

# CHAPTER 2

## MEDICINES AND ANTIBIOTICS



Figure 1. Bryophytes and other herbs on sale in a Chinese market. Photo by 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.

### Herbal Medicines

Not surprisingly, herbal medicines of China (Figure 1), India, and Native Americans include bryophytes. Native Americans have used them for drugs, fibers, and clothing (University of Michigan, Dearborn 2003). 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.

### Liver Ailments

The most widely known use of bryophytes determined by its appearance is that of *Marchantia polymorpha* (Figure 2) 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).



Figure 2. *Marchantia polymorpha* thallus illustrating the surface that the Chinese considered to resemble the cross section of the liver. Photo by Michael Lüth.

### Ringworm

*Riccia* spp. were used in the Himalayas to treat ringworm because of the resemblance of the growth habit of those liverworts to the rings made by the worm (Figure 3). Recent tests on *Riccia fluitans* from Florida indicated no ability to inhibit growth of bacteria (*Pseudomonas aeruginosa*, *Staphylococcus aureus*) or yeast (*Candida albicans*) (Pates & Madsen 1955), and it is unlikely that *Riccia* species do any better with ringworm.



Figure 3. Circular formations of *Riccia* species, such as this *Riccia austinii*, suggested its use for curing ringworm, according to the Doctrine of Signatures. Photo by Janice Glime.

### Heart 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 4) and *R. roseum* to treat nervous prostration and cardiovascular diseases, the latter being a use that may have scientific merit (Wu 1982).

Chinese scientists have attempted to demonstrate the basis for the healing powers of some of the mosses, including *Rhodobryum giganteum* (Figure 4), 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%.



Figure 4. *Rhodobryum giganteum* in Yunnan, China. Photo by David Long.

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 4, Figure 5), in dry condition, a traditional Tibetan medicine for heart trouble. It was selling for US \$0.50 per 10g.

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*, 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!



Figure 5. Dried *Rhodobryum giganteum* (left container) at a shop in Yunnan, China. Photo by David Long.

### Inflammation and Fever

*Polytrichum commune* (Figure 6) has been used in China to reduce inflammation and fever (Ding 1982), and the Seminole native people in North America used the small mosses *Barbula unguiculata* and *Bryum capillare*, as

well as larger mosses like *Octoblepharum albidum*, as external applications for fever and body aches (Sturtevant 1954).



Figure 6. *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.

*Fontinalis antipyretica* reputedly got its name from its ability to work against fever, as recorded in the journal of Linnaeus (Nils Cronberg, pers. comm.). However, many people have interpreted the name to be derived from its use to insulate chimneys, where in actuality it seems to have little value.

### Diuretics and Laxatives

The Chinese also use *Polytrichum commune* as a detergent diuretic, laxative, and hemostatic agent (Hu 1987).

### Gynecology

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

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

### Disinfectant and Infections

The Native American Nitinahts also used *Sphagnum* as a disinfectant (Turner *et al.* 1983). *Fissidens* (Figure 7) 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*, *Atrichum*, *Polytrichum*, and *Thuidium*, primarily as anti-bacterial and anti-inflammatory agents. *Polytrichum juniperinum* (Figure 8) is used there for some prostate and urinary difficulties.

In China, *Polytrichum commune* (Figure 6) is boiled to make a tea for treating the common cold and reputedly helps to dissolve stones of the kidney and gall bladder (Gulabani 1974). Dried *Sphagnum* is sold to treat hemorrhages (Bland 1971), and *S. teres* (Figure 9) is used to treat eye diseases (Ding 1982). *Haplocladium microphyllum* is sold to treat cystitis, bronchitis, tonsillitis, and tympanitis (Ding 1982).



Figure 7. *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.



Figure 8. *Polytrichum juniperinum*, a hairy cap moss, is used in China to treat urinary and prostrate 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.



Figure 9. *Sphagnum teres* is used to treat eye diseases in Asia. Photo by Michael Lüth.

### Lung Diseases

The similarity of *Marchantia polymorpha* (Figure 2) thalli to the texture of lung tissue caused Europeans to use that liverwort to treat pulmonary tuberculosis (Bland 1971).

The other side of the coin is the ability of some mosses, especially *Sphagnum*, to harbor fungi that cause lung disease. *Sphagnum* was once thought to harbor *Mycobacteria*, 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* does cause pulmonary **sporotrichosis**, an infection of the lung resulting from breathing the fungi (McCain & Buell 1968).

### Skin Treatments

Himalayan Indians use a mixture of moss ashes with fat and honey to soothe and heal cuts, burns, and wounds (Pant *et al.* 1986), claiming that these ashes heal wounds more quickly (Pant & Tewari 1989). Among the Native Americans, the Cheyenne in Montana use *Polytrichum juniperinum* (Figure 8) in medicines (Hart 1981). In Utah, USA, the Gosiute native peoples used *Bryum*, *Mnium*, *Philonotis* (Figure 10), and various matted hypnaceous forms crushed into a paste applied to reduce the pain of burns, bruises, and wounds (Flowers 1957).

A mixture of the thallose liverworts *Conocephalum conicum* (Figure 11) and *Marchantia polymorpha* (Figure 2) with vegetable oils is used in China on bites, boils, burns, cuts, eczema, and wounds (Wu 1977; Ding 1982; Ando 1983). *Sphagnum* was used by Native Americans as a carrier for berries that were rubbed on children's sores (Carrier Linguistic Committee 1973).

Himalayan Indians have used *Marchantia polymorpha* 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 10. *Philonotis fontana* is a wetland moss used by Gosiute native people to relieve pain of burns. Photo by Michael Lüth.



Figure 11. Thallose liverwort, *Conocephalum conicum*. Photo by Janice Glime.

Alaskan native peoples have used *Sphagnum*, 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*, 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.

The CDC (Center for Disease Control and Prevention) describes it: "The first symptom is usually a small painless bump resembling an insect bite. It can be red, pink, or purple in color. The bump (nodule) usually appears on the finger, hand, or arm where the fungus first enters through a break on the skin. This is followed by one or more additional bumps or nodules which open and may resemble boils. Eventually lesions look like open sores (ulcerations) and are very slow to heal. The infection can spread to other areas of the body."

### Filters

Kumaun Indians of the Himalayas use slender bryophytes such as *Herbertus* (Figure 12), *Anomodon* (Figure 13), *Entodon* (Figure 14), *Hypnum*, *Meteoriopsis*, and *Scapania*, wrapped in a cone of *Rhododendron campanulatum* 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 12. The leafy liverwort *Herbertus sendtneri* is used as a filter for smoking. Photo by Michael Lüth.



Figure 13. *Anomodon rugellii*, a moss of vertical surfaces, filters substances out of items for smoking. Photo by Michael Lüth.

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 14. The pleurocarpous moss *Entodon concinnus* is likewise used as a smoking filter. Photo by Michael Lüth.

## Surgical and Wounds

Bryophytes have been used both in treating and in cushioning wounds. In Utah, the Gosuite native people used poultices of *Bryum*, *Mnium*, *Philonotis* (Figure 10), and various matted hypnaceous forms as padding under splints to set broken bones.

But it is *Sphagnum* that has gained fame for its use as a bandage. 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 of dressing per month (Nichols 1918c, 1920), saving about \$200,000 (Bland 1971), the Canadian Red Cross about 200,000 pounds per month, and the United States about

500,000 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* 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 15). 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).

*Sphagnum* 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 16) to bandage wounds. The Anglo-Saxons gave it the name of maidenhair moss because to them it resembled a maiden's pubic hair.

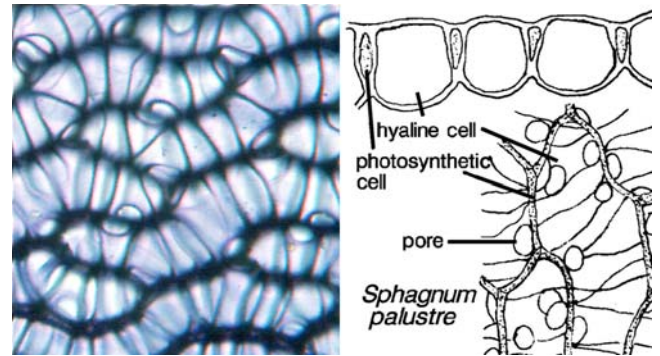


Figure 15. Stained cells of *Sphagnum* showing large hyaline cells with pores and small photosynthetic cells. Photo and drawings by Janice Glime.



Figure 16. *Fissidens adianthoides* is the maidenhair moss used by the Nitinaht native people for bandages. Photo by Michael Lüth.

Soothing a wound of a different sort (human pride), the Chinese use *Fissidens* (Figure 7; Figure 16), burned, to put on their heads to encourage hair growth! (Harris 2002).

The use of *Sphagnum* 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).

<i>Atrichum</i>	6.9
<i>Barbula</i>	8.3
<i>Bazzania pompeana</i>	4.0
<i>Haplomitrium mnioides</i>	12.0
<i>Hylocomium cavifolium</i>	9.8
<i>Plagiomnium maximoviczii</i>	6.7
<i>Rhodobryum</i>	10.0
<i>Sphagnum</i>	12.4
<i>Trachycystis microphylla</i>	3.2

## Antibiotics and Other Biologically Active Substances

Bryophyte species actually produce broad-range antibiotics. 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), and Germany (Frahm 2004), as well as in China (Ding 1982; Wu 1982) and India (Watts 1891).

One indication of the presence of unique and potentially pharmaceutically important chemicals in bryophytes is the presence of unique odors. This is especially true for liverworts. *Leptolejeunea* and *Moerckia* are distinctly aromatic (Schuster 1966), *Lophozia bicrenata* (Figure 17) has a pleasant odor, species of *Solenostoma* smell like carrots, *Geocalyx graveolens* (Figure 18) has a turpentine-like odor, and *Conocephalum conicum* (Figure 11) smells like mushrooms. The tropical *Plagiochila rutilans* smells like peppermint, caused by several menthane monoterpenoids (Heinrichs *et al.* 2001).



Figure 17. The leafy liverwort *Lophozia bicrenata*. Photo by Michael Lüth.

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



Figure 18. The leafy liverwort *Geocalyx graveolens*. Underleaf is indicated by the red star. Photo by Michael Lüth.

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).

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*, *S. strictum*, *Conocephalum conicum*, and *Dumortiera hirsuta*. Pavletic and Stilinovic (1963) found that *Dicranum scoparium* strongly inhibited all bacteria tested but gram negative *Escherichia coli*. 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*, *Dicranum*, *Mnium*, *Polytrichum*, and *Sphagnum*. Reminiscent of *Dicranum scoparium*, *Atrichum undulatum* (Figure 19) was effective on everything tested except *Aerobacter aerogenes* and *E. coli*.



Figure 19. *Atrichum undulatum* is a moss that is very effective against a wide range of bacteria. Photo by Michael Lüth.

Gupta and Singh (1971) found high occurrence of antibacterial activity in extracts of *Barbula* species, reaching as high as 36.2%, whereas it was only half that in *Timmia* species (18.8%). In 1982, Asakawa *et al.* (1982) isolated three prenyl bibenzyls from *Radula* spp. and demonstrated that these bibenzyls could inhibit growth of *Staphylococcus aureus* at concentrations of 20.3  $\mu\text{g ml}^{-1}$ . 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 *Pyricularia oryzae*. Belcik and Wiegner (1980) reported antimicrobial activity in extracts of the liverworts *Pallavicinia* and *Reboulia*, and Isoe (1983) reported it from *Porella*.

Another three species of mosses (*Anomodon rostratus*, *Plagiomnium cuspidatum*, *Orthotrichum rupestre*) produce substances that inhibit bacteria and fungi, but these inhibitors seem to be unstable products that vary considerably among species and possibly also 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.

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 tosona* 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).

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

### 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, *Hypnum cupressiforme* (Figure 20) has remarkable antibacterial and antifungal effects.

The absence of fungal diseases in liverworts led Pryce (1972) to suggest that lunularic acid, an aging hormone found in liverworts but not in mosses, might be responsible for liverwort antifungal activity. Banerjee and Sen (1979) 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*, *Pythium debaryanum*, and *Rhizoctonia solani* by

the liverwort *Herbertus aduncus* was age-dependent. They subsequently isolated three aging substances from it: (-)-alpha-herbertenol; (-)-Beta-herbertenol, and (-)-alpha-formylherbertenol.



Figure 20. *Hypnum cupressiforme* is effective against fungi that cause skin infections. Photo by Michael Lüth.

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 21). Frahm (2004) 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 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).

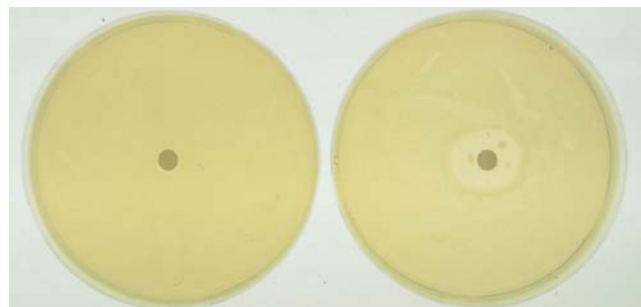


Figure 21. Bryophytes are known to inhibit growth of some kinds of bacteria and fungi. **Left:** Microbes grow uninhibited around a disk with only extraction fluid. **Right:** A zone of inhibition occurs around the disk with bryophyte extract. Photo by Jan-Peter Frahm.

And one extract has 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* and *Bryum argenteum*. 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.

### Antiviral Activity

The Maoris of New Zealand have used bryophytes to treat venereal disease by packing wet plants on the infected organs (Frahm 2004). Even viruses may some day be cured by extracts of mosses, but we cannot simply identify them as "moss" as our ecologist friends have been wonton to do in reporting the ground cover. For example, 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* produces several antivirally active humic acids, and *Camptothecium* extracts can inhibit growth of the poliovirus (Withauer *et al.* 1976). Nevertheless, actual usage of bryophytic extracts has not developed outside of Asia.

### 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*. But application of the antitumor activity fared no better and was apparently not rediscovered in bryophytes for two decades. 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 22) and *D. taxifolium*, shows significant activity (ED50 4-16 µg/ml) against human epidermoid carcinoma (KB cell culture).



Figure 22. The leafy liverwort *Diplophyllum albicans* is active against human epidermoid carcinoma. Photo by Michael Lüth.

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

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 test mice. The most activity was found in Brachytheciaceae, Dicranaceae, Grimmiaceae, Hypnaceae, Mniaceae, Neckeraceae, Polytrichaceae, and Thuidiaceae. 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* was greatest in samples contaminated with the Cyanobacterium *Nostoc cf. microscopicum*, 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.

Asakawa (1981) has shown that several compounds from leafy liverworts exhibit antileukemic activity. From the thallose species, Marchantin A from *Marchantia palacea*, *M. polymorpha*, and *M. tosona*, riccardin from *Riccardia multifida* (Figure 23), and perrottetin E from *Radula perrottetii* all show cytotoxicity against the leukemic KB cells (Asakawa *et al.* 1982).



Figure 23. *Riccardia multifida* is a thallose liverwort known for its antileukemic activity. Photo by Michael Lüth.

For some reason, this 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.

### Transgenic 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 24) for medicinal purposes. Yes, bryophytes have indeed finally penetrated the forefront of modern medicine!

One advantage of *Physcomitrella patens* is its ability to grow in a "bioreactor" (Figure 25; 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<sub>2</sub> (Greenovation).



Figure 24. *Physcomitrella patens*, a source of human proteins and blood-clotting factor IX. Photo by Michael Lüth.



Figure 25. This type of bioreactor is used to grow *Physcomitrella patens* for human proteins and human blood-clotting factor IX. Photo by Ralf Reski.

Among its many assets, *Physcomitrella patens* 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.

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.

### Medical Dangers



Figure 26. *Frullania tamarisci*, a species with both allergic and medicinal properties. **Upper:** Typical epiphytic plant habit. **Lower:** Underside of branch showing lobules by which the genus may be determined. Photos by Michael Lüth.

Caution is in order in exercising any medicinal use of bryophytes, particularly liverworts, because of their

potential for causing allergic reactions. 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* 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 26) 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*, 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.

## 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.

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.

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.

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.

## Literature Cited

- Adamek, W. 1976. Introductory report on oncogenic and therapeutic nature of the peat preparation in human neoplastic disease. In Proc. 5th Internat. Peat Congr., Poznabn, Poland, Vol. 1. Peat and Peatlands in the Natural Environment Protection. pp. 417-429.
- Adams, J. E., Dion, W. M., and Reilly, S. 1982. Sporotrichosis due to contact with contaminated *Sphagnum* moss. Can. Med. Assoc. J. 126: 1071-1073.
- Ando, H. 1983. Use of bryophytes in China 2. Mosses indispensable to the production of Chinese galls. Proc. Bryol. Soc. Jap. 3: 124--125.
- Ando, H. and Matsuo, A. 1984. Applied bryology. In: Schultze-Motel, W. (ed.). Advances in Bryology, Vol. 2, pp. 133-224.
- Asakawa, Y. 1981. Biologically active substances obtained from bryophytes. J. Hattori Bot. Lab. 50: 123-142.
- Asakawa, Y. 1982. Chemical constituents of the Hepaticae. Prog. Chem. Org. Natur. Prod. 42: 1-285.
- Asakawa, Y., Toyota, M., Taira, Z., and Takemoto, T. 1982. Biologically active cyclic bisbenzyls and terpenoids isolated from liverworts. 25th symposium on chemistry of natural products. Symposium papers, pp. 337--344.
- Banerjee, R. D. 1974. Studies on antibiotic activity of bryophytes and pteridophytes. Ph. D. thesis. University of Kalyani, Kalyani, India.
- Banerjee, R. D. and Sen, S. P. 1979. Antibiotic activity of bryophytes. Bryologist 82: 141-153.
- Belcik, F. P. and Wiegner, N. 1980. Antimicrobial activities or antibiosis of certain eastern U.S. liverwort, lichen and moss extracts. J. Elisha Mitchell Sci. Soc. 96: 94.
- Belkin, M., Fitzgerald, D. B., and Felix, M. D. 1952-1953. Tumor-damaging capacity of plant materials. II. Plants used as diuretics. J. Nat. Cancer Inst. 13: 741-744.
- Bland, J. 1971. Forests of Lilliput. Prentice-Hall, Inc., Englewood Cliffs. 210 pp.
- Carrier Linguistic Committee 1973 Plants of Carrier Country. Fort St. James, BC. Carrier Linguistic Committee, p. 87.
- Coles, F. B., Schuchat, A., Hibbs, N. J., *et al.* 1992. A multistate outbreak of sporotrichosis associated with *Sphagnum* moss. Amer. J. Epidemiol. 136: 475-478.
- Crum, H. 1973. Mosses of the Great Lakes Forest. Contributions from the University of Michigan Herbarium 10: 404 pp.
- Crum, H. 1988. A focus on Peatlands and Peat mosses. University of Michigan Press, Ann Arbor. 306 Pp.
- D'Alessio, D. J., Leavens, L. J., Strumpf, G. B., and Smith, C. D. 1965. An outbreak of sporotrichosis in Vermont associated with *Sphagnum* moss as the source of infection. New England J. Med. 272: 1054--1058.
- Decker, E. L. and Reski, R. 2004. The moss bioreactor. Curr. Opin. Plant Biol. 7: 166-170.
- Decker, E. L., Gorr, G., and Reski, R. 2003. Moss-an innovative tool for protein production. BioForum Europe 7: 96-97.
- Deriu, G. M., Levre, E., and Caroli, G. 1995. Preliminary survey on *Sphagnum* moss, an ecological niche of microorganisms of medical significance. Igiene Moderna 103(2): 115-124.
- Ding, H. 1982. Medicinal spore-bearing plants of China. Shanghai. 409 pp.

- Flowers, S. 1957. Ethnobotany of the Goshute Indians of Utah. *Bryologist* 60: 11-14.
- Frahm, J.-P. 2004. New frontiers in bryology and lichenology: Recent developments of commercial products from bryophytes. *Bryologist* 107: 277-283.
- Frankel, E. H. and Frankel, D. F. 1982. Sporotrichosis of the abdomen. *Cutis* 29: 189-190.
- Greenovation, accessed 24 January 2003 at <[http://www.greenovation.com/Projects\\_Production.htm](http://www.greenovation.com/Projects_Production.htm)>
- Gulabani, A. 1974. Bryophytes as economic plants. *Botanica* 14: 73-75.
- Gupta, K. G. and Singh, B. 1971. Occurrence of antibacterial activity in moss extracts. *Res. Bull. Punjab Univ.* 22: 237-239.
- Hajjeh, R., McDonnell, S., Reef, S., Licitra, C., Hankins, M., Toth, B., Padhye, A., Kaufman, L., Pasarell, L., Cooper, C., Hutwagner, L., Hopkins, R., and McNeil, M. 1997. Outbreak of sporotrichosis among tree nursery workers. *J. Infect. Diseases* 176(2): 499-504.
- Harris, E. 2002. An examination of phylogenetic characters in mosses: Examples from *Fissidens* Hedw. (Fissidentaceae: Musci). Presentation and abstract presented at the annual meeting of the American Bryological and Lichenological Society, 26-27 July 2002, Storrs, CN, USA.
- Hart, J. A. 1981. The ethnobotany of the northern Cheyenne Indians of Montana. *J. Ethnopharma* 4: 1-55, 8 append.
- Hayashi, S., Kami, T., Matsuo, A., Ando, H., and Seki, T. 1977. The smell of liverworts. *Proc. Bryol. Soc. Jap.* 2: 38-40.
- Heinrichs, J., Groth, H., Gradstein, S. R., Rycroft, D. S., Cole, W. J., and Anton, H. 2001. *Plagiochila rutilans* (Hepaticae): A poorly known species from tropical America. *Bryologist* 104: 350-361.
- Hohe, A., Decker, E. L., Gorr, G., Schween, G., and Reski, R. 2002. Tight control of growth and cell differentiation in photoautotrophically growing moss (*Physcomitrella patens*) bioreactor cultures. *Plant Cell Rept.* 20: 1135-1140.
- Hoof, L. van, Berghe, D. A. Vanden, Petit, E., and Vlietnick, A. J. 1981. Antimicrobial and antiviral screening of Bryophyta. *Fitoterapia* 52: 223-229.
- Horikawa, Y. 1952. The amount of water absorption by some mosses. *Hikobia* 1: 150.
- Hotson, J. W. 1918. *Sphagnum* as a surgical dressing. *Science*, N.S. 48: 203-208.
- Hotson, J. W. 1919. *Sphagnum* from bog to bandage. *Puget Sound Biol. St. Bull.* 2: 211-247.
- Hotson, J. W. 1921. *Sphagnum* used as a surgical dressing in Germany during the world war. *Bryologist* 24: 74-78, 89-96.
- Hu, R. 1987. *Bryology*. Higher Education Press, Beijing, China. 465 pp.
- Ichikawa, T. 1982. Biologically active substances in mosses. *Bryon (Kanagawa Koke no kai)* 2: 1-2.
- Ichikawa, T., Namikawa, M., Yamada, K., Sakai, K., and Kondo, K. 1983. Novel cyclopentenonyl fatty acids from mosses, *Dicranum scoparium* and *Dicranum japonicum*. *Tetrahedron Lett.* 24: 3327-3340.
- Isoe, S. 1983. Terpene diols. Biological activity and synthetic study. 48th Annual Meeting of the Chemical Society of Japan. *Proceedings Papers II.* pp. 849-850.
- Jennings, O. E. 1926. Mosses immune to molds. *Bryologist* 29: 75-76.
- Keller, W. E. 1988. Impact of "lethal moss" may go beyond the bog. *Environment* 30: 22-23.
- Kleb, B., Benkovic, L., Torok, A., and Domsodi, J. 1999. Peat exploration for medical use. *Period Polytech. Civ. Eng.* 43(2): 233-242.
- Klöcking, R., Thiel, K.-D., and Sprössig, M. 1976. Antiviral activity of humic acids from peat water. In *Proc. 5th Internat. Peat Congr., Poznan, Poland, Vol. 1. Peat and Peatlands in the Natural Environment Protection.* Pp. 446-455.
- Lahlou, E. H., Hashimoto, T., and Asakawa, Y. 2000. Chemical constituents of the liverworts *Plagiochasma japonica* and *Marchantia tosonana*. *J. Hattori Bot. Lab.* 88: 271-275.
- Lewington, A. 1990. *Plants for People*. Oxford University Press, New York.
- Madsen, G. C. and Pates, A. L. 1952. Occurrence of antimicrobial substances in chlorophyllose plants growing in Florida. *Bot. Gaz.* 113: 293-300.
- Matsuo, A., Nozaki, A., Kubota, N., Uto, S., and Nakayama, M. 1984. Structures and conformation of (-)-isobicyclgermacrenal and 9(-)-lepidozenal, two key sesquiterpenoids of the *cis*- and *trans*-10,3-bicyclic ring system, from the liverwort *Lepidozia vitrea*. *J. Chem. Soc. Perkin Trans. 1*: 203-214.
- Matsuo, A., Atsumi, K., Nadaya, K., Nakayama, M., and Hayashi, S. 1981a. <sup>13</sup>C NMR chemical shifts of ovalifoliene and related compounds with 2,3-seco-alloaromadendrane skeleton. Structure of (+)-9 alpha-acetoxyovalifoliene, a plant growth inhibitor. *Phytochemistry* 20: 1065-1068.
- Matsuo, A., Atsumi, K., Nakayama, M., and Hayashi, S. 1981b. Structure of *ent*-2,3-seco-alloaromadendrane sesquiterpenoids having plant growth inhibitory activity from *Plagiochila semidecurrrens* (liverwort). *J. Chem. Soc. Perkin Trans. 1*: 2816-2824.
- Matsuo, A., Nakayama, M., and Hayashi, S. 1971. Aromatic esters from the liverwort *Isotachis japonica*. *Z. Naturforsch.* 26: 1023-1025.
- Matsuo, A., Kubota, N., Nakayama, M., and Hayashi, S. 1981c. (-)-Lepidozenal, a sesquiterpenoid with a novel *trans*-fused bicyclo[8.1.0] undecane system from the liverwort *Lepidozia vitrea*. *Chem. Lett.* pp. 1097-1100.
- Matsuo, A., Kubota, N., Uto, S., Nozaki, H., Nakayama, M., and Hayashi, S. 1980. Structure of three novel sesquiterpene aldehydes, (-)-isobicyclgermacrenal, (-)-lepidozenal, and (+)-vitrenal, displaying plant growth inhibitory effect from the liverwort *Lepidozia vitrea*. 23rd Symposium on Chemistry of Natural Products. *Symposium papers.* Pp. 420-427.
- Matsuo, A., Yuki, S., and Nakayama, M. 1983. (-)-Herbertenediol and (-)-herbertenolide, two new sesquiterpenoids of the *ent*-herbertane class from the liverwort *Herberta adunca*. *Chem. Lett.* pp. 1041-1042.
- Matsuo, A., Yuki, S., Higashi, R., Nakayama, M., and Hayashi, S. 1982a. Structure and biological activity of several sesquiterpenoids having a novel herbertane skeleton from the liverwort *Herberta adunca*. 25th Symposium on Chemistry of Natural Products. *Symposium papers.* pp. 242-249.
- Matsuo, A., Yuki, S., Nakayama, M., and Hayashi, S. 1982b. Three new sesquiterpene phenols of the *ent*-herbertane class from the liverwort *Herberta adunca*. *Chem. Lett.* pp. 463-466.
- McCain, W. H. and Buell, W. F. 1968. Primary pulmonary sporotrichosis in Illinois. *Ill. Med. J.* 131: 255-258.
- McCleary, J. A. and Walkington, D. L. 1966. Mosses and antibiosis. *Rev. Bryol. Lichenol.* 34: 309-314.
- McCleary, J. A., Sypherd, P. S., and Walkington, D. L. 1960. Mosses as possible sources of antibiotics. *Science* 131: 108.

- Miller, N. G. and Miller, H. 1979. Make ye the bryophytes. *Horticulture* 57(1): 40-47.
- Mitchell, J. and Rook, A. 1979. *Botanical Dermatology. Plants and plant products injurious to the skin.* Greengrass Ltd. Vancouver.
- Mitchell, J. C., Schofield, W. B. T., Singh, B., and Towers, G. H. N. 1969. Allergy to *Frullania*, allergic contact dermatitis occurring in forest workers caused by exposure to *Frullania nisquallensis*. *Arch. Dermatol.* 100: 46-49.
- Nichols, G. E. 1918a. The vegetation of northern Cape Breton Island, Nova Scotia. *Trans. Conn. Acad. Arts Sci.* 22: 249-467.
- Nichols, G. E. 1918b. The American Red Cross wants information regarding supplies of surgical *Sphagnum*. *Bryologist* 21: 81-83.
- Nichols, G. E. 1918c. War work for bryologists. *Bryologist* 21: 53-56.
- Nichols, G. E. 1918d. The *Sphagnum* moss and its use in surgical dressings. *New York Bot. Gard. J.* 19: 203-220.
- Nichols, G. E. 1920. *Sphagnum* moss; war substitute for cotton in absorbent surgical dressings. *Publ. Smiths. Inst.* 2558 (U.S. Nat. Mus. Rep. 1918): 221-234.
- Ohta, Y., Andersen, N. H., and Liu, C.-B. 1977. Sesquiterpene constituents of two liverworts of genus *Diplophyllum*. Novel eudesmanolides and cytotoxicity studies for enantiomeric methylene lactones. *Tetrahedron* 33: 617-628.
- Padhye, A. A. and Ajello, L. 1990. Sporotrichosis – an occupational hazard for nursery workers, tree planters and orchid growers. *Amer. Orchid Soc.* 59: 613-616.
- Pant, G. and Tewari, S. D. 1989. Various human uses of bryophytes in the Kumaun region of Northwest Himalaya. *Bryologist* 92: 120-122.
- Pant, G. and Tewari, S. D. 1990. Bryophytes and mankind. *Ethnobotany* 2: 97-103.
- Pant, G., Tewari, S. D., Pargaien, M. C., and Bisht, L. S. 1986. Bryological activities in North-West Himalaya – II. A bryophyte foray in the Askot region of district Pithoragarh (Kumaun Himalayas). *Bryol. Times* 39: 2-3.
- Pates, A. L. and Madsen, G. C. 1955. Occurrence of antimicrobial substances in chlorophyllose plants growing in Florida. II. *Bot. Gaz.* 116: 250-261.
- Pavletic, Z. and Stilinovic, B. 1963. Untersuchungen über die antibiotische Wirkung von Moosextrakten auf einige Bakterien. *Acta Bot. Croat.* 22: 133-139.
- Pinheiro da Silva, M. F., Lisboa, C. L., and Vasconcelos Brazao, R. de. 1989. Contribucao ao estudo de briofitas como fontes de antibióticos. *Avcta Amazonica* 19: 139-145.
- Porter, J. B. 1917. *Sphagnum* surgical dressings. *Intern. J. Surgery* 30: 129-135.
- Powell, K. E., Taylor, A., Phillips, B. J., Blakey, D. L., Campbell, G. D., Kaufman, L., and Kaplan, W. 1978. Cutaneous sporotrichosis in forestry workers. *J. Amer. Med. Assoc.* 240: 232-235.
- Pryce, R. J. 1972. Metabolism of lunularic acid to a new plant stilbene by *Lunularia cruciata*. *Phytochemistry* 11: 1355-1364.
- Quirce, S., Tabar, A. I., Muro, M. D., and Olaguibel, J. M. 1994. Airborne contact dermatitis from *Frullania*. *Contact Dermat.* 30(2): 73-76.
- Radwan, S. S. 1991. Sources of C<sub>20</sub>-polyunsaturated fatty acids for biotechnological use. *Appl. Microbiol. Biotech.* 35: 421-430.
- Rosenberg, N. 1988. Malady traced to state moss. *Milwaukee Journal Tuesday, Nov. 1, 1988, Sect. B, p. 1.*
- Schofield, W. B. 1969. Some Common Mosses of British Columbia. *Brit. Col. Prov. Museum. Handbook No 28.* Victoria. 262 pp.
- Schuster, R. M. 1966. The Hepaticae and Anthocerotae of North America. Vol. 1. Columbia Univ. Press. N. Y. 1344 pp.
- Solheim, B., and Zielke, M. 2002. Associations Between Cyanobacteria and mosses. In: Rai, A. N., Bergman, B., and Rasmussen, U. (eds.). *Cyanobacteria in Symbiosis.* Kluwer Academic Publishers, Boston.
- Spjut, R. W., Cassady, J. M., McCloud, T., Suffness, M., Norris, D. H., Cragg, G. M., and Edson, C. F. 1988. Variation in cytotoxicity and antitumor activity among samples of the moss *Claopodium crispifolium* (Thuidiaceae). *Econ. Bot.* 42: 62-72.
- Spjut, R. W., Suffness, M., Cragg, G. M., and Norris, D. H. 1986. Mosses, liverworts, and hornworts screened for antitumor agents. *Econ. Bot.* 40: 310-338.
- Stanley, A. 1995. *Mothers and Daughters of Invention.* Rutgers University Press, N.J. pp. 212-275.
- Sturtevant, W. 1954. The Mikasuki Seminole: Medical Beliefs and Practices. Ph. D. Dissertation. Yale University, p. 203.
- Tamblyn, S. E. 1981. Sporotrichosis and *Sphagnum* moss. *Alberta Social Services & Community Health Newsletter* 4(2): 1-3.
- Turner, N. J., Thomas, J., Carlson, B. F., and Ogilvie, R. T. 1983. Ethnobotany of the Nitinaht Indians of Vancouver Island. Victoria. British Columbia Provincial Museum, p. 59.
- Turner, R. G. 1993. Peat and people: A review. *Adv. Bryol.* 5: 315-328.
- University of Michigan, Dearborn. 2003. Native American Ethnobotany, A database of plants used as drugs, foods, dyes, fibers, and more, by native Peoples of North America. Accessed 8 January 2004 at <<http://herb.umd.umich.edu/>>.
- Varley, S. J. and Barnett, S. E. 1987. *Sphagnum* moss and wound healing II. *Clinical Rehabilitation* 1: 153-160.
- Watts, G. 1891. *A Dictionary of the Economic Products of India.* Part V. Delhi.
- Weber, K. and Ploetner, G. 1976. The effectivity of cures with therapeutic peat baths of different consistencies in cases of a rheumatoid arthritis. In: *Proc. 5th Internat. Peat Congr., Poznabn, Poland, Vol. 1. Peat and Peatlands in the Natural Environment Protection.* pp. 467-476.
- Witthauer, J., Klöcking, R., Helbig, B., and Drabke, P. 1976. Chemical and physicochemical characterization of antivirally active humic acids. In: *Proc. 5th Internat. Peat Congr., Poznabn, Poland, Vol. 1. Peat and Peatlands in the Natural Environment Protection.* pp. 456-466.
- Wren, R. W. 1956. *Potters New Encyclopedia of Botanical Drugs and Preparations.* 7th ed. Harper & Row, London.
- Wu, P. C. 1977. *Rhodobryum giganteum* (Schwaegr.) Par can be used for curing cardiovascular disease. *Acta Phytotax. Sin.* 15: 93.
- Wu, P. C. 1982. Some uses of mosses in China. *Bryol. Times* 13: 5.