

Lichens- Role in Traditional Medicine and Drug Discovery

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Abstract

Lichens represent a unique division in the plant kingdom. They have been used in Traditional systems of medicine including Traditional Indian Medicine (TIM), Traditional Chinese Medicine (TCM), Homeopathic and Western Medical Herbals. Lichens have been used in the treatment of diverse diseases like arthritis, alopecia, constipation, kidney diseases, leprosy, pharyngitis rabies, infection, worm and infestation. The medicinal utility of lichens is regarded to presence of secondary compounds like of usnic acid and atranorin. Animal investigations on lichens have demonstrated antimicrobial, antitumor and immunomodulaor activity. One of the reasons for exploring biological compounds in lichens is the potential for medical use. However, much work remains to link medical effects with specific lichen species.

INTRODUCTION

The Lichen Division is comprised of at least 8 orders, 45 families, and 6,000 species. Information on the edible and medicinal uses of the lichens is scattered (Chevallier, 1996). Many lichens are known to have potent antibiotic properties, and many are edible. However, some lichens do contain toxic substances, so you should not graze randomly on them (Agelet & Joan, 2003).

LICHENS IN FOLK AND TRADITIONAL MEDICINE

“Doctrine of Signatures” written in the 15th century stated “A plant could treat a diseases it most looked like” This formed the basis of phyto-therapeutics in traditional systems of medicines like Traditional Indian Medicine (TIM) or Ayurveda, Traditional Chinese Medicine (TCM), and Western Medical Herbalism (Bown, 2001). Interestingly enough, the word lichen is derived from Greek word ‘Leprous’ and refers to use of lichens in treating skin diseases due to their peeling-skin appearance. Lichen like *Lobaria pulmonaria* (L.) Hoffm. (Stictacea) and *Parmelia sulcata* Taylor (Parmeliaceae) have been used in the treatment of pulmonary and cranial diseases, respectively (Rizzini, 1952). Similarly, *Xanthoria parietina* (L.) Th. Fries (Lobariaceae), being yellow, was used to cure jaundice (Bown, 2001).

Medicinal uses of lichens are linked with folklore. The medicinal use of lichens can be traced back to the 18th dynasty (1700-1800 BC) when *Evernia furfuracea* (L.) Mann

or (Parmeliaceae) was first used as a drug (Launert, 1981). Some lichens were claimed to be good for coughs, jaundice, rabies and restoring lost hair (Pereira, 1853). Herbal medicine texts included account of several species of lichens including *Cladonia*, *Evernia*, *Lobaria*, *Parmelia*, *Peltigera*, *Pertusaria*, *Physica*, *Rocella*, *Usnea* and *Xanthoria* (Llano, 1944 b). During the middle age, lichens figured prominently in the herbals used by practitioners.

Peltigera sp., mixed with 2 drachms of black pepper, for four-days, in half-pint of warm milk, was used for rabies or hydrophobia. Linnaeus named *Peltigera*, in 1753 as *Lichen caninus* (the Dog Lichen) as it has rhizines on the lower surface that resembles teeth, hence specific epithet of canina. In traditional medicine, *Peltigera canina* (L.) Willd is used as liver tonic and laxative. In Ireland, *Peltigera aphthosa* (L.) Willd. was used as vermifuge.

People of Northern California used *Letharia vulpina* (L.) Hue. (Parmeliaceae) in stomach diseases. A novel species of *Dictyonema* was used by the Waorani as hallucinogen (Davis & Yost, 1983). In Arabian medicine, *Alectoria usneoides* was used in the treatment of splenomegaly (enlarged spleen).

In China, *Usnea diffracta* Vain (Parmeliaceae) was used in medicine around 500 A.D. (Strickmann.). Hippocrates prescribed *Usnea barbata* for uterine ailments. In Sweden, *Parmelia saxatilis* (L.) Ach. is used to treat warts. In China, *Lethariella cashmeriana* Krog-Wei, *L. sernanderi* (Motyka) Obermayer, *L. sinensis* J. C. Wei & Jiang (Parmeliaceae)

and *Thamnolia vermicularis* Hytter i Norden Danske (Icmadophilaceae) are used as medicated teas (Wang, et al. 2001).

Usnea sp. are used in Traditional Chinese Medicine (TCM), Homeopathic system of medicine and traditional medicine in Pacific islands and New Zealand. *Usnea* sp are valued for demulcent properties and finds use for mild inflammation of the oral and pharyngeal mucosa. *Usnea filipendula* Stirt was used in former Soviet Union for cuts and wounds (Chevallier, 1996).

Spanish folk medicine has documented use of lichens in various medical ailments. Decoction of *Pseudoevernia furfuracea* (L.) Zopf. (Parmeliaceae) is used in Alfacar and Viznar in respiratory ailments. *Ramalina bourgeana* Mont. ex Nyl. (Ramalinaceae) is consumed for diuretic and stone-dissolving (lithontriptic) properties (González -Tejero, 1995). *Xanthoparmelia scabrosa* (Taylor) Hale (Parmeliaceae) is ingredient of various aphrodisiac formulations sold in international market. Tea prepared from *Flavocetraria nivalis* (L.) Kärnefelt & Thell (Parmeliaceae) is used in the treatment of motion-sickness and heart attacks of by natives of Qollahuaya Andeans in Poland (Bastien, 1983).

Cetraria islandica (L.) Ach. (Parmeliaceae) commonly known as Irish moss, is valued folk remedy for lung diseases, kidney and bladder complaints as well as externally for poorly healed wounds (Bown, 2001). Traditionally it is used mild inflammation of the oral and pharyngeal mucosa. It is also valued in dyspepsia and loss of appetite. In European folk medicine, it is used in cancer treatment (Chevallier, 1996).

Reindeer lichens are important medicinal agents. *Cladonia rangiferina* (L.) F. H. Wigg. syn. *Cladina rangiferina* (L.) Nyl. (Cladoniaceae) is commonly studied Reindeer lichen. Northern native people used reindeer lichen in medicinal teas to treat colds, arthritis, fevers and other problems (Perez- Llano, 1944). Reindeer lichens were also used as a poultice to relieve the ache of arthritic joints. Reindeer lichens have been taken to treat fever, jaundice constipation, convulsions, coughs, and tuberculosis (Bown, 2001). *Cladonia pyxidata* (L.) Hoffm. is useful remedy for whooping cough (Chevallier, 1996).

Three *Parmelia* sp. (*Parmelia chinense* (Osbeck) Hale & Ahti., syn *P. perlata* (Huds.) Ach, *P. sancti-angeli* (Lyngé) Hale and *P. peforatum* (Jacq.) A. Massal. are used for Indian

drug *chharila*, which is used as aphrodisiac (Lal & Upreti, 1995; Kumar & Upreti, 2001). In India *Parmelia chinense* is used as diuretic and as liniment for headache and powder to help wounds heal. *Parmelia sancti-angeli* is used in Central India to treat Tinea (ringworm) like disease. Ash of the lichen, mixed with mustard or linseed oil, is applied to the affected area. *Parmelia peforatum* is medically recognized in Afghanistan (Chandra & Singh, 1971).

Parmelia nepalense (Talyor) Hale ex Sipman is used in Nepal in the treatment of toothache and sore throat (Kumar, Banskota & Manandhar, 1996). In Western Himalayas *Thamnolia vermicularis* (Schwartz) Ach. (Icmadophilaceae) is used as antiseptic (Negi & Kareem, 1996). In Sikkim, *Heterodermia diademata* (Talyor) D.D. Awas. (Physciaceae) is used for cuts and wounds (Saklani & Upreti, 1992).

PHYTOCHEMICAL AND PHARMACOLOGICAL INVESTIGATIONS

Lichen metabolites exert a wide variety of biological actions including antibiotic, antimycobacterial, antiviral, anti-inflammatory, analgesic, antipyretic, antiproliferative and cytotoxic effects. Even though these manifold activities of lichen metabolites have now been recognized, their therapeutic potential has not yet been fully explored and thus remains pharmaceutically unexploited (Müller, 2002). The utility of lichens is due of range of secondary compounds produced by them (Boustie & Grube, 2005).

ANTIMICROBIAL ACTIVITY

ANTIBACTERIAL

Antibiotic properties of the lichens are of special interest to the scientists (Lawrey, 1986). According to one estimate, 50 % of all lichens have antibiotic properties (Sharnoff, 1997). Burkholder (1944) was pioneer initiating research on lichens as antibacterial agents. He tested 42 lichens for antibiotic property and 27 were reported to inhibit growth of bacteria (Burkholder et al 1944; Bylicka, 1952; Vartia, 1973).

Parmelia Physodes (L.) Ach. was reported to be antibiotic (Mordraksi, 1956). Usnic acid is wide-spectrum antibiotic characterized from the lichens (Shibamoto & Wei, 1984, Rowe et al. 1991; Dobrescu et al. 1993; Abo-Khatwa et al. 1996; Cocchietto, Skert & Nimis, 2002). Vulpinic acid has mild antibiotic property (Lauterwein et al. 1995). Atranorin has been found to be much less biologically active than usnic acid and vulpinic acid (Lawrey, 1986). Usnic acid, evernic acid, and vulpinic acid inhibited the growth of gram positive bacteria *Staphylococcus aureus*, *Bacillus subtilis*, and

Bacillus megaterium, but the acids had no effect on the gram negative bacteria *Escherichia coli* or *Pseudomonas aeruginosa* (Lawrey, 1986).

Usnic acid isolated from lichens from south Spain has high activity against Gram-positive bacteria (Rowe et al. 1999). Acetone, diethyl ether and ethanol extracts of the lichen *Cetraria aculeata* (Schreber) Fr. and its active constituent protolichesterinic acid were tested positive against *Escherichia coli*, *Staphylococcus aureus*, *Aeromonas hydrophila*, *Proteus vulgaris*, *Streptococcus faecalis*, *Bacillus cereus*, *Bacillus subtilis*, *Pseudomonas aeruginosa*, and *Listeria monocytogenes* (Turk et al. 2003).

Alectosarmentin, (-)-usnic acid, physodic acid and 8'-O-ethyl-beta-alectoronic acid isolated from the alcoholic extract of the lichen *Alectoria sarmentosa* (Ach.) Ach. (Alectoriaceae) showed antimicrobial activity (Gollapudi et al. 1994) *Hypogymnia apinnata* (atranorin), *Letharia columbiana* (vulpinic acid), *Lobaria pulmonaria* (Stictic acid, constictic acid, & norstictic acid) and *Usnea filipendula* (Usnic acid & salazinic acid) have been reported to have significant antibiotic activity against *Micrococcus luteus*, *Staphylococcus aureus*, *Salmonella gallinarum* and *Serratia marcescens* respectively (Crockett et al. 2003).

The acetone and methanol extracts of *Lasallia pustulata* (L.) Méret. (Umbilicariaceae), *Parmelia sulcata* Taylor, and *Umbilicaria crustulosa* (Ach.) Frey (Umbilicariaceae), manifested antibacterial activity against the majority of species of bacteria tested, in addition to selective antifungal activity (Rankovic, Misic & Sukdolak, 2007). Acetone, chloroform, diethyl ether, methanol, and petroleum ether extracts of *Parmelia sulcata* and its constituent (salazinic acid) demonstrated antibacterial activity against *Aeromonas hydrophila*, *Bacillus cereus*, *Bacillus subtilis*, *Listeria monocytogenes*, *Proteus vulgaris*, *Yersinia enterocolitica*, *Staphylococcus aureus*, *Streptococcus faecalis*, *Candida albicans*, *Candida glabrata*, *Aspergillus niger*, *Aspergillus fumigatus*, and *Penicillium notatum* (Candan et al 2007).

3-hydroxyphysodic acid isolated from *Hypogymnia tubulosa* (Schaerer) Havaas (Parmeliaceae) showed antimicrobial activity against *Aeromonas hydrophila*, *Bacillus cereus*, *Bacillus subtilis*, *Escherichia coli*, *Klebsiella pneumoniae*, *Listeria monocytogenes*, *Proteus vulgaris*, *Salmonella typhimurium*, *Staphylococcus aureus*, *Streptococcus faecalis*, and *Candida albicans* (Yilam et al. 2005). Extracts of *Xanthoparmelia pokornyii* (Vainio) Hale (Parmeliaceae) and its constituents (gyrophoric and stenoporic acid) have

been reported to be potential antimicrobials (Candan et al 2006). Extracts of *Pseudevernia furfuracea* and its constituents (physodic acid, chloroatranorin, atranorin, and olivetoric acid) have significant antimicrobial activity (Turk et al. 2006). *Hirtusneanoside* isolated from *Usnea hirta* (L.) Wigg. (Parmeliaceae) showed growth inhibitory activities against Gram-positive bacteria (Renzaka & Sigler, 2007).

ANTIFUNGAL

Parietin, anthraquinone isolated from methanol extract of *Caloplaca cerina* (Ehrh. ex Hedwig) Th.Fr. (Teloschistaceae) has been reported to have significant antifungal activity (Manojlovic et al. 2005). Extracts of Andean lichens *Protousnea poeppigii* (Nees & Flot.) Vain. (Parmeliaceae) and *Usnea florida* var. *rigida* Acharius demonstrated antimicrobial activity against the pathogenic fungi *Microsporum gypseum*, *Trichophyton mentagrophytes* and *T. rubrum*. isodivaricatic acid, 5-propylresorcinol, divaricatinic acid and usnic acid were identified as antifungal agents (Schmeda-Hirschmann et al. 2007).

ANTIVIRAL

Usnic acid isolated from *Teloschistes chrysophthalmus* (L.) Th. Fr. (Teloschistaceae) and parietin isolated from *Ramalina celastri* demonstrated antiviral activity against the arena viruses Junin and Tacaribe (Fazio et al. 2007).

ANTIOXIDANT ACTIVITY

Phenolic constituents from the lichen *Parmotrema stuppeum* (Nyl.) Hale (Parmeliaceae) including methyl orsenillate, orsenillic acid, atranorin and lecanoric acid showed moderate antioxidant activity (Jayapraksha & Rao, 2000). An animal study reported antioxidant activity of lichen *Cetraria islandica* (Gülçin et al. 2002). Stictic acid derivatives from the lichen *Usnea articulata* (Ach.) Motyka were reported to have significant (Lohèzic-Le Dèvehat F 2007).

ANTITUMOR ACTIVITY

Pannarin inhibited cell growth and induces cell death in human prostate carcinoma DU-145 cells (Maier et al. 1999). The orcinol derivatives tenuiorin and methyl orsellinate present in extract of *Peltigera leucophlebia* (Nyl.) Gyeln. (Peltigeraceae) exhibited in vitro inhibitory activity against 15-lipoxygenase from soybeans. A correlation has been observed between 5-lipoxygenase inhibition and antiproliferative effects for related lichen metabolites. On this account, tenuiorin and methyl orsellinate were further tested for antiproliferative activity on cultured human breast,

pancreatic and colon cancer cell lines. Methyl orsellinate lacked antiproliferative activity but tenuiorin depicted moderate activity (Ingolfssdottir et al. 2002). Bianthraquinone glycosides, colleflaccinosides isolated from *Collema flaccidum* (Ach.) Ach. (Collemaaceae) collected in Israel and Russia, were reported to have antitumor activity (Rezanka & Dembitsky, 2006).

IMMUNOMODULATOR ACTIVITY

Heteroglycans and a beta-glucan isolated from *Thamnolia vermicularis* var. *subuliformis* were tested for in vitro immunomodulating activity and reported to have various influences on the immune system (Omarsdottir, Freysdottir & Olafsdottir, 2007).

TYROSINASE-INHIBITORY ACTIVITY

Methanol extracts of *Graphina glaucorufa* (Vain.) Zahlbr., *Graphina multistriata* Müll. Arg., *Graphina salacinilabiata* Patw. & CR Kulk., *Graphis assamensis* Nagarkar & Patw., *Graphis nakanishiana* Patw. & CR Kulk., and *Phaeographopsis indica* (Patw. & Nagarkar) Sipman & Aptroot (Graphidaceae) have significant tyrosinase-inhibitory activity (Behera, Adawadkar & Makhija, 2006). Methanolic extracts of the edible and medicinal lichens, *Umbilicaria* (*Gyrophora*) *esculenta* and *Usnea longissima* manifested in vitro melanogenesis inhibitory. It was concluded that lichen extracts affected the activity of tyrosinase via the inhibition of tyrosinase glycosylation (Kim & Cho, 2007).

RECENT PHYTOCHEMICAL INVESTIGATIONS ON LICHENS

Two tridepsides (2,4-Di-O-methylgyrophoric acid and 2,4,5-tri-O-methylhiassic acid) have been isolated from *Parmelia damaziana* Zahlbr., (Elix, Jayanthi & Leznoff., 1981). Lasallic acid, a tridepside has been reported from *Lasallia asiae-orientalis* Whittaker & Margulis (Umbilicariaceae) (Narui et al. 1996). -butyrolactone acid, (-)-isomuronic acid and gyrophoric acid have been isolated from *Punctelia microsticta* (Mull. Arg.) Krog (Parmeliaceae) (Maier et al. 1999). Dasyvogalactone, a lactone has been reported from *Usnea dasygopa* Rohl growing in Indonesia (Suwarso et al 1999).

A new red anthraquinone, draculone, has been isolated from the corticolous tropical lichen *Melanotheca cruenta* (Mont.) Miill. (Trypetheliaceae) together with anthraquinone pigment haematommone (Mathey, Spitteller & Steglich, 2002). Beta-orcinol metabolites viz hypotrachynic acid,

deoxystictic acid, cryptostictinolide and 8'-methylconstictic acid have been reported from the lichen *Hypotrachyna revoluta* (Flörke) Hale. (Parmeliaceae) (Papadopoulou et al. 2007).

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