis fontana*** likewise can be used to treat adenopharyngitis (Asakawa 2015). ***Bryum argenteum*** (Figure 47) and ***Weissia controversa*** (Figure 44) have chemical properties used to treat **rhinitis** (inflammation of the mucous membrane of the nose) (Asakawa 2015).

Lung Diseases

Funaria hygrometrica (Figure 33) has been used in India to treat pulmonary tuberculosis (Pant 1998; Chandra *et al*. 2017), and Asakawa (2015) indicates it has compounds useful for that purpose, as does ***Polytrichum commune*** (Figure 4). The similarity of ***Marchantia polymorpha*** (Figure 5) thalli to the texture of lung tissue caused Europeans to use that liverwort to treat pulmonary tuberculosis (Bland 1971). It is likely that this Doctrine of Signatures was also responsible for the Chinese use of liverworts to treat pulmonary tuberculosis (Asakawa 2012). It is interesting that its thallus has been interpreted as resembling both liver tissue and lung tissue.

In Cambridge, England, the moss ***Homalothecium sericeum*** (Figure 36) was used to treat whooping cough (Belcher & Swale 1998). In the Himalayas the moss ***Haplocladium microphyllum*** (Figure 52) is used to treat bronchitis (Kumar *et al*. 2007). ***Haplocladium microphyllum*** has also been used to treat tonsillitis and pneumonia (Ding 1982; Pant 1998; Chandra *et al*. 2017); ***H. capillatum*** (see Figure 52) is known for its use in treating in pneumonia (Asakawa 2015).

Treatments of colds, not surprisingly, has made use of bryophytes. ***Hyophila involuta*** (Figure 59) has been used for the symptoms of a cold, cough, and sore throat. This treatment is a leaf decoction with a pinch of ground pepper, used daily (Lubaina *et al*. 2014; Chandra *et al*. 2017). Also in India, natives in the Western Ghats have used ***Weissia controversa*** (Figure 44) to treat colds.

Figure 59. ***Hyophila involuta*** drying. This species has been used to treat cold, cough, and sore throat. Photo by Bob Klips, with permission.

The other side of the coin is the ability of some mosses, especially ***Sphagnum*** (Figure 58), to harbor fungi that cause lung disease. ***Sphagnum*** was once thought to harbor *Mycobacteria* (Figure 60), the genus in which the tuberculosis bacterium resides, but now it seems that it is not the reservoir for this genus it was thought to be (Deriu *et al*. 1995). On the other hand, the fungus *Sporothrix schenckii* (Figure 61), common on ***Sphagnum***, does cause pulmonary **sporotrichosis**, an infection of the lung resulting from breathing the fungi (McCain & Buell 1968).

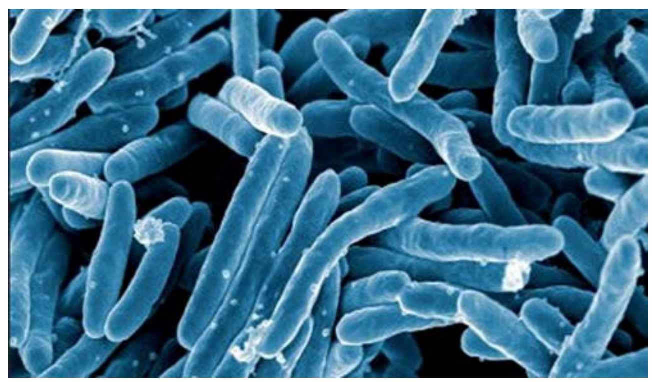

Figure 60. ***Mycobacterium tuberculosis*** SEM, member of a pathogenic genus once thought to live among ***Sphagnum***. Photo from NIAID, through Creative Commons.

Figure 61. ***Sporothrix schenckii*** conidia, a species that grows among ***Sphagnum*** and causes **sporotrichosis**. Photo from USDHHS, through public domain.

Skin Ailments and Burns

The antibiotic properties of many bryophytes suggest that they should promote healing of skin infections. The thallose liverwort ***Reboulia hemisphaerica*** (Figure 32) is used to treat skin blotches, external wounds, and bruises and ***Oreas martiana*** (Figure 38) is used to treat external wounds (Asakawa 2007b, 2015; Chandra *et al*. 2017). ***Fissidens nobilis***, ***Conocephalum conicum*** (Figure 18), and ***Marchantia polymorpha*** (Figure 5) have compounds that help in the healing of burns (Asakawa 2015). ***Funaria hygrometrica*** (Figure 33) is useful in treating bruises and Athlete's foot. ***Rhodobryum giganteum*** (Figure 25, Figure 30), ***Conocephalum conicum***, and ***Marchantia polymorpha*** can be used to treat cuts (Asakawa 2015).

Himalayan Indians use a mixture of moss ashes with fat and honey to soothe and heal cuts, burns, and wounds (Pant *et al.* 1986; Pant 1998; Chandra *et al*. 2017), claiming that these ashes heal wounds more quickly (Pant & Tewari 1989). ***Taxiphyllum taxirameum*** (Figure 35) is among those mosses used to treat surface wounds (Pant 1998; Asakawa 2007b; Chandra *et al*. 2017). In the Himalayas, the Gaddi tribe uses ***Philonotis fontana*** (Figure 62) and ***Plagiochasma appendiculatum*** (Figure 63) to treat burns and skin diseases (Flowers 1957; Pant 1998; Asakawa 2007b; Kumar *et al*. 2007; Shirsat 2008; Alam 2012; Chandra *et al*. 2017). ***Bryum thomsonii*** is used in the Northwest Himalayas for healing wounds (Kumar *et al*. 2007). Himalayan Indians have used ***Marchantia polymorpha*** (Figure 5; Figure 64) or ***M. palmata*** to treat boils and abscesses because the young archegoniophore resembles a boil as it emerges from the thallus (Pant & Tewari 1989).

Figure 62. ***Philonotis fontana*** is a wetland moss used by Gosuite native people to relieve pain of burns. Photo by Michael Lüth, with permission.

In India, the pendent moss ***Aerobryum lanosum*** is used to treat burns. The whole plant is boiled in goat urine and applied externally (Lubaina *et al*. 2014; Chandra *et al*. 2017). Species of ***Mnium*** (*sensu lato*?) (Figure 3) have been used in a poultice to reduce pain from bruises, wounds, and burns (Azuelo *et al*. 2011; Chandra *et al*. 2017). Similarly, these authors found that ***Plagiomnium*** (Figure 12, Figure 34) has been used for treating infections and swellings.

Also in India, the thallose liverwort ***Targionia hypophylla*** (Figure 65) is used, mixed with leaves of the flowering plant *Actiniopteris radiata*, and ground into a paste, then mixed with two tablespoons of coconut oil. This paste is smeared over the body of the children affected by itching skin, scabies, and other skin diseases (Remesh & Manju 2009; Chandra *et al*. 2017).

Figure 63. ***Plagiochasma appendiculatum*** with archegoniophores, a species used in the Himalayas to treat burns and skin diseases. Photo by Michael Lüth, with permission.

Figure 64. Young archegoniophores of ***Marchantia polymorpha***, somewhat resembling a boil. Photo by Rudolf Macek, with permission.

Figure 65. ***Targionia hypophylla***, a species used in India to treat skin diseases. Photo by Martin Hutten, with permission.

Marchantia palmata is made into a fleshy leaf paste and applied directly to acute inflammation caused by heat (burns) (Tag *et al*. 2007; Chandra *et al*. 2017).

Another skin-related use in India is that of the cosmopolitan moss ***Funaria hygrometrica*** (Figure 33) to treat bruises and skin infections (Pant 1998; Chandra *et al*. 2017).

Among the Native Americans, the Cheyenne in Montana use ***Polytrichum juniperinum*** (Figure 50) in medicines (Hart 1981). In Utah, USA, the Gosuite native peoples used ***Bryum*** (Figure 41, Figure 47), ***Mnium*** (Figure 3), ***Philonotis*** (Figure 62), and various matted hypnaceous forms crushed into a paste applied to reduce the pain of burns, bruises, and wounds (Flowers 1957). ***Sphagnum*** (Figure 10) was used by Native Americans as a carrier for berries that were rubbed on children's sores (Carrier Linguistic Committee 1973).

As one might expect, the Chinese have used liverworts in the treatment of skin ailments, including cuts, burns, and bruises (Asakawa 2012). A mixture of the thallose liverworts ***Conocephalum conicum*** (Figure 18) and ***Marchantia polymorpha*** (Figure 5) with vegetable oils is used in China on bites, boils, burns, cuts, eczema, and wounds (Wu 1977; Ding 1982; Ando 1983; Yan *et al.* 1999).

In China and India, ***Conocephalum conicum*** (Figure 18) has a number of medical uses. Its antimicrobial, antifungal, antipyretic, and antidotal activities contribute to its usefulness to treat cuts, swollen tissue, scalds, burns, fractures, and poisonous snake bites (Ding 1982; Alam 2012; Chandra *et al*. 2017). Likewise, ***Marchantia polymorpha*** (Figure 5) has been used to treat snake bites (Hu 1987; Shirsat 2008; Azuelo *et al*. 2011; Asakawa 2015; Chandra *et al*. 2017). ***Bryum argenteum*** (Figure 47), ***Polytrichum commune*** (Figure 4), and one or more species of ***Philonotis*** (Figure 62) have been used as antidotes (Asakawa 2007b, 2015; Chandra *et al*. 2017).

Alaskan native peoples have used ***Sphagnum*** (Figure 10), mixed with fat, to make a salve (Schofield 1969; Miller & Miller 1979). In Britain ***Sphagnum*** was used to treat boils (Bland 1971), its derivative **sphagnol** to relieve the itch of a mosquito bite (Crum 1988), and for medicinal baths (Crum 1973; Weber & Ploetner 1976; Turner 1993), although the small amounts of active substances put into an average bath are not likely to have any effect.

Nevertheless, Mitchell and Rook (1979) caution us about the possible allergenic effects of ***Sphagnum*** (Figure 10), especially because of its ability to harbor the fungus causing **sporotrichosis** (Adams *et al.* 1982). It is a known danger to nursery workers and harvesters who are in constant contact with the ***Sphagnum*** (D'Alessio *et al.* 1965; McCain & Buell 1968; Tamblyn 1981; Keller 1988; Padhye & Ajello 1990; Coles *et al*. 1992), even affecting areas like the abdomen (Frankel & Frankel 1982). In 1988, sporotrichosis reached sufficient proportions that "*Sphagnum* the culprit" made its debut in the *Milwaukee Journal* (Rosenberg 1988). In 1995, nine of the 65 workers involved in making topiary art at a Florida nursery became infected with lymphocutaneous sporotrichosis (Hajjeh *et al* 1997). Even forestry workers who don't handle the moss directly can contract the disease from working in peatlands (Powell *et al.* 1978). The threat is sufficient to cause the American Orchid Society to warn its members of this occupational hazard (Padhye & Ajello 1990). The Macauley Institute in Aberdeen, England, is investigating the use of hydroponics to produce ***Sphagnum*** that is free of microorganisms and other contaminants. Wearing gloves helps to protect against the lymphocutaneous sporotrichosis (Hajjeh *et al*. 1997), but longer exposures can still lead to pulmonary infections.

Eye Problems and Diseases

In the northwest Himalayas, ***Sphagnum teres*** (Figure 58) is used to treat ophthalmic diseases (Kumar *et al*. 2007). There seems to be medical evidence that at least some of the bryophytes can be used effectively to treat age-related blindness (age-related macular degeneration) (Albert-Ludwigs-Universität Freiburg 2010). Factor H is necessary to maintain healthy eyes (Coffey 2007). The Freiburg research lab has produced a protein in a bioreactor using factor H from mosses. Factor H is otherwise known only from blood and is important for the immune system. 50 million people suffer blindness due to lack of this protein, especially in industrial countries.

Büttner-Mainik *et al.* (2011) developed a protocol to produce Factor H using ***Physcomitrella patens*** (Figure 6, Figure 7). Factor H is a protein that is difficult to produce in animal lines, but these researchers successfully produced it in transgenic ***P. patens***.

Flatbergium sericeum (Figure 66), a relative of ***Sphagnum***, has been used to treat eye diseases (Azuelo *et al*. 2011; Chandra *et al*. 2017). Similarly, ***Sphagnum teres*** (Figure 58) has been used for this purpose in China (Ding 1982).

Figure 66. ***Flatbergium sericeum***, a species that has been used to treat eye diseases. Photo courtesy of Jon Shaw.

Ear Ache and Hearing Problems

Entodon flavescens is used by the Kani tribes in the Western Ghats for treating ear ache (Lubaina *et al*. 2014; Chandra *et al*. 2017). They use a leaf juice as ear drops, especially in cold weather. ***Haplocladium capillatum*** (see

Figure 52) has been used to treat tinnitis, but recent news reports suggest this is not really related to the ears.

Hair Treatments

Soothing a wound of a different sort (human pride), the Chinese use ***Fissidens*** (Figure 54; Figure 79), burned, to put on their heads to encourage hair growth! (Harris 2002). In India, ***Fissidens nobilis*** (Figure 48) has likewise been used to grow hair (Pant 1998; Azuelo *et al*. 2011). And Asakawa (2015) found compounds in ***Fissidens nobilis*** (Figure 48) that should promote hair growth

Most likely following the Doctrine of Signatures, Himalayan natives use ***Polytrichum commune*** (Figure 4) to promote hair growth (Kumar *et al*. 2007). The Doctrine of Signatures is a theory that the plant tells us what it is useful for by its morphology or other properties. Since ***Polytrichum commune*** has a hairy calyptra (Figure 67), that would suggest it is good for growing hair. Similarly, the hairs on the calyptra most likely account for the use of ***Dawsonia longifolia*** (Figure 69) to grow hair (Azuelo *et al*. 2011; Chandra *et al*. 2017).

Figure 67. ***Polytrichum commune*** capsules with hairy calyptrae (and one with calyptra removed). This species is used to help grow hair. Photo by Michael Lüth, with permission.

Frullania ericoides (Figure 68) is used to treat the hair and scalp in India (Remesh & Manju 2009; Chandra *et al*. 2017). It purportedly gets rid of head lice and nourishes the hair.

Figure 68. ***Frullania ericoides***, a species used in India to treat the hair and scalp. Photo by Paul Davison, with permission.

Figure 69. ***Dawsonia longifolia*** with capsule, showing long hairs on the calyptra. Photo by Vita Plasek, with permission.

Sedatives

The use of bryophytes as sedatives seems to be uncommon. The moss ***Hypnum*** (Figure 70) was named for sleep, but that is because it was used to stuff pillows, not for any known sedative effect (Dillenius 1741). However, ***Plagiopus oederianus*** (Figure 71) has been used in India as a sedative, as well as for treating epilepsy (Pant 1998; Asakawa 2015; Chandra *et al*. 2017). And the widely used ***Rhodobryum roseum*** and ***R. giganteum*** (Figure 26) likewise have been used as sedatives (Wu 1977; Pant 1998; Asakawa 2007b, 2015; Chandra *et al*. 2017).

Figure 70. ***Hypnum cupressiforme***, a moss that filters substances out of items for smoking and is used to stuff pillows. Photo by Michael Lüth, with permission.

Figure 71. ***Plagiopus oederianus***, a species used in India as a sedative and to treat epilepsy. Photo by Michael Lüth, with permission.

Antidotes

The mosses ***Bryum argenteum*** (Figure 47), ***Haplocladium capillatum*** (see Figure 52). ***Philonotis fontana*** (Figure 62), ***Polytrichum commune*** (Figure 4), and ***Weissia controversa*** (Figure 44) can be used as an antidote, as well as ***Conocephalum conicum*** (Figure 18) and ***Marchantia polymorpha*** (Figure 5). But Asakawa does not state what things these will treat (Asakawa 2015). For ***Conocephalum conicum***, Asakawa reports that it can be used to treat snake bites.

Filters

Kumaun Indians (also Kumaon) of the Himalayas use slender bryophytes such as ***Herbertus*** (Figure 51), ***Anomodon*** (Figure 72), ***Entodon*** (Figure 76), ***Hypnum*** (Figure 70), ***Meteoriopsis*** (Figure 73), and ***Scapania*** (Figure 74), wrapped in a cone of *Rhododendron campanulatum* (Figure 75) leaves, to serve as a filter for smoking (Pant & Tewari 1989). One must wonder if any of those heated phenolic compounds in bryophytes might be as harmful as the substances they filter out!

Figure 72. ***Anomodon rugelii***, a moss of vertical surfaces, filters substances out of items for smoking. Photo by Michael Lüth, with permission.

Figure 73. ***Meteoriopsis squarrosa***, a pendent species in the Western Ghats. The genus ***Meteoriopsis*** is used as a smoking filter in the Himalayas. Photo by M. C. Nair, K. P. Rajesh, and P. V. Madhusoodanan, through Creative Commons.

Figure 74. ***Scapania gracilis***. Members of this genus are used as smoking filters in the Himalayas. Photo by Michael Lüth, with permission.

Figure 75. ***Rhododendron campanulatum***. Leaves of this species are used to wrap bryophytes to serve as smoking filters. Photo by Kurt Stüber, through Creative Commons.

One peat product has actually entered modern medicine as a means to cleanse the body of pollutants: humic acids. HUMET-R syrup entered medicine as a transporter of trace elements, reducing excess trace elements that are bombarding the human body from pollutants and other sources (Kleb *et al*. 1999). The active substance is humin acid.

Figure 76. The pleurocarpous moss ***Entodon concinnus*** is used as a smoking filter. Photo by Michael Lüth, with permission.

Surgical and Larger Wounds

Bryophytes have been used both in treating and in cushioning wounds. In Utah, the Gosuite native people used poultices of ***Bryum*** (Figure 41, Figure 47), ***Mnium*** (Figure 3), ***Philonotis*** (Figure 62), and various matted hypnaceous forms as padding under splints to set broken bones.

But it is ***Sphagnum*** (Figure 10) that has gained fame for its use as a bandage (Figure 77) (Painter 2003). It appears that even before the First World War, ***Sphagnum*** was used to bandage the wounded in the Russo-Japanese War (1904-05). In the First World War, the Americans (USA) and Canadians used ***Sphagnum*** (peat moss) to make bandages, conserving the valuable cotton for making and packing gunpowder (Porter 1917; Hotson 1918, 1919, 1921; Nichols 1918a, b, c, d, 1920). The wounds apparently healed better than those with sterile surgical bandages, benefitting from the moisture and fewer infections. The British Army used about 1,000,000 pounds (453590 kg) of dressing per month (Nichols 1918c, 1920), saving about US $200,000 (Bland 1971), the Canadian Red Cross about 200,000 pounds (90720 kg) per month, and the United States about 500,000 pounds (226800 kg) during the last six months of war (Bland 1971). After the war, these countries returned to traditional gauze bandages, but the Chinese have continued to use ***Sphagnum*** for this purpose (Ding 1982).

The superiority of ***Sphagnum*** (Figure 10) bandages is attributed in part to its ability to absorb 3-4 times as much liquid as a cotton bandage at a rate three times as fast (Porter 1917). This is due to the interlaced hyaline cells that are dead and possess pores (Figure 78). These cells retain water and readily absorb water when dry. Hence, the bandage retains liquids longer and more uniformly, necessitating less frequent change. It is more comfortable for the user because it is cooler, softer, less irritating, and retards bacterial growth (Banerjee 1974). In fact, tests indicate that the amount of wound area covered by new epidermis doubles with use of ***Sphagnum*** dressing compared to no dressing (Varley & Barnett 1987).

Figure 77. ***Sphagnum*** for surgical dressings. Photo from National Museum of American History, with online permission.

This news article appeared on page 4 of *The Seattle Star* (Washington, USA), 3 April 1918:

"U" STUDENTS TO MAKE 50,000 MOSS DRESSINGS

Fifty thousand sphagnum dressings, for use in France, will be made at the University of Washington before June 15. The dressings will follow a new design and will be submitted for experiment. If successful, it is expected that a call will come for 50,000 each week.

Between 800 and 900 freshman and sophomore girls are now registered for work on sphagnum moss dressings.

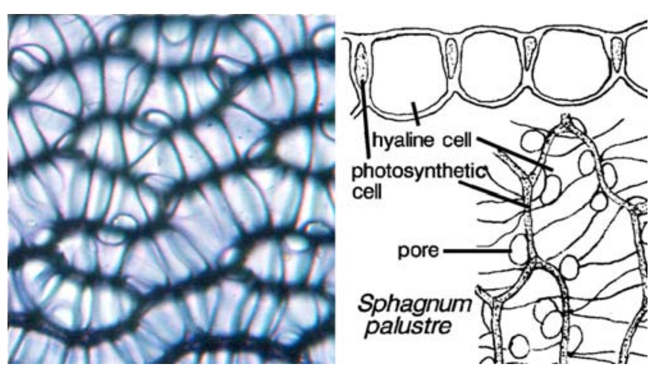

Figure 78. Stained cells of ***Sphagnum*** showing large hyaline cells with pores and small photosynthetic cells. Photo and drawings by Janice Glime.

The pectin complex in the ***Sphagnum*** (Figure 78) cell wall is similar structurally to immunostimulatory pectin from tracheophytes that has traditionally been used for healing wounds (Painter 2003).

Sphagnum (Figure 10) is not the only moss that has been used for bandages. The Nitinaht native people of Vancouver Island, Canada, used a moss known as maidenhair moss (***Fissidens adianthoides***; Figure 79) to bandage wounds. The Anglo-Saxons gave it the name of maidenhair moss because to them it resembled a maiden's pubic hair.

Figure 79. ***Fissidens adianthoides*** is the maidenhair moss used by the Nitinaht native people for bandages. Photo by Michael Lüth, with permission.

Perhaps one of the more unusual uses of liverworts is the Chinese use to promote healing of fractures (Asakawa 2012); he reports ***Conocephalum conicum*** (Figure 18) and ***Marchantia polymorpha*** (Figure 5) to be useful for this (Asakawa 2015). Lubaina *et al*. (2014) reported the use of the leafy liverwort ***Plagiochila beddomei*** (see Figure 80) for healing wounds in the Western Ghats.

Figure 80. ***Plagiochila*** sp. ***Plagiochila beddomei*** is used in the Western Ghats for healing wounds. Photo by Lin Kyan, with permission.

The use of ***Sphagnum*** (Figure 10) as a bandage is not without its hazards, as mentioned earlier. Perhaps other mosses may serve an absorptive function as well or better than ***Sphagnum*** and impose fewer hazards. Horikawa (1952) compared a number of mosses and their ability to absorb water. He found several that could rival ***Sphagnum*** in absorptive ability (Table 1).

Table 1. Weight gain measured as wet weight to dry weight ratio of selected bryophytes (Horikawa 1952).

Atrichum	6.9	Figure 56
Barbula	8.3	Figure 40, Figure 43
Bazzania pompeana	4.0	*cf.* Figure 81
Haplomitrium mnioides	12.0	Figure 82
Loeskeobryum cavifolium	9.8	*cf.* Figure 83
Plagiomnium maximoviczii	6.7	Figure 84
Rhodobryum	10.0	Figure 25
Sphagnum	12.4	Figure 58
Trachycystis microphylla	3.2	Figure 85

Figure 81. ***Bazzania trilobata***. ***Bazzania pompeana*** gains water up to 4 time its dry weight. Photo by Janice Glime.

Figure 82. ***Haplomitrium mnioides***, a species that gains water up to 12 times its dry weight. Photo by Yang, Jia-Dong, through Creative Commons.

Figure 83. ***Loeskeobryum brevirostre***. ***Loeskeobryum cavifolium*** gains water up to 9.8 times its dry weight. Photo by Bob Klips, with permission.

Figure 84. ***Plagiomnium maximoviczii***, a species that gains water up to 6.7 times its dry weight. Photo through Creative Commons.

Figure 85. ***Trachycystis microphylla***, a species that gains water up to 3.2 times its dry weight. Photo by Li Zhang, with permission.

Breaking News

After "completing" the revision of this chapter, I received an email announcing the completion of a safety study for the pharmaceutical use of a bryophyte-produced compound, Moss-aGal (Kirstein 2017). Six patients were monitored for 28 days following a single dose of the pharmaceutical and showed no negative effects. This is only phase 1 of the study, but it provides promise in relieving symptoms in patients suffering from Fabry disease. This is the first moss-based clinical product to be tested in humans. The research has been done at Greenovation, a privately-owned biopharmaceutical company based in Heilbronn, Germany. It was founded in 1999 by Prof. Dr. Ralf Reski and Prof. Dr. Gunter Neuhaus.

Fabry disease is a rare genetic disease causing a deficiency of the enzyme **alpha-galactosidase A** (a-Gal A), hence the name Moss-aGal for the moss compound to treat it. This disease causes a buildup of a type of fat called **globotriaosylceramide** (Gb3, or GL-3) in the body. Fabry disease is classified as a type of lysosomal storage disorder. There is no known cure, only treatments of the deficiency.

Summary

Bryophytes have been traditionally used for their medicinal properties in China, India, and among Native Americans. Their use in Europe became more widespread following the development of the Doctrine of Signatures. Among the most commonly used, ***Marchantia polymorpha*** was used for liver ailments and is still used in some places, but is also used for boils and abscesses. ***Rhodobryum giganteum*** is used for cardiovascular problems, a use supported by clinical tests.

Traditional uses of bryophytes include treatment for liver ailments, ringworm, heart problems, inflammation, fever, urinary and digestive problems, female problems, infections, lung disease, skin problems, and as filters and cleansing agents against pollutants.

The ability of ***Sphagnum*** to promote healing of flesh wounds is well documented. **Sphagnol** is used to treat boils and mosquito bites, and ***Sphagnum*** in diapers prevents diaper rash.

Acknowledgments

I appreciate the continued support of Robin Stevenson in providing me with interesting articles such as the one on the medical use of mosses growing on skulls. Eric Harris generously shared his papers and images of medicinal bryophytes.

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CHAPTER 2-2

MEDICAL USES: BIOLOGICALLY ACTIVE SUBSTANCES

TABLE OF CONTENTS

CHAPTER 2-2 MEDICAL USES: BIOLOGICALLY ACTIVE SUBSTANCES

Figure 1. Bryophytes and other herbs on sale in a Yunnan, China, market. ***Rhodobryum giganteum*** (upper bag) and ***Leucobryum*** (lower bag), both called Hui Xin Cao. Photo by courtesy of Eric Harris.

Antibiotics and Other Biologically Active Substances

Bryophyte species actually produce broad-range antibiotics (Asakawa 2007a, b, 2008; Asakawa *et al*. 2013). Their usage in surgical dressings, diapers, and other human medicinal applications is well known. And their use has not been confined to Asia (Frahm 2004), but is known in Brazil (Pinheiro da Silva *et al*. 1989), England (Wren 1956), North America (Pejin *et al*. 2011a, b), and Germany (Frahm 2004), as well as in China (Ding 1982; Wu 1982) and India (Watts 1891). Frahm (2007) has reviewed the literature on bryophytes and their antibiotic activity.

Bryophytes discourage the feeding by a variety of organisms, as discussed in the chapters on terrestrial insects, arthropods, and other interaction chapters. Frahm and Kirchhoff (2002) showed that extracts of the epiphytic moss ***Neckera crispa*** (Figure 2) and leafy liverwort ***Porella obtusata*** (Figure 3) both discouraged feeding by the Portuguese slug ***Arion lusitanicus*** (Figure 4).

Figure 2. ***Neckera crispa***, a species that discourages the Portuguese slug from eating it. Photo by Jan-Peter Frahm, with permission.

Figure 3. ***Porella obtusata***, a species that discourages the Portuguese slug from eating it. Photo by Michael Lüth, with permission.

Figure 4. ***Arion lusitanicus***, a slug that avoids eating extracts of the moss ***Neckera crispa*** and leafy liverwort ***Porella obtusata***. Photo by Ondřej Zicha, through Creative Commons.

One indication of the presence of unique and potentially important pharmaceutically and anti-feedant chemicals in bryophytes is the presence of unique odors. This is especially true for liverworts, with more than several hundred new compounds identified among them (Asakawa 2012). In addition, more than 40 new carbon skeletal acetogenins, phenolic compounds, and terpenoids were identified. Testing of these compounds has led to the commercial development of a natural pesticide (Frahm 2004).

Leptolejeunea (Figure 5) and ***Moerckia*** (Figure 6) are distinctly aromatic (Schuster 1966), ***Lophozia bicrenata*** (Figure 7) has a pleasant odor, species of ***Solenostoma*** (Figure 8) smell like carrots, ***Geocalyx graveolens*** (Figure 9) has a turpentine-like odor, and ***Conocephalum conicum*** (Figure 10) smells like mushrooms. The tropical ***Plagiochila rutilans*** (Figure 11) smells like peppermint, caused by several methane monoterpenoids (Heinrichs *et al*. 2001).

Figure 5. ***Leptolejeunea elliptica***, a species with a distinct odor. Photo by Yan Jia-dang, through Creative Commons.

Figure 6. ***Moerckia flotoviana*** female, a species with a distinct odor. Photo by Michael Lüth, with permission.

Figure 7. The leafy liverwort ***Lophozia bicrenata***. Photo by Michael Lüth.

Figure 8. ***Solenostoma hyalina***, a species that smells like carrots. Photo by Janice Glime.

Figure 9. The leafy liverwort ***Geocalyx graveolens***. Underleaf is indicated by the red star. Photo by Michael Lüth.

Figure 10. ***Conocephalum conicum***, a species that smells like mushrooms. Photo by Hermann Schachner, through Creative Commons.

But can you imagine using mosses to lower your cholesterol? Yes, mosses contain polyunsaturated fatty acids that are already known to have important potentials in human medicine, such as preventing atherosclerosis and cardiovascular disease, reducing collagen-induced thrombocyte aggregation, and lowering triacylglycerols and cholesterol in plasma (Radwan 1991).

Figure 11. ***Plagiochila*** sp. ***Plagiochila rutilans*** smells like peppermint. Photo by Lin Kyan, with permission.

It appears that these unique odors result from a combination of many compounds, including monoterpene hydrocarbons such as α-pinene, ß-pinene, camphene, sabinene, myrcene, alpha-terpinene, limonene, fatty acids, and methyl esters of low molecular weight (Hayashi *et al.* 1977). For example, ***Isotachis japonica*** (Figure 12) has at least three aromatic esters: benzyl benzoate, benzyl cinnamate, and B-phenylethyl cinnamate (Matsuo *et al.* 1971).

Figure 12. ***Isotachis*** sp. ***Isotachis japonica*** has at least three aromatic esters. Photo by George Shepherd, through Creative Commons.

But progress in purifying and identifying bryophyte biochemical components and demonstrating their antibiotic effects has been slow. As early as 1952, Madsen and Pates found inhibition of microorganisms in products of bryophytes, including ***Sphagnum portoricense*** (Figure 13), ***S. strictum*** (Figure 14), ***Conocephalum conicum*** (Figure 10), and ***Dumortiera hirsuta*** (Figure 15) (see also Sabovljević *et al*. 2011; Chandra *et al*. 2017). Pavletic and Stilinovic (1963) found that ***Dicranum scoparium*** (Figure 16) strongly inhibited all bacteria tested but Gram-negative *Escherichia coli* (Figure 17). McCleary and Walkington (1966) considered that non-ionized organic acids and polyphenolic compounds might contribute to the antibiotic properties of bryophytes and found eighteen mosses that strongly inhibited one or both of Gram-positive and Gram-negative bacteria, the most active being ***Atrichum*** (Figure

20), ***Dicranum*** (Figure 16), ***Mnium*** (Figure 18), ***Polytrichum*** (Figure 19), and ***Sphagnum***. Reminiscent of ***Dicranum scoparium*** (Figure 16), ***Atrichum undulatum*** (Figure 20) was effective on everything tested except *Enterobacter aerogenes* (drug resistant and infectious to people with weak immune systems; Figure 21) and *E. coli*.

Figure 13. ***Sphagnum portoricense***, a species that inhibits microorganisms. Photo by Blanka Shaw, with permission.

Figure 14. ***Sphagnum strictum***, a species that inhibits microorganisms. Photo by Jan-Peter Frahm, with permission.

Figure 15. ***Dumortiera hirsuta,*** a species that inhibits microorganisms. Photo by Michael Lüth, with permission.

Figure 16. ***Dicranum scoparium***, a species that inhibited all bacteria tested but Gram-negative *Escherichia coli*. Photo by Janice Glime.

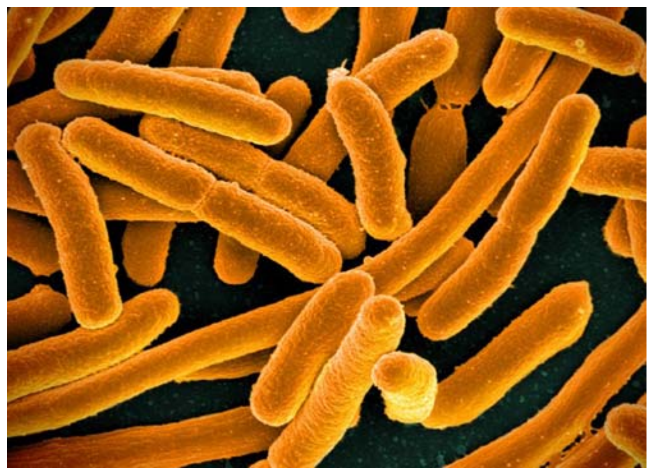

Figure 17. *Escherichia coli*, a species that is inhibited by acetone-soluble extracts of several thallose liverwort species. Photo by NIAID, through Creative Commons.

Figure 18. ***Mnium spinulosum***. Members of the genus ***Mnium*** are among the most active against one or both of Gram-positive and Gram-negative bacteria. Photo by Michael Lüth, with permission.

Figure 19. ***Polytrichum commune***. Members of the genus ***Polytrichum*** are among the most active against one or both of Gram-positive and Gram-negative bacteria. Photo by Michael Lüth, with permission.

Figure 20. ***Atrichum undulatum*** is a moss that is very effective against a wide range of bacteria. Photo by Michael Lüth.

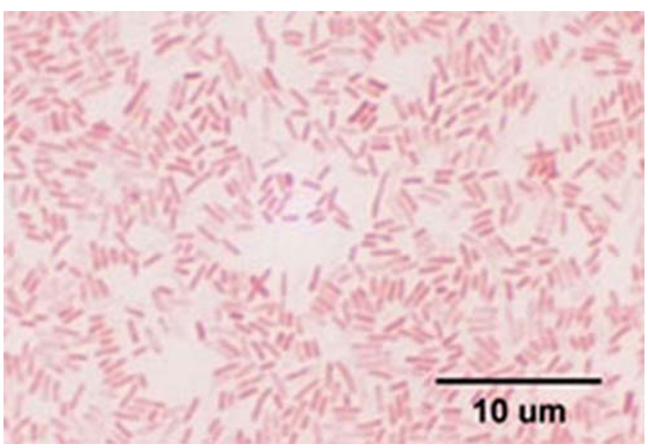

Figure 21. *Enterobacter aerogenes*, a bacterium that seems to be resistant to extracts of 18 moss species that negatively affect other bacteria. Photo by Alexa Rakusin Muna, through Creative Commons.

Gupta and Singh (1971) found high occurrence of antibacterial activity in extracts of ***Barbula*** species (Figure 22), reaching as high as 36.2%, whereas it was only half that in ***Timmiella*** species (Figure 23) (18.8%). In 1982, Asakawa *et al.* (1982) isolated three prenyl bibenzyls from ***Radula*** spp. (Figure 24) and demonstrated that these bibenzyls could inhibit growth of *Staphylococcus aureus* (Figure 25) at concentrations of 20.3 µg ml^{-1}. Out of more than 80 species tested, Ichikawa (1982) and coworkers (1983) found antimicrobial activity in nearly all. Acyclic acetylenic fatty acid and cyclophentenonyl fatty acid extracts from the mosses completely inhibited the growth of the rice blast fungus *Magnaporthe grisea* (Figure 26). Belcik and Wiegner (1980) reported antimicrobial activity in extracts of the liverworts ***Pallavicinia*** (Figure 27) and ***Reboulia*** (Figure 28), and Isoe (1983) reported it from ***Porella*** (Figure 29).

Figure 22. ***Barbula convoluta***, member of a genus with high antibacterial activity. Photo by Michael Lüth, with permission.

Figure 23. ***Timmiella*** sp., a genus with high antibacterial activity. Photo by Ken-ichi Ueda through Creative Commons.

Figure 24. ***Radula complanata***, a species with bibenzyls that could inhibit growth of *Staphylococcus aureus*. Photo by Michael Lüth, with permission.

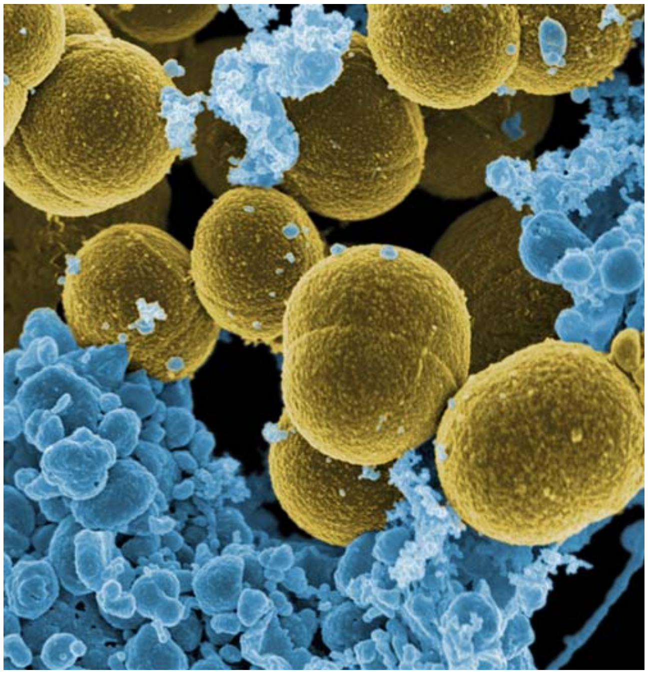

Figure 25. *Staphylococcus aureus*, a bacterium that is not inhibited by the thallose liverwort ***Riccia fluitans***. Photo by NIAID, through Creative Commons.

Figure 26. *Magnaporthe grisea*, a plant pest that is inhibited by several liverworts. Photo by IRRI Photos, through Creative Commons.

Figure 27. ***Pallavicinia lyellii***, member of a genus with reported antimicrobial activity. Photo by Jan-Peter Frahm, with permission.

Figure 28. ***Reboulia hemisphaerica***, member of a genus with reported antimicrobial activity. Photo by Malcolm Storey <www.discoverlife.org>, with online permission.

Figure 29. ***Porella platyphylla***, member of a genus with reported antimicrobial activity. Photo by Tim Waters through Creative Commons.

Another three species of mosses [***Anomodon rostratus*** (Figure 30), ***Plagiomnium cuspidatum*** (Figure 31), ***Orthotrichum rupestre*** (Figure 32)] produce substances that inhibit bacteria and fungi, but these inhibitors seem to be unstable products that vary considerably among species and possibly also among seasons (McCleary *et al*. 1960). Indeed, it would appear that some of these antibiotic compounds are the very ones that bryophytes produce in response to stress. However useful they may be, it seems that these discoveries have not yet found their way into medical practice.

Figure 30. ***Anomodon rostratus***, a species that inhibits bacteria and fungi. Photo by Dale A. Zimmerman Herbarium, Western New Mexico University, with permission.

Figure 31. ***Plagiomnium cuspidatum***, a species that inhibits bacteria and fungi. Photo by Štěpán Koval, with permission.

Figure 32. ***Orthotrichum rupestre***, a species that inhibits bacteria and fungi. Photo by Michael Lüth, with permission.

Scientists have found innumerable kinds of biological activity in compounds from bryophytes. Even in a single species, one might find multiple kinds of activity. For example, the liverworts ***Plagiochasma japonica*** and ***Marchantia emarginata*** subsp. ***tosana*** (Figure 33) exhibit antitumor activity, antifungal and antimicrobial activity, inhibition of superoxide release, inhibition of thrombin activity, and muscle relaxation (Lahlou *et al.* 2000). As is often the case with herbal medicine, the effect of the total extract is better than that of the isolated compounds, perhaps due to a synergistic effect (Frahm 2004).

Figure 33. ***Marchantia emarginata*** subsp. ***tosana***, a subspecies with a wide range of medicinal properties. Photo by Taiwan Mosses, through Creative Commons.

On the other hand, some researchers claim that antibiotic properties of some mosses, including ***Sphagnum*** (Figure 13, Figure 14), may actually be the work of associated microorganisms. In some cases, *e.g.* ***Sphagnum***, it may be *Penicillium* sp. (Figure 34) effecting this antibiotic ability (Lewington 1990). Or is it the closely associated **Cyanobacteria**, such as ***Nostoc*** (Figure 35) (Spjut *et al*. 1988; Solheim & Zielke 2002)?

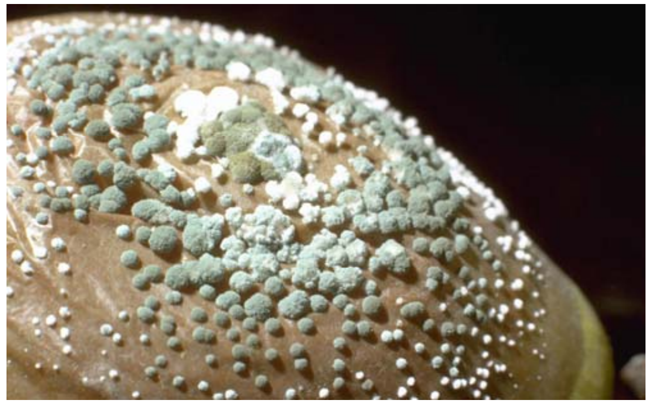

Figure 34. ***Penicillium expansum*** on pear, in a genus that can grow on ***Sphagnum*** and may contribute to its antibiotic effects. Photo by H. J. Larsen, through Creative Commons.

Figure 35. ***Nostoc pruniforme***, in a genus with close associations with ***Sphagnum*** and other bryophytes and could contribute to antibiotic properties. Photo by Lairich Rig, through Creative Commons.

Painter (2003) notes that ***Sphagnum*** (Figure 13, Figure 14) can be 3-4 times as absorbent as cotton equivalents. But its call to fame seems to be its ability to react chemically with all sorts of proteins. ***Sphagnum*** species have the potential to immobilize whole bacterial cells, enzymes, exotoxins, and lysins that are secreted by most of the invasive pathogens. Once these are immobilized, they are inactivated by a **Maillard reaction**.

The **Maillard reaction** makes this story complex. It is known to suppress the virulence gene expression operon in the bacterium *Listeria monocytogenes* (Figure 36) (Sheikh-Zeinoddin *et al*. 2000), so that is a good thing. On the other hand, a variety of foods form potential cancer-causing acrylamides, especially fried foods (Stadler *et al*. 2002). Such acrylamides can be released by thermally treating certain amino acids such as asparagine, especially in combination with reducing sugars through the Maillard reaction. The early Maillard reaction products are N-glycosides. Painter (1998) found that the Maillard reaction inhibits microbial growth in animal products preserved in bogs by sequestering ammonia, amino acids, and peptides, whereas the polymeric end-products (melanoidins) inhibit their growth by cross-linking the polypeptide chains and sequestering essential multivalent metal cations. In short, the Maillard reaction appears to be an important component of the ***Sphagnum*** (Figure 13, Figure 14) antibiotic activity. Furthermore, its preservative ability correlates with α-keto-carboxylate groups in a glycuronoglycan (**sphagnan**) that comprises ~60% of the holocellulose in the ***Sphagnum*** hyaline cell walls.

Figure 36. *Listeria monocytogenes*, a bacteria species that is inhibited by extracts of the leafy liverwort ***Porella cordaeana***. Photo from CDC, through public domain.

Harris (2009) considered phylogenetic, elevational, and latitudinal relationships of the production of flavonoids in medicinal mosses. He was unable to show any significant correlation between phylogenetic independent contrasts of total phenolic content, number of flavonoids, or percent luteolin derivatives. He furthermore found no correlation with elevation or latitude. He could not rule out the possible correlation with fine-scale ecological features, and he considered flavonoid variation to reflect recent evolution.

Labbé *et al.* (2007) tested the thallose liverwort ***Riccardia polyclada*** for potential pesticidal properties. They identified four compounds that contributed to lethality in the brine shrimp (*Artemia salina*; Figure 37). Two of the compounds had moderate activity as an antifeedant for the African cotton leafworm (*Spodoptera littoralis*; Figure 38). They also inhibited culture growth of the fungal plant pathogen *Cladosporium herbarum* (Figure 39).

Figure 37. ***Artemia salina***, a species that is killed by extracts from the liverwort ***Riccardia polyclada***. Photo by Hans Hillewaert, through Creative Commons.

Figure 38. ***Spodoptera littoralis***, a species that is discouraged from eating the liverwort ***Riccardia polyclada*** by its chemical compounds. Photo from Forestry Images, through Creative Commons.

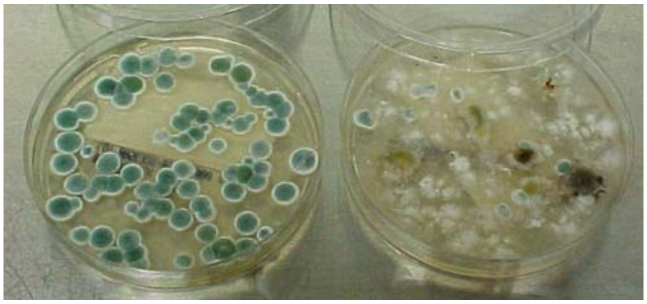

Figure 39. ***Cladosporium*** spp., fungal pathogens that are inhibited by extracts from the liverwort ***Riccardia polyclada***. Photo from Mold Treatment Centers of America, through Creative Commons.

Antimicrobial Activity

Our knowledge of antimicrobial activity of bryophytes is mostly based on ***Sphagnum*** (Figure 13, Figure 14). However other bryophytes are now known to have antibiotic properties. Some of these may just be folklore as they have not been tested experimentally. For example, Cheng *et al.* (2008) reported the folk use of ***Polytrichum*** to treat pneumonia. And we have already seen that ***Polytrichum commune*** (Figure 19) is used in a tea for treating colds (Gulabani 1974; Beike *et al.* 2010).

Nevertheless, antibiotic properties have been demonstrated in the laboratory. Moss activity against Gram-positive and Gram-negative bacteria have been demonstrated (Basile *et al.* 1999; Merkuria *et al.* 2005; Zhu *et al.* 2006). Asakawa (2007a, b) has demonstrated many effects of liverworts.

Kumar *et al.* (2007), in their review of classical ethnobotanical Indian uses, reported the antibacterial value of the mosses ***Anomodon rostratus*** (Figure 30), ***Atrichum angustatum*** (Figure 40), ***A. undulatum*** (Figure 41), and ***Hyophila involuta*** (Figure 42) and the thallose liverworts ***Conocephalum conicum*** (Figure 10) and ***Dumortiera hirsuta*** (Figure 15). These bryophytes reportedly produce antibiotics. The leafy liverwort ***Radula complanata*** (Figure 24) similarly has antimicrobial properties. To these we can add the antiseptic properties of ***Frullania tamarisci*** (Figure 43) (Asakawa 2007b; Chandra *et al.* 2017) and antimicrobial activity of ***Pallavicinia*** sp. (Figure 27) (Azuelo *et al.* 2011; Chandra *et al.* 2017).

Figure 40. ***Atrichum angustatum***, a species with antibacterial properties. Photo by Janice Glime.

Figure 41. ***Atrichum undulatum***, a species with antibacterial properties. Photo by Brian Eversham, with permission.

Figure 42. ***Hyophila involuta***, a species with antibacterial properties. Photo by Michael Lüth, with permission.

Figure 43. ***Frullania tamarisci***, an epiphytic species with antiseptic properties, having both allergenic and medicinal properties. Photo by Michael Lüth, with permission.

Recent tests on the floating thallose liverwort ***Riccia fluitans*** (Figure 44) from Florida indicated no ability to inhibit growth of the tested bacteria [*Pseudomonas aeruginosa* (Figure 45), *Staphylococcus aureus* (Figure 25)] or yeast (*Candida albicans*; Figure 46) (Pates & Madsen 1955). Vashistha *et al*. (2007) determined the antimicrobial activity of three other thallose liverworts. They found that water soluble extracts from ***Conocephalum conicum*** (Figure 10), ***Marchantia polymorpha*** (Figure 47), and ***Plagiochasma appendiculatum*** (Figure 48) had no effect on any of the pathogens tested [Gram-negative bacteria *Escherichia coli* (Figure 17) and *Salmonella typhi* (a variant of *S. enterica*; Figure 49)] and fungi *Aspergillus niger* (Figure 50) and yeast *Candida albicans* (Figure 46). However, acetone-soluble extracts of all three bryophyte species were inhibitory against the pathogens. They were more effective against the growth of *S. typhi* than against *E. coli*. ***Plagiochasma appendiculatum*** had a strong inhibitory effect against *A. niger* and ***Conocephalum conicum*** was strongly inhibitory to *Candida albicans*.

Figure 44. ***Riccia fluitans***, a species that was unable to inhibit the growth of several tested bacteria. Photo by Štěpán Koval, with permission.

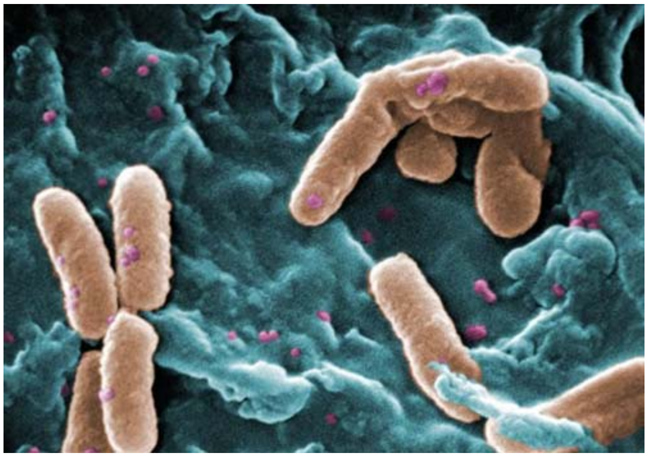

Figure 45. ***Pseudomonas aeruginosa***, a species that is not inhibited by ***Riccia fluitans***. Photo by Janice Haney Carr, through Creative Commons.

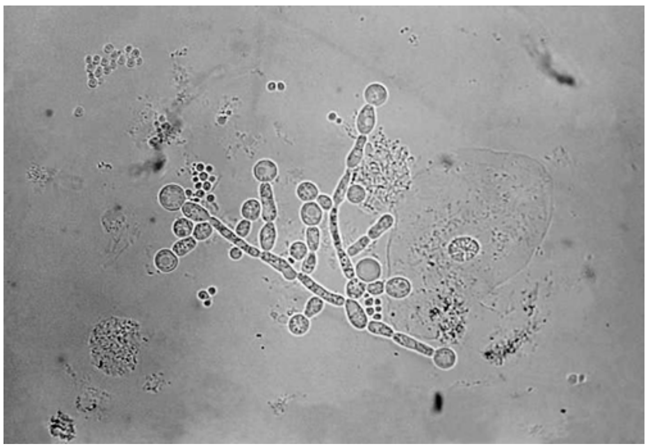

Figure 46. *Candida albicans*, a yeast species that is inhibited by extracts of the liverworts ***Conocephalum conicum***, ***Marchantia polymorpha***, and ***Plagiochasma appendiculatum***, but not ***Riccia fluitans***. Photo from Public Health Image Library, through public domain.

Figure 47. ***Marchantia polymorpha*** subsp. ***ruderalis***. This species had no effect on the fungi or Gram negative bacteria tested by Vashistha *et al*. Photo by Malcolm Storey, through Creative Commons

Figure 48. ***Plagiochasma appendiculatum***, a species that is effective against some pathogens. Photo by Ying Jia-dong, through Creative Commons.

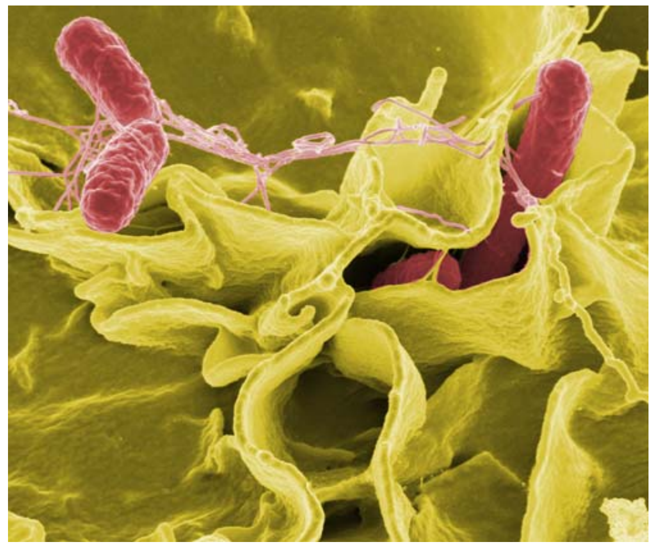

Figure 49. ***Salmonella enterica*** invading human cells. Photo by NIAID, through public domain.

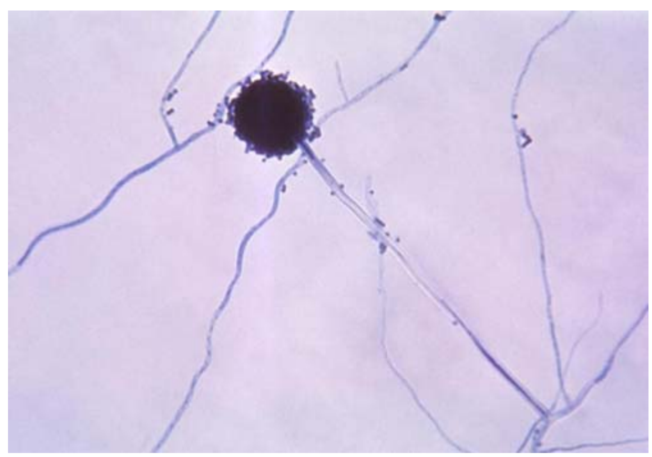

Figure 50. *Aspergillus niger*, a fungal species that is inhibited by extracts of the liverworts ***Conocephalum conicum***, ***Marchantia polymorpha***, and ***Plagiochasma appendiculatum***. Photo from Public Health Image Library, through public domain.

Bukvicki *et al*. (2012), using solid-phase microextraction-gas chromatography mass spectrometry, explored the volatile components of the leafy liverwort ***Porella cordaeana*** (Figure 51). Using methanol, ethanol, and ethyl acetate to extract terpenoids, they were able to identify sesquiterpene hydrocarbons and monoterpene hydrocarbons. These same hydrocarbons were active against the eleven food microorganisms tested, but at different concentrations among the microorganisms. The fungi among these will be discussed blow. Affected bacterial strains were *Salmonella enteritidis* (food poisoning that causes diarrhea, fever, and abdominal cramps; Figure 52), *Escherichia coli* (commonly found in lower intestine of warm-blooded organisms with some strains causing food poisoning; Figure 17), and *Listeria monocytogenes* (very virulent food pathogen that causes the infection listeriosis; Figure 36). Methanol extracts showed the best activity.

Figure 51. ***Porella cordaeana***, a species that is able to inhibit a variety of yeasts and bacteria. Photo by J. C. Schou, with permission.

Figure 52. *Salmonella enteritidis*, a bacteria species that is inhibited by extracts of ***Porella cordaeana***. Photo through OGL (public domain).

It appears that differences in bryophyte extract activity among various pathogens may be common. Extracts of the liverworts ***Marchantia polymorpha*** (Figure 47), ***Porella platyphylla*** (Figure 29), and the moss ***Dicranum scoparium*** (Figure 16) showed antimicrobial effects on the Gram-positive bacteria *Bacillus subtilis* (Figure 53), *Staphylococcus aureus* (Figure 25), and *Micrococcus luteus* (Figure 54) (Pavletic & Stilinovic 1963; Frahm 2004). These same bryophytes exhibited no activity against Gram-negative *Escherichia coli* (Figure 17).

Figure 53. SEM of ***Bacillus subtilis***, a species that is inhibited by extracts of several bryophyte species. Photo by Davehwng, through Creative Commons.

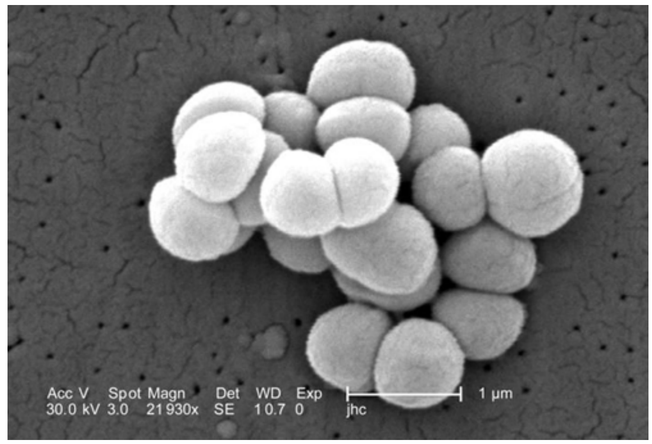

Figure 54. *Micrococcus luteus*, a bacteria species that is inhibited by extracts of several bryophyte species. Photo by Janice Carr, through public domain.

Basile *et al*. (1999) isolated seven pure flavonoids from five species of mosses. Some of these exhibited strong antibacterial effects against the bacteria *Enterobacter cloaceae* (Figure 55), *E. aerogenes* (Figure 56), and *Pseudomonas aeruginosa* (Figure 45). They were mainly active against Gram-negative bacteria that caused severe opportunistic infections and were at the same time resistant to commonly used antibacterial therapy. This means that the bryophyte products could become important tools in treating some bacterial infections.

Figure 55. ***Enterobacter cloaceae***, a species that is active against Gram-negative bacteria. Photo by Nathan Reading, through Creative Commons.

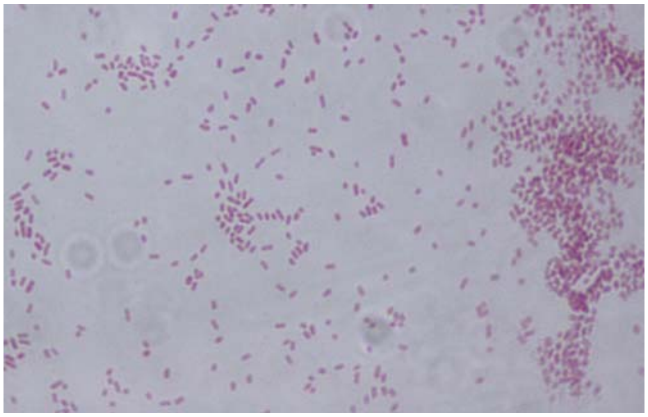

Figure 56. ***Enterobacter aerogenes***, a species that is active against Gram-negative bacteria. Photo by Riraq25, through Creative Commons.

Ariyo *et al*. (2011) compared the efficacy of extracts from the Nigerian thallose liverwort ***Riccia nigerica*** as antimicrobial agents. These extracts were tested against the bacteria *Bacillus subtilis* (Figure 53), *Pseudomonas aeruginosa* (Figure 45), *Shigella dysenteriae* (Figure 57), and *Staphylococcus aureus* (Figure 25) and fungi *Rhizopus* spp. (Figure 58), *Aspergillus flavus* (Figure 59), *A. niger* (Figure 50), *Penicillium* spp. (Figure 34), and and demonstrated strong significant antibacterial and antifungal activity.

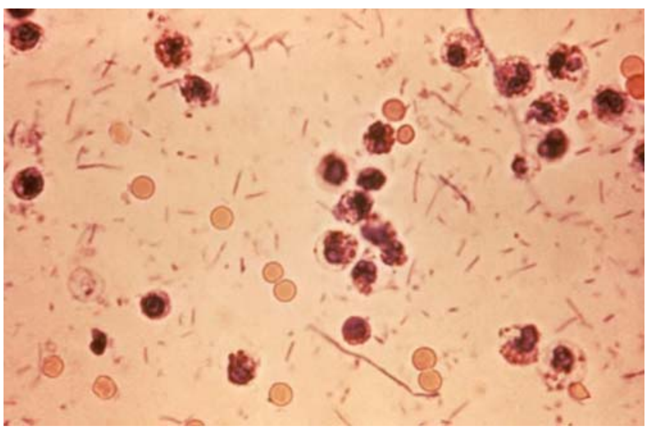

Figure 57. *Shigella dysenteriae*, a bacterial species that is inhibited by extracts of ***Riccia nigerica***. Photo by Public Health Image Library, through public domain.

Figure 58. ***Rhizopus*** on yam, a fungal species that is inhibited by extracts of ***Riccia nigerica***. Photo by Charles Averre, through Creative Commons.

Figure 59. ***Aspergillus flavus***, a fungal species that is inhibited by extracts of ***Riccia nigerica***. Photo by Medmyco, through Creative Commons.

The leafy liverwort ***Ptilidium pulcherrimum*** (Figure 60) exhibits antimocrobial activity against both Gram + bacteria and Gram negative bacteria, but the effect is greater on the Gram positive bacteria (Veljić *et al*. 2010).

Figure 60. ***Ptilidium pulcherrimum***, a species that is effective against both Gram positive and Gram negative bacteria. Photo by Hermann Schachner, through Creative Commons

Antifungal Activity

Although mosses are known to harbor fungi and will quickly become infected if kept moist in a plastic bag, some fungi are inhibited by many species of bryophytes, including many that cause skin infections. Jennings (1926) reported moss immunity to molds as early as 1926, but the possibility of using them as a source of antifungal activity seems to have been largely overlooked. Among these, the cosmopolitan moss ***Hypnum cupressiforme*** (Figure 61) has remarkable antibacterial and antifungal effects. Ven Hoof *et al*. (1981) demonstrated strong antibacterial and antifungal effects by extracts of ***Hypnum cupressiforme***.

Figure 61. ***Hypnum cupressiforme***, a species that is effective against fungi that cause skin infections. Photo by Michael Lüth.

Kumar *et al*. (2007) report antifungal properties for the widespread leafy liverwort ***Porella platyphylla*** (Figure 29). Ando and Matsuo (1984) demonstrated antifungal effects of bryophytes on human pathogenic fungi, but they warned that while the bryophyte extracts have fungicidal and antifeedant effects, they also may cause allergic reactions and dermatitis for some humans.

Bukvicki *et al*. (2012), using solid-phase microextraction-gas chromatography mass spectrometry, explored the volatile components of the related liverwort ***Porella cordaeana*** (Figure 51). Using methanol, ethanol, and ethyl acetate to extract terpenoids, they were able to identify sesquiterpene hydrocarbons and monoterpene hydrocarbons. These same hydrocarbons were active against the eleven food microorganisms tested, but at different concentrations among the microorganisms. These included the yeasts *Saccharomyces cerevisiae* (yeast used in wine making, baking, and brewing, but antibodies against *S. cerevisiae* are found in 60-70% of patients with Crohn's disease; Figure 62), *Zygosaccharomyces bailii* (species causing significant spoilage in the food industry; Figure 63), *Aureobasidium pullulans* (an inhabitant of humidifiers or air conditioners that can lead to hypersensitivity pneumonitis; Figure 64), *Pichia membranifaciens* (species causing grey mold of fruits; Figure 65) (2 strains), *Pichia anomala* (used in winemaking) (2 strains), and *Yarrowia lipolytica* (used in industrial microbiology for production of specialty lipids). Methanol extracts showed the best activity.

Figure 62. *Saccharomyces cerevisiae* SEM, a yeast species that is inhibited by extracts of the leafy liverwort ***Porella cordaeana***. Photo by Mogana Das Murtey and Patchamuthu Ramasamy, through Creative Commons.

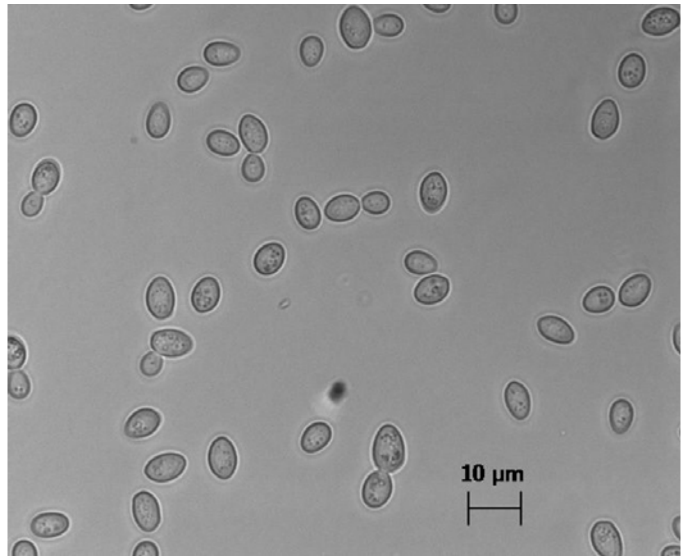

Figure 63. *Zygosaccharomyces bailii*, a yeast species that is inhibited by extracts of ***Porella cordaeana***. Photo by DTDT, through Creative Commons.

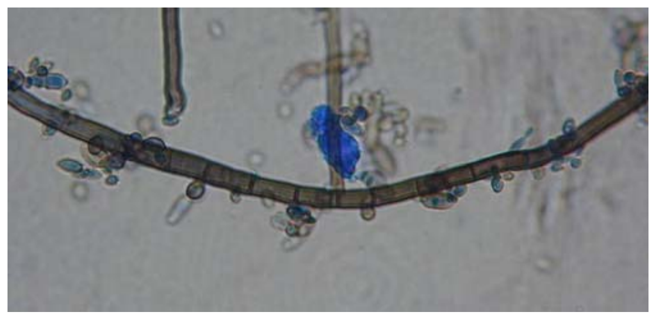

Figure 64. *Aureobasidium pullulans*, a yeast species that is inhibited by extracts of the leafy liverwort ***Porella cordaeana***. Photo by Tom Volk, through Creative Commons.

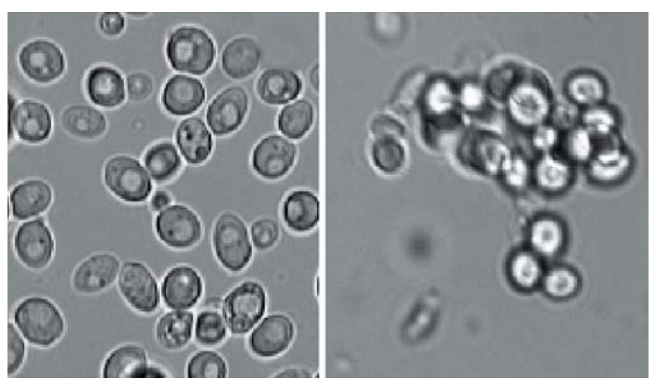

Figure 65. *Pichia membranaefaciens*, a yeast species that is inhibited by extracts of ***Porella cordaeana***. Photo by Luciana Francisco Fleuri & Hélia Harumi Sato, through Creative Commons.

The leafy liverwort ***Ptilidium pulcherrimum*** (Figure 60) is not only effective against bacteria, but also against fungi (Veljić *et al*. 2010). Its best antifungal activity was against *Trichoderma viride* (Figure 66), compared to the activity of the synthetic bifonazol.

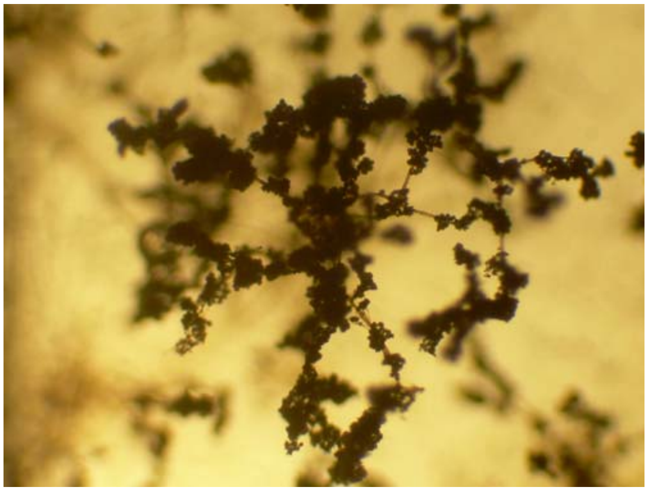

Figure 66. ***Trichoderma viride*** conidiophores, a fungal species that is inhibited by ***Atrichum undulatum***, ***Physcomitrella patens***, and ***Marchantia polymorpha***. Photo by Ninjatacoshell, through Creative Commons.

The absence of fungal diseases in liverworts led Pryce (1972) to suggest that **lunularic acid**, a hormone that affects aging in liverworts but not in mosses, might be responsible for liverwort antifungal activity. Banerjee and Sen (1979; Bannerjee 1974) found that the degree of antibiotic activity in a given species may depend on the age of the gametophyte; Matsuo *et al*. (1982a, 1982b, 1983) supported this conclusion by demonstrating that antifungal activity against *Botrytis cinerea* (Figure 67), *Pythium debaryanum* (Figure 68), and *Rhizoctonia solani* (Figure 69) by the liverwort ***Herbertus aduncus*** (Figure 70) was age-dependent. They subsequently isolated three aging substances from it: (-)-alpha-herbertenol; (-)-Beta-herbertenol, and (-)-alpha-formylherbertenol.

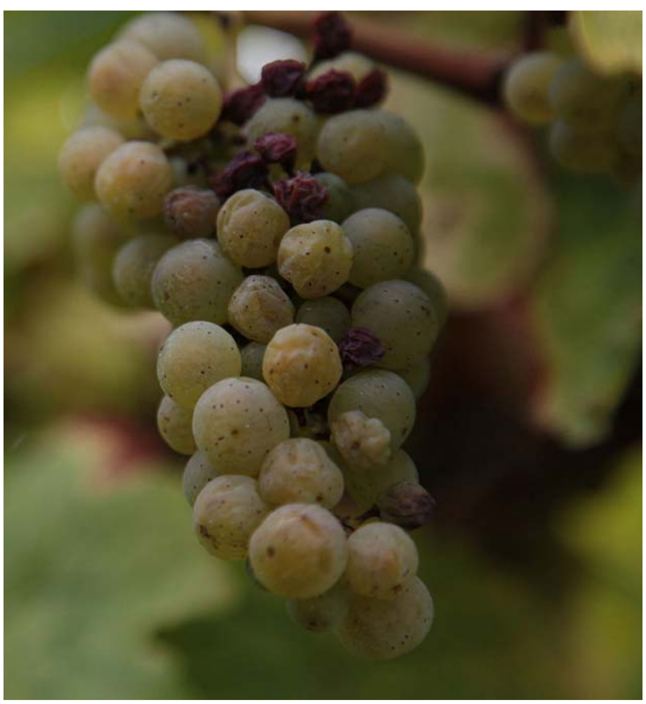

Figure 67. ***Botrytis cinerea*** on grapes. The liverwort ***Herbertus aduncus*** can exercise antifungal activity against this fungus, but activity is age-dependent. Photo by Alexandre Dulaunoy, through Creative Commons.

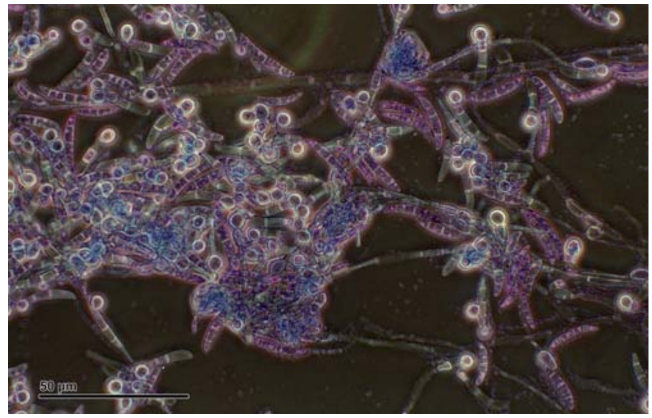

Figure 68. ***Pythium*** sp. The liverwort ***Herbertus aduncus*** can exercise antifungal activity against this fungus, but activity is age-dependent. Photo by Josef Reischig, through Creative Commons.

Figure 69. ***Rhizoctonia solani*** infecting leaves. The liverwort ***Herbertus aduncus*** can exercise antifungal activity against this fungus, but activity is age-dependent. Photo by Howard F. Schwartz, through Creative Commons.

Figure 70. ***Herbertus aduncus***, a leafy liverwort that can exercise antifungal activity against several fungi, but activity is age-dependent. Photo by Martin Hutten, with permission.

Vashistha *et al*. (2007) determined the antimicrobial activity for the thallose liverworts ***Plagiochasma appendiculatum*** (Figure 48), ***Marchantia polymorpha*** (Figure 47), and ***Conocephalum conicum*** (Figure 10). Acetone-soluble extracts of all three bryophyte species were inhibitory against the fungal pathogens tested. ***Plagiochasma appendiculatum*** had a strong inhibitory effect against *Aspergillus. niger* and ***C. conicum*** was strongly inhibitory to *Candida albicans*. When Niu *et al*. (2006) tested ***Marchantia polymorpha*** (Figure 47) for antifungal activities against the yeast *Candida albicans* (Figure 46), they found **plagiochin** E, 13,13'-O-isoproylidenericcardin D, and neomarchantin A were active against the yeast. The other identified compounds had only weak effects.

Sabovljević *et al*. (2011) used DMSO extracts of both cultured and wild grown mosses ***Atrichum undulatum*** (Figure 20) and ***Physcomitrella patens*** (Figure 71-Figure 72) and thallose liverwort ***Marchantia polymorpha*** ssp. ***ruderalis*** (Figure 47) to test for antifungal activity. Using *Aspergillus versicolor* (Figure 73), *Aspergillus fumigatus* (Figure 74), *Penicillium funiculosum* (see Figure 34), *Penicillium ochrochloron*, and *Trichoderma viride* (Figure 66), these researchers demonstrated antifungal activity by all three bryophytes against all five fungal species. Most of the bryophytes grown in culture had greater antibiotic activity than the wild-grown ones.

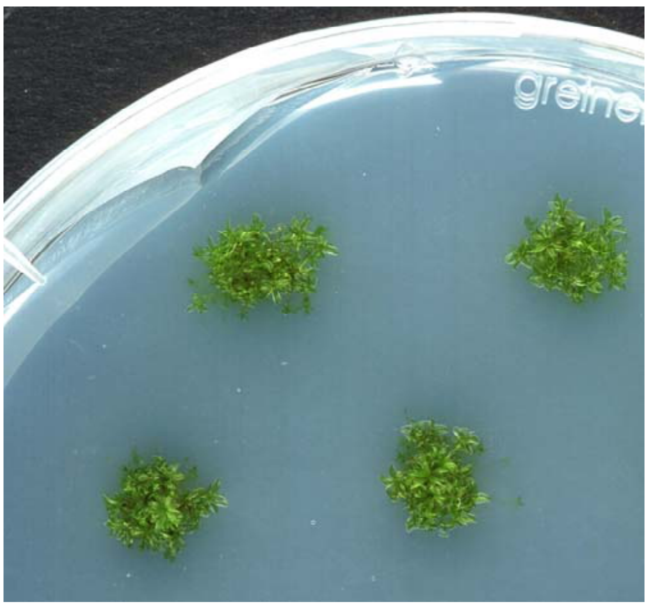

Figure 71. ***Physcomitrella patens*** growing on agar plates. Photo by Sabisteb, through Creative Commons.

Figure 72. ***Physcomitrella patens***, a source of human proteins and blood-clotting factor IX. Photo by Michael Lüth.

Figure 73. ***Aspergillus versicolor***, a fungal species that is inhibited by ***Atrichum undulatum***, ***Physcomitrella patens***, and ***Marchantia polymorpha***. Photo by James Scott, through Creative Commons.

Figure 74. ***Aspergillus fumigatus***, a fungal species that is inhibited by ***Atrichum undulatum***, ***Physcomitrella patens***, and ***Marchantia polymorpha***. Photo through Creative Commons.

Alcoholic extracts of all twenty bryophytes tested at Bonn University had antifungal activity on infected crops (Frahm 2004), as demonstrated in a Petri dish (Figure 75). Frahm reports curing a fungal infection of the skin with a bryophyte extract. The success was reported in a TV magazine and a published book, causing a number of people to use the extract for fungal infections, mostly with favorable results. However, Frahm warns that the biologically active substances are terpenoids, and these may cause allergic effects to some people (Ando & Matsuo 1984). One reputedly can cure athlete's foot by walking through a peat bog, presumably because of these same terpenoids (Frahm 2004).

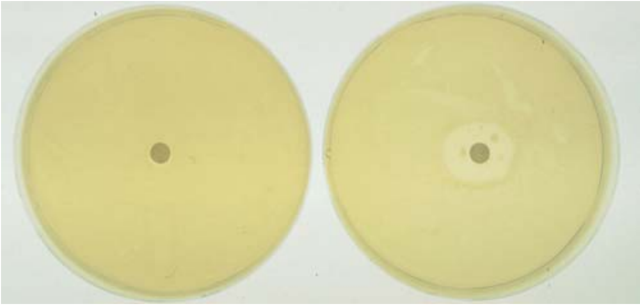

Figure 75. Bryophytes are known to inhibit growth of some kinds of bacteria and fungi. **Left:** Microbes grow uninhibited around a disk with only extraction fluid. **Right:** A zone of inhibition occurs around the disk with bryophyte extract. Photo by Jan-Peter Frahm.

One extract has actually been patented to cure fungal infections of horses (Frahm 2004). An industrious horse owner was inspired by what he read about the Bonn experiments and made a paste of ***Ceratodon purpureus*** (Figure 76) and ***Bryum argenteum*** (Figure 77). The fungus disappeared from the horse in 24 hours! This same extract is also sold as a human foot cream to refresh and fight odor. Unfortunately, the use for curing fungal infections cannot be mentioned in advertising because then it would require the extensive testing necessary to meet medical approval, which might be difficult because it can cause allergies and dermatitis in some people. It also works as an antifeedant against slugs. Unfortunately, to date it must be extracted from field-collected material, creating conservation concerns.

Figure 76. ***Ceratodon purpureus***, a species was used with ***Bryum argenteum*** and killed a fungal infection on a horse. Photo by Janice Glime.

It appears that some bryophytes may contribute to antifungal compounds by hosting a fungus that manufactures both antifungal and antitumor compounds (Guo *et al*. 2008). The leafy liverwort ***Scapania verrucosa*** hosts the fungus ***Chaetomium fusiforme*** (Figure 78). Not only does the latter produce both antifungal and antitumor compounds, but the liverwort itself likewise produces them. However, the fungus compounds provide superior properties and the liverwort might contribute to the medicinal field through this fungal **endophyte** (organisms growing within cells of plant, ranging from symbiotic to parasitic).

Figure 77. ***Bryum argenteum***, a species that was used in a paste with ***Ceratodon purpureus*** and killed a fungal infection on a horse. Photo by Martin Hutten, with permission.

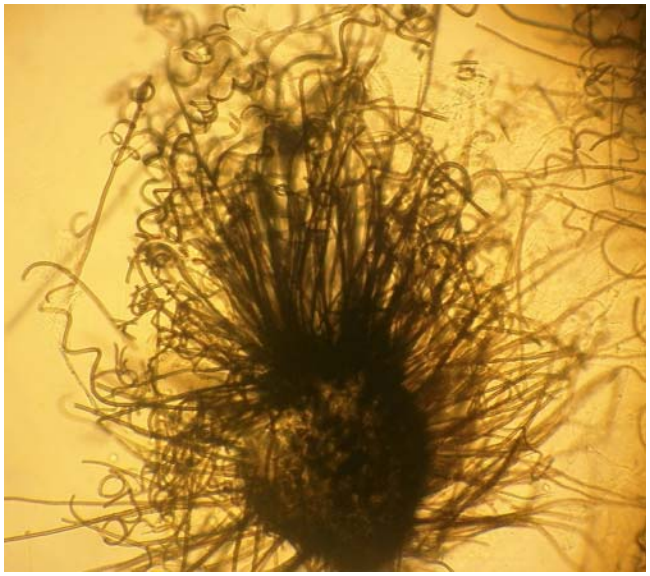

Figure 78. ***Chaetomium globosum***. The fungus ***Chaetomium fusiforme*** occurs on ***Scapania verrucosa*** and produces both antifungal and antitumor compounds. Photo by Ulitca, through Creative Commons.

Antiviral Activity

Even viruses may some day be cured by extracts of mosses, but we cannot simply identify them as "moss" as many of our ecologist friends have been wanton to do in reporting the ground cover. The Maoris of New Zealand have used bryophytes to treat venereal disease by packing wet plants on the infected organs (Frahm 2004). Nevertheless, van Hoof and coworkers (1981) found no effect of 20 species of moss extracts on the herpes virus, but earlier Klöcking *et al.* (1976) found that at least some peat humic acids possess antiviral activity against herpes simplex virus types 1 and 2, interfering primarily with the adsorption of viruses to host cells.

Sphagnum (Figure 13, Figure 14) produces several antivirally active humic acids, and ***Camptothecium*** (Figure 79) extracts can inhibit growth of the poliovirus (Witthauer *et al.* 1976; van Hoof *et al.* 1981). Nevertheless, actual usage of bryophytic extracts has not developed outside of Asia.

Figure 79. ***Camptothecium lutescens***, in a genus that can inhibit growth of the poliovirus. Photo by David T. Holyoak, with permission.

Cancer and Anti-tumor Properties

In the same year as the Madsen and Pates (1952) report of antibiotics in bryophytes, Belkin *et al.* (1952-53) reported anticancer activity against Sarcoma 37 in mice, using extracts of ***Polytrichum juniperinum*** (Figure 80). But application of the antitumor activity fared no better and was apparently not rediscovered in bryophytes until the next century. Finally, Anterola *et al*. (2009) considered the anticancer drug precursors in mosses to be so important that they titled their presentation on them "Turning precursors into gold: Production of anticancer drug precursors in moss."

Figure 80. ***Polytrichum juniperinum*** with antheridial splash cups, a species that produces anticancer compounds. Photo by Paul Slichter, with permission.

Fu *et al*. (2009) attempted to show anti-cancer capabilities of the moss ***Polytrichum commune*** (Figure 19). To this end, they isolated two "unusual" flavones and other compounds from this moss. However, when tested against a small panel of cancer cell lines, they failed to find any activity.

Kumar *et al*. (2007) found that Indians have used ***Polytrichum juniperinum*** (Figure 80) to treat cancer. The anti-tumor use of bryophytes in India included ***Chiloscyphus polyanthos*** (Figure 81), ***Diplophyllum albicans*** (Figure 82), ***D. taxifolium*** (Figure 85), ***Marchantia palmata***, and ***M. polymorpha*** (Figure 47). ***Frullania tamarisci*** (Figure 43) is used as an antileukemic agent. To this list, others added ***Riccardia*** sp. (Figure 84) (Azuelo *et al*. 2011; Alam 2012; Chandra *et al*. 2017) and ***Plagiochila*** sp. (Figure 11) (Asakawa 2007; Alam 2012; Chandra *et al*. 2017).

Figure 81. ***Chiloscyphus polyanthos***, a species that may cause allergic reactions. Photo by Barry Stewart, with permission.

Figure 82. ***Diplophyllum albicans***, used as an anti-tumor treatment in India and as an agent against epidermoid carcinoma. Photo by Michael Lüth, with permission.

Asakawa (1981) has shown that several compounds from leafy liverworts exhibit antileukemic activity. From the thallose species, Marchantin A from ***Marchantia palacea*** (Figure 83), ***M. polymorpha*** (Figure 47), and ***M. emarginata*** subsp. ***tosana*** (Figure 33), riccardin from ***Riccardia multifida*** (Figure 84), and perrottetin E from ***Radula perrottetii*** all show cytotoxicity against the leukemic KB cells (Asakawa *et al*. 1982).

Figure 83. ***Marchantia paleacea***, a thallose liverwort known for its antileukemic activity. Photo by Jan-Peter Frahm, with permission.

Figure 84. ***Riccardia multifida***, a thallose liverwort known for its antileukemic activity. Photo by Michael Lüth, with permission.

In 1976, Adamek reported that peat preparations hold some promise against some types of human cancer. In 1977, Ohta and coworkers (1977) reported that diplophyllin, isolated from the liverworts ***Diplophyllum albicans*** (Figure 82) and ***D. taxifolium*** (Figure 85), shows significant activity (ED50 4-16 µg/ml) against human epidermoid carcinoma (KB cell culture).

Figure 85. ***Diplophyllum taxifolium***, a species that produces diplophyllin, a compound that is active against human epidermoid carcinoma. Photo by Hermann Schachner, through Creative Commons.

Hughes and Anterola (2010) attempted to transplant genes for producing **Taxol** (a potent anticancer agent) into the moss ***Physcomitrella patens*** (Figure 71, Figure 72). They found evidence of small amounts of the anticancer precursors in the moss. If the moss can be taught (genetically) to produce Taxol, it could become a laboratory means to manufacture this important anti-cancer drug without destroying the diminishing number of *Taxus* (Figure 86) shrubs that produce it naturally. Bryophytes are ideal organisms for such gene transplants because of their dominant state with a single set of chromosomes and the relative ease with which genes can be put into them.

Figure 86. ***Taxus baccata***, member of the genus that produces the anticancer agent Taxol. Photo through Creative Commons.

When Asakawa (1981, 1982) entered the arena, he isolated the sesquiterpenoids costunolide and tulipinolide from ***Conocephalum supradecompositum***, ***Frullania monocera***, ***F. tamarisci*** (Figure 43), ***Marchantia polymorpha*** (Figure 47), ***Wiesnerella denudata*** (Figure 87) and ***Porella japonica*** (Figure 88). To this list, Matsuo and coworkers (1980, 1981a, b, c, 1984) added ***Lepidozia vitrea*** (Figure 89) and ***Plagiochila semidecurrens*** (Figure 90). These substances, already known from higher plants, have activity to combat carcinoma of the nasopharynx, at least in cell culture.

Figure 87. ***Wiesnerella denudata***, a species that produces sesquiterpenoids that are likely to have antibiotic properties. Photo by Ying Jia-dong, through Creative Commons.

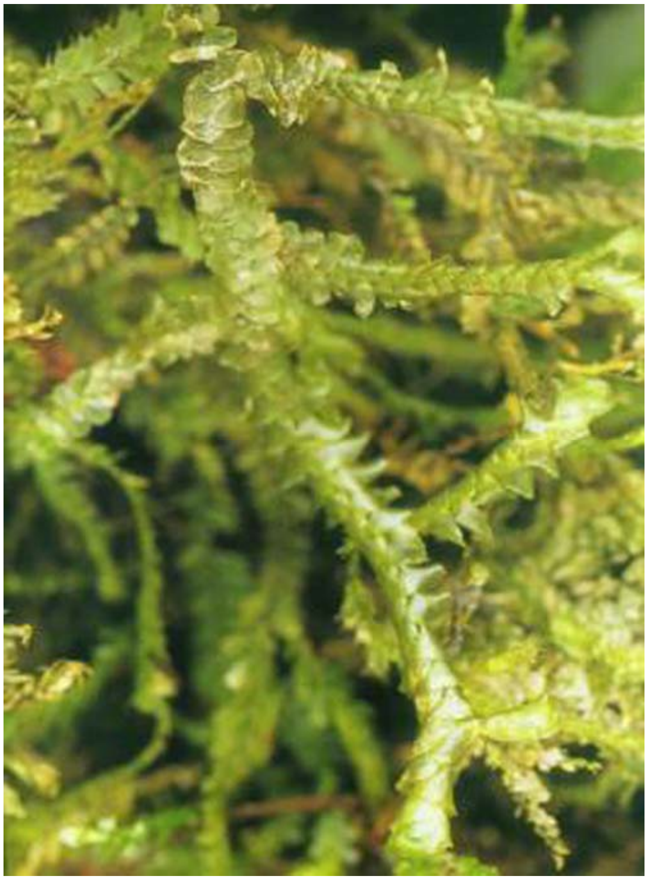

Figure 88. ***Porella japonica***, a species that produces compounds that combat carcinoma of the nasopharynx. Photo from Taiwan mosses color illustrations, through Creative Commons.

Figure 89. ***Lepidozia vitrea***, a species that produces compounds that combat carcinoma of the nasopharynx. Photo by Lin Shanxiong, through Creative Commons.

Figure 90. ***Plagiochila semidecurrens***, a species that produces compounds that combat carcinoma of the nasopharynx. Photo by Martin Hutten, with permission.

When the National Cancer Institute became interested, Spjut and his coworkers (1986) tested 184 species of mosses and 23 species of liverworts for antitumor activity. Of these, 43 species contained active substances, while those of 75 species were toxic to tested mice. The most activity was found in **Brachytheciaceae** (Figure 91), **Dicranaceae** (Figure 16), **Grimmiaceae** (Figure 92), **Hypnaceae** (Figure 61), **Mniaceae** (Figure 18, Figure 31), **Neckeraceae** (Figure 2), **Polytrichaceae** (Figure 19, Figure 80), and **Thuidiaceae** (Figure 93). However, in 1988, doubt was cast on the role of the moss when this team reported that the antitumor activity of the moss ***Claopodium crispifolium*** (Figure 94) was greatest in samples contaminated with the Cyanobacterium ***Nostoc*** cf. ***microscopicum*** (Figure 95), suggesting that ***Nostoc*** could be the direct source of the activity or a necessary partner for interaction between the species (Spjut *et al.* 1988). Interaction could result from the transfer of a precursor from the ***Nostoc*** to the moss, which could then transform it into an active substance. Alternatively, the moss might produce the substance as an allelopathic response to the ***Nostoc***. In any event, this raises important and intriguing questions, both medically and ecologically.

Figure 91. ***Brachythecium salebrosum*** (**Brachytheciaceae**). Some members of this family exhibit high antitumor activity. Photo by Hermann Schachner, through Creative Commons.

Figure 92. ***Grimmia nutans*** (**Grimmiaceae**). Some members of this family exhibit high antitumor activity. Photo by Michael Lüth, with permission.

Figure 93. ***Thuidium tamariscinum*** (**Thuidiaceae**). Some members of this family exhibit high antitumor activity. Photo by Malcolm Storey (DiscoverLife.com), with online permission.

Figure 94. ***Claopodium crispifolium***, a moss that provides habitat for ***Nostoc***, which in turn has anti-tumor properties. Photo from Botany Website, UBC, with permission.

Figure 95. ***Nostoc*** sp., a moss contaminant that can increase anti-tumor activity. Photo from Retina, through Creative Commons.

For some reason, much of the biochemical work has concentrated on the liverworts. Similar studies on activities of moss compounds are sparse and there may be good reason to presume a greater medical treasure chest among the liverworts. Since these compounds generally benefit the bryophytes by discouraging their would-be herbivores, it is the tiny, slow-growing liverworts that stand to benefit most. Where other, larger plants have spent their evolutionary history developing a diversity of structure, it would seem that small size has afforded these plants only the benefits of diversity of biochemistry as a means of combating the hungry herbivores.

Burgess *et al*. (2000) found that the leafy liverwort ***Bazzania novae-zelandiae*** (Figure 96) produces a sesquiterpene caffeate that has selective activity against certain human tumor cells. The active compound has been identified as the new compound naviculyl caffeate.

Figure 96. ***Bazzania novae-zealandiae***, a species that is active against human tumor cells. Photo by Shirley Kerr, with permission.

Even breast cancer sufferers might benefit from bryophytes. Huang *et al*. (2010) found that **marchantin A** produced by ***Marchantia emarginata*** subsp. ***tosana*** (Figure 33) induced apoptosis in MCF-7 breast cancer cells. This compound demonstrates strong antioxidant activity, scavenging free radicals.

The leafy liverwort ***Scapania verrucosa*** and its endophytic fungal inhabitant ***Chaetomium fusiforme*** (see Figure 78) produce several compounds that act as antitumor agents (Guo *et al*. 2008).

The thallose liverwort ***Dumortiera hirsuta*** (Figure 15) produces **riccardin D**, a macrocyclic bisbibenzyl compound that induces apoptosis of human leukemia cells (Xue *et al*. 2012). Xue and coworkers verified anticancer activity by riccardin D against human non-small cell lung cancer. In mice it produced a 44.5% inhibition of cancer growth with no apparent toxicity.

Pharmaceutical Production

Welcome to Greenovation! Moss for a healthy future. So began the website <http://www.greenovation.com/> of an upstart company that is growing the tiny ***Physcomitrella patens*** (Figure 71, Figure 72) for medicinal purposes. Yes, bryophytes have indeed finally penetrated the forefront of modern medicine!

Physcomitrella patens (Figure 71, Figure 72) is able to accept transferred human genes and express them to produce human antibodies in a liquid culture, making the antibodies easy to harvest (ETH Zurich 2009). So far, this is not possible when the genes are transplanted into "higher' organisms. One advantage of ***Physcomitrella patens*** is its ability to grow in a "bioreactor" (Figure 97; Decker & Reski 2004), a fermenter in which only water and minerals are needed to nourish the moss, of course in the presence of light and CO_2 (Greenovation). These tiny plants are actually superior (and cheaper) production systems for many complex recombinant pharmaceuticals (Bauer *et al*. 2005; Decker & Reski 2007, 2012; Gitzinger *et al*. 2009). Contrary to many mammalian systems that have been used to produce pharmaceuticals but that cause serious immune responses, those produced by ***Physcomitrella patens*** are non-immunogenic, a huge advantage for the patient, and making them superior to currently used mammalian cell lines for producing antibodies.

Among its many assets, ***Physcomitrella patens*** (Figure 71, Figure 72) is able to produce human proteins (Hohe *et al*. 2002; Decker *et al*. 2003) and is the only plant being used to produce the blood-clotting factor IX for pharmaceutical use. This discovery, patented by Prof. Reski of the Institute of Biotechnology of Plants at the University of Freiburg in Germany, led to the founding of the Greenovation Company in 1999. By 2002, the company was already employing 30 people to produce this valuable blood factor (Frahm, Bryonet discussion 2002).

Bryophytes offer the researchers, and the company, a number of advantages over "higher" plants. They can be grown without antibiotics, hence avoiding the danger of contamination of the final product. The moss is quite small and thus is cultured only in the lab with little danger of the transgenic plants escaping into the environment. But the real advantage comes from the dominant gametophytic generation of mosses as opposed to the dominant sporophyte of the tracheophytes. As a result, mosses are the only plants known to have a high frequency of homologous recombination. The result – stable integration of inserted genes into the genome. Furthermore, the highly complex moss system, compared to bacteria and fungi, permits a much wider array of expression than is possible in those systems. Thus, mosses are extremely useful as production systems for targeted substances that can be produced through gene manipulation.

Figure 97. This type of bioreactor is used to grow ***Physcomitrella patens*** for human proteins and human blood-clotting factor IX. Photo by Ralf Reski.

Unfortunately, most biologically active substances so far obtained have not proved economical for use, at least in part due to the slow-growing nature and difficulty of culturing bryophytes. And, while their pharmaceutical use seems promising, we lack any understanding of their potential harmful side effects.

In the words of Ma *et al*. (2003), "Imagine a world in which any protein, either naturally occurring or designed by man, could be produced safely, inexpensively and in almost unlimited quantities using only simple nutrients, water and sunlight. This could one day become reality as we learn to harness the power of plants for the production of recombinant proteins on an agricultural scale. Molecular farming in plants has already proven to be a successful way of producing a range of technical proteins. The first plant-derived recombinant pharmaceutical proteins are now approaching commercial approval, and many more are expected to follow."

Medical Dangers

Caution is in order in exercising any medicinal use of bryophytes, particularly liverworts, because of their potential for causing allergic reactions (Mitchell *et al.* 1969, 1970; Benezra *et al*. 1985, Asakawa 2012). Often the very compounds that have these medical potentials can cause allergic reactions. For example, it is a sesquiterpene lactone (Asakawa 1981) that gives the common epiphyte ***Frullania*** (Figure 98-Figure 99) its ability to cause contact dermatitis, especially to forest workers (Mitchell *et al.* 1969). Now there is a patch test with a sesquiterpene lactone mix to determine sensitivity to ***Frullania*** (Quirce *et al*. 1994).

Yet sesquiterpene lactones are well known for their antimicrobial activity. In southern Europe, ***Frullania tamarisci*** (Figure 43, Figure 98) imparts an allergic reaction to olive pickers, yet is listed as one of the medicinal species (J. Curnow, pers. comm.). D. H. Wagner (pers. comm.) reports an allergy to ***Chiloscyphus polyanthos*** (Figure 81), especially when he squeezes it to remove excess water. By 1981, 24 liverwort species were known to have potential allergenic sesquiterpene lactones (Asakawa 1981). These compounds undoubtedly endow the same advantage to bryophytes that they do to flowering plants – discouraging consumption by hungry herbivores.

Figure 98. ***Frullania tamarisci***, showing underside of branch with lobules by which the genus may be determined. Photo by Michael Lüth, with permission.

Frullania tamarisci (Figure 43, Figure 98) grows on trees and can cause skin irritations for loggers and even for their wives who handle their clothes. Allergic reactions to ***Frullania nisquallensis*** (Figure 99) occurred in patch tests on seven forest workers who had contact dermatitis (Mitchell *et al*. 1969). These forest workers exhibited the dermatitis only when they were working on forest areas. The problem was worse in wet weather and appeared within 1-2 days of starting work. The condition persisted for 2-4 weeks after leaving work in forested areas where the liverwort grew. The condition is often known locally in British Columbia, Canada, as cedar poisoning, but in fact it is caused by the liverworts that commonly grow on the cedars (*Thuja*; Figure 100).

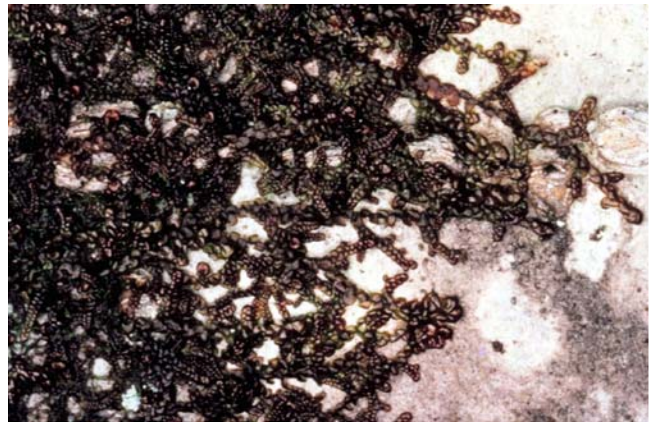

Figure 99. ***Frullania nisquallensis***, a leafy liverwort epiphyte that causes allergic reactions among forest workers. Photo by Dale Vitt, with permission.

Figure 100. ***Thuja plicata***, host plant for ***Frullania*** species. Photo from <www.nwplants.com>, through Creative Commons.

Summary

Bryophytes, especially liverworts, often have distinct odors, suggesting aromatic compounds such as phenols. However, few bryophytes have been linked to actual curative properties and identifiable associated compounds.

One danger in using bryophytes is that the same compounds that may have antibiotic properties may also be toxic or allergenic, or be associated with such compounds. Furthermore, peatland mosses may have associated fungi that cause **sporotrichosis**.

Many antibiotics have been isolated from bryophytes, but few have been developed for medical use, despite their demonstrated effectiveness. In Germany, ***Ceratodon purpureus*** and ***Bryum argenteum*** are used to cure fungal infections of horses. Several medical uses seem promising, such as antileukemic properties and anticancer agents.

The most promising uses of bryophytes in medicine seem to lie in genetic engineering. Bryophytes are being used already to produce human blood-clotting proteins, while others are known to reduce thrombin activity.

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I appreciate the continued support of Robin Stevenson in providing me with interesting articles such as the one on the medical use of mosses growing on skulls. Eric Harris generously shared his papers and images of medicinal bryophytes.

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