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BIOLOGICAL PROPERTIES OF LICHENS - A REVIEW

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Abstract

Even today plant materials do play a major role in primary health care in developing countries for example *Azadirachta indica* natural products have contributed important role in therapeutic drugs in modern medicine. Not only plants, the lower plants like bryophytes also have been reported to display diverse biological activities. For example, its composite organism (fungi and alga or cyanobacteria). Lichens are known for their secondary metabolites and have several medicinal properties as photoprotection allelopathy, antioxidant, anti-microbial and anti-viral. This paper deals with a brief review of the pharmaceutical potentiality of the lichen and its chemical compounds.

Key words: *Azadirachta indica,* bryophytes, pharmaceutical.

Introduction

Erik Acharius created the first National System for lichens and has been called the Father of Lichenology. Lichens are an important constituent of the Indian flora. India has rich vegetational wealth and diversity, mainly because of the immense variety of climatic and altitudinal range, coupled with variant ecological habitats. Lichens have been used in many countries as a cure for diseases of humans for example *Lobaria pulmonaria, Parmelia sulota* used for Pulmonary and cranial diseases. Similarly *Parietina* sp. and *Latharia vulpina* used to cure jaundice and stomach diseases. (Hune, S. *et al.,* 1999; Kirumizigul, S. *et al.,* 2003; Malhotrassubban R. *et al.,* 2008).

In recent years, both in practice and in theory, there has been great interest in new preparations of natural origin for the control and prevention of various human, animal and plant diseases. It is known that the long-term use of synthetic drugs can cause numerous side effects and sometimes resistance (Karaman *et al.,* 2003). Unlike synthetic drugs, bioactive natural products have beneficial effects on the whole organism. In the search for new bioactive preparations of natural origin, lichens are a subject of interest to many research teams.

Lichen Symbiosis

Lichens are symbiotic organisms consisting of algae and fungi and are more important constituents of many eco systems. They usually grow on rocks, soil, tree barks, shrubs, trunks and animal carapaces and on manmade undisturbed surfaces like bricks, leather, wood, bone, glass, metal, plastic, etc. (Shukla *et al.,* 2010; Edwards *et al.,* 1997; Seymour *et al.,* 2005). Lichens produce about 1000 metabolites through their acetyl-polymalonyl, skimic acid and mevaloc acid pathways (Nash *et al.,* 1996). Lichen metabolites spur diverse biological activities such as antimicrobial, antitumor, antimutagenic, antiherbivore and allergenic (Atalay *et al.,* 2011).

Lichens are also known for having higher phenolic content, which has various applications. The development of multi drug resistance in pathogenic bacteria is a serious problem in current clinical chemistry, as it occurs because of the excessive use ofexisting antibacterial drugs (Candan *et al.,* 2007). These organisms are used for human and animal nutrition and in the production of colors, perfumes and alcohol.

Lichens have been used for various purposes, in particular as dyes, perfumes and remedies in folk medicines. In Indian spice market lichens are sold by name of 'Chharilla', which consists of mixture of two or more species of *Parmelia, Usnea longissima, Ramalina sub. complanata* and *Heterodermia tremulans*. Chharila has astringent, resolvent, laxative and carminative properties and is also supposed to posse's aphrodisiac property. The smoke of Chharillaisbelieved to relive headache (Kumar *et al.,* 1996). Medicinal properties of

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Table 1: Antimicrobial activity reported in lichens from different regions are tabulated.

S. No.	Area	Lichen	Solvent		References
1	Eastern Ghats	*Parmotrema reticulatum*	Polar solvents	Acetone high activity	Ayyappadasan Ganesan *et al*., 2017
2	Kopaonik Serbia	*P-Caperata P-Sulcata P-Saxatilis*	Acetone	*P-Saxatilis*- strong *P-Capetata*-low	Marijana M. Kosanic *et al*., 2011
3	Kopaonik Serbia	*Cladonia furcata, Lecanora atra Lecanora muralis*	Acetone	*Cladonia furcata,* - strong *Lecanora muralis*-low	Branislav R. Rankovic *et al.*, 2011
4	Nepal	*Alectoria sarmetosa, R-Farinacea,P-Glauca, E-Divaricata,B-Fuscescens.*	Acetone Chloroform	*Alectoria sarmentosa* -Strong	Baidya Nath Jha *et al*., 2017
5	Shevaroy hills, Eastern Ghats	*Parmotremaaustrosinese, P-hababianumP-Tinctorum*	Polar Solvents	Benzene - high activity.	Ayyappadasan Ganesan *et al.*, 2015
6	Kopaonik Serbia	*P-arseneana,A-fuscata (Ny.l)Arnold.*	Acetone	Lichen's Component gyrophoric high	Marijana M. Kosanic *et al*., 2011
7	Mavhuradonha Mountains	*Cladonia digitata*	Ethanol	Highest activity against *Clatridium perfringens*	Dzomba *et al.*, 2012
8	Kandira district Turkey	*C-rangiformics,* *C-Convoluta*	Methanol Chloroform Acetone Chloroform	Chloroform extract-against *C. albicans*.	Acikgozbirkan *et al.*, 2 013
9	Pithoragarh district Uttarakhand	*Bulbothrix setschwanensis, Parmelariathomasnoni, Everniastrumnepalenase, Heterodermiadiademata*	Acetone, Methanol, Chloroform	Acetone extract -*Bulbothrix setschwanensis, Parmelariathoma snoni and Heterodermiadia demata*	Tiwari *et al.*, 2011
10	Pichavaram Mangrove Forest	*Roccella belangeriana*	Polar Solvents	Aqueous — *Klebsiella pneumonia* Acetone — *Staphyloc occus sp* Methonal — *Staphylo coccus sp, Proteus sp,* Ethyl acetate — *Staphyloc occus sp.* Chloroform — *Enteroco cci sp* Ethanol — *Proteus sp,* Diethyl ether — *Staphyloco ccus sp.* Petroleum ether — *Escherichia coli.*	Karthikaidevi *et al.*, 2009

lichens are mentioned in Ayurvedic system of therapy as they are useful in diseases of blood, heart, bronchitis, scabies, leprosy, enlarged spleen, burning sensation, bleeding pile, thirst, vomiting, asthma while in Unani system, lichens find use in curing inflammations, stomach disorder, dyspepsia, vomiting, pain in liver, amenorrhea and vesicular calculus (Kirtikar *et al.,* 1984). *Lobaria pulmonaria* and *P. sulcata* have been used in treatment of pulmonary and cranial diseases respectively, *Xanthoria parietina* has been used to cure jaundice and *Letharia vulpine* has been used in treatment of stomach diseases (Huneck *et al.,* 1999; Kirmizigul *et al.,* 2003;

Malhotra *et al.,* 2008). The usage of some lichens in traditional medicine for many years has been justified by subsequent research confirming their various biological activities.

Antimicrobial Activity

Lichen forming fungi produce antibiotic secondary metabolites that protect many animals from pathogenic microorganisms (Lawrey *et al.,* 1989). A number of investigators have studied the antibacterial and antifungal activity of lichens. The first study of the antibiotic properties of lichens was carried out by Burkholder *et al.,* 1944. Vartia [20] reported antibacterial activity for several lichens and other researchers have since then studied the antibacterial activity of several lichens against the gram positive and gram negative bacteria, as well as the antifungal activity of lichen extract (Acikgoz *et al.,* 2013). Several lichen extracts have been used for various remedies in folk medicine and screening the lichens has revealed the frequent occurrence of metabolites with antibiotic, antimycobacterial, antiviral, antitumor, analgesic and antipyretic properties (Lawrey *et al.,* 1989; Singh *et al.,* 2011; Acikgoz *et al.,* 2013; Lawrey *et al.,* 1986; Ingolfsdottir *et al.,* 1997).

The anti microbial activity of many lichen taxa such as *Alectoria, Cladonia*, *Lecanora, Evernia, Ramalina, Usnea*, against gram positive and gram-negative bacteria is due to the presence of natural isomers of usnic acid (Ingolfsdottir *et al.,* 2002). The ethanol, chloroform and n-hexane extracts of *R. farinacea* was found active against *E. coli* and *P. aeruginosa b*y (Esimone *et al.,* 1999) Antibacterial activity against these two bacteria was observed (Kekuda *et al.,* 2009).

The extracts of *B. capillaries* and its substance barbatolic acid showed considerable antimicrobial effects. On the basis of these results, the lichen *B. capillaria* and its secondary metabolite barbatolic acid appear to be good and safe natural antimicrobial agent and could be used in the control of various human, animal and plant diseases due to pathogens (Sariozlu *et al.,* 2016).

The acetone extracts of *Parmotrema reticulatum* showed highest antibacterial activity followed by methanol and ethanol extracts. Acetone extract was found superior to the standard antibiotic ampicillin and inferior to the chloramphenicol extract against the several micro-organisms (Ayyapadasan Ganesan *et al.,* 2017).

In HPLC analysis, revealed the presence of major phytochemical compounds such as atranorin, lecanoricacid, salazinic acid and chloroatranorin in different species of parmeliod lichens such as *P. tinctorum, P. hababiam, P. austrosinense*. In addition, finding of these activities could lead to the formulation of pharmaceutically important products for various ailments (Ingolfsdottir *et al.,* 2002).

Antioxidant Activity

Previously a lot of attention has been paid to lichens as source of natural antioxidant (Behera *et al.,* 2006; Gulcin *et al.,* 2002). Natural antioxidants consists of antifungal, antibacterial, antiviral, anti-inflammatory and anti-allergic properties (Muanda *et al.,* 2010). According to their chemical structure, most lichen substances are phenolic compounds, dibenzofuranes, usnicacids, depsidones, depsones, lactones, quinines and pulvunic acid derivatives. In various systems of traditional medicine worldwide, including the Indian system of medicine, lichen species are said to effectively cure dyspepsia, bleeding piles, bronchitis, scabies, stomach disorders and many disorders of blood and heart (Shukla *et al.,* 2010; Shahidi *et al.,* 1992; Rankovic, B. *et al.,* 2010). In recent years much attention has been devoted to natural antioxidant and their association with health benefits (Ayyappadasan Ganesan *et al.*, 2015).

The antioxidant activity of lichens are shown in table 2.

The DCM (Dichloromethane) fractions of *Parmotrema centratum, Peltigera polydactyla and Ramalina roesleri* and methanol fractions of *Peltigerapoly dactyla* and *Parmoterma sp*. showed comparatively strong DPPH reducing activity. The methanol extract of *Parmoterma sp*. from Nepal origin showed stronger antioxidant activity (IC_{50},11.4±0.1ug/ml) than the same species collected from Malaysia (IC_{50}>500ug/ml) [41]. *Ramalina bourgena* is consumed as a folk medicine for diuretic and stone-dissolving properties (Gonzalez-Tejero *et al.,* 1995).

Other Biological Activities

Now a day's cancer is one of the most common and dangerous diseases. Researches focused developing new anticancer drug therapies from various natural sources such as plants, fungi, prokaryotes, marine organisms etc.. More than 1000 secondary chemicals were identified. These chemicals used for anticancer drugs dates back to the late 1960 (Fukuora *et al.*, 1968); (Bezivin *et al.,* 2003). *Parmelia spp*. are used in wound healing in parts of Eastern ghats, India. Many other lichen compounds either in crude extract or purified form have been reported against various malignant cell lines showing cytotoxic effects on various cancer cell lines (Ren, M.R. *et al.,* 2009); (Kumar and Muller, 1999; Zeytinogl *et al.,* 2008).

Lichens are effective against various cancer cell lines both in crude form (Backorova, M. *et al.,* 2011; Backorova *et al.,* 2012) and purified form (Burlando, B. *et al.,* 2009; Russo, A. *et al.,* 2006; Einarsdottir, E. *et al.,* 2010). The literature also shows that lichen metabolites are strongly cytotoxic and have the capality of terminating cell proliferation at micro-molar

Table 2: Antioxidant Activity of Lichens.

S. No	Area	Lichen	Solvent	Activity		References
1	Eastern Ghats	*Parmotrema reticulatum.*	Ethanol Methanol	DPPH free Radial	Methanol extract- highest activity Ethyl acetate extract highest phenolic content	Ayyappa dasan *et al.*, 2017
2	Kopaonik Serbia	Parmelia Species *P. caperata, P. sulcata, P. saxatilis.*	Acetone	DPPH free Radial	Acetone extract of *P. saxatilis* showed highest activity	Marijana M Kosanic *et al.*, 2011
				Reducing Power	*P. saxatilis* showed highest Reducing Power	
				Superoxide anion radical scavenging	Acetone extracts of *P. caperata* have highest superoxide activity	
				Phenolic & flavonoid content	Acetone extract of *P. saxatilis* highest Phenolic content	
3	Kopaonik Serbia	*Cladonia furcata, Lecanora atra, Lecanora muralis.*	Acetone Extract	DPPH free Radial	*Lecanora atra* showed highest DPPH radi Scavenging activity	Branislav Rankovic *et al.*,
				Reducing Power	*Lecanora atra* showed highest reducing power	
				Phenolic & flavonoid content	Highest Phenolic content in *Lecanora atra,*	
4	Shevaroy hills Eastern Ghats	Parmeliodlichen, *Parmotremaa ustrosinense, P. hababianum, P. tinctorum.*	Petroleum ether, Ethyl acetate acetone, ethanol & Water	DPPH Free Radial	Acetone extract *P. tinctorum* showed very good antioxidant activity	Ayyappadasan Ganesan *et al.*, 2015
				Reducing Power	Ferric reducing power showed highest reducing power in acetone extracts of *P. tinctorum*	
				Superoxide anion radical scavenging	Hydrogen peroxide scavenging activity showed the highest activity in methanol and benezene extract of *P. hababianum* & Benzene extract of *P. tinctorum*	
5	Kopaonik Serbia	*Parmella arseneana, Acarospora fuscata*	Acetone	DPPH free Radial	Acetone extract of *P.arseneana* have highest Acetone extract of *P. arseneana* have highest	Marijana Kosanic *et al.*, 2011
				Reducing Power Reducing Power	Isolated compound gyrophoric acid has high reducing Power.	
				Superoxide anion radical scavenging	Isolated compound gyrophoric acid have high radical scavengings activity	
				Phenolic & flavonoid content	Acetone extract of *P. arseneana*	

concentrations (Einarsdottir, E. *et al.,* 2010). Structural modification of lichen compounds has also been shown to enhance the cytotoxic capacity of many lichen compounds (Bazin, M.A. *et al.,* 2008; Tokiwano, T. *et al.,* 2009). In addition, the position of different functional groups in lichen compounds also affects levels of cytotoxicity (Correche, E.R. *et al.,* 2002). Regulation of the cell cycle is critical in controlling the growth and development of cancer cells. Various lichen acids have been found to stop cancer cell growth at the sub-G_1 (Ren, M.R. *et al.,* 2009) of the cell cycle. The mechanism of cell death in various cancer cell lines caused by lichen metabolites include apoptosis (Burlando, B. *et al.,* 2009; Ren, M.R. *et al.,* 2009; Einarsdottir, E. *et al.,* 2010) necrosis (Einarsdottir, E. *et al.,* 2010) and angiogenesis inhibition (Bezivin, C. *et al.,* 2004; Liu, H. *et al*., 2010) and caspase independent (Bezivin, C. *et al.,* 2004) pathways were found to initiate apoptosis. In addition to the lichen secondary compounds, polysaccharides derived from lichens, especially β-glucan and galactomannan, have been shown to be active against several cancer cell lines (Koparal, A.T. *et al.,* 2010; Correche, E. *et al.,* 2004). Recently, there has been additional research examining the use of lichen polysaccharides as immunostimulatory compounds and their potential role in fighting cancer (Nishikawa, Y. *et al.,* 1981; Watanabe, M. *et al.,* 1986). The cytotoxic activity of acetone extracts *Cladonica furcata, Lecanora atra* and *Lecanora muralis* was studied against Femx cell and LS174 cell. From this study *Lecanora atra* was exhibited the best cytotoxic activity, *Cladonica furcata* showed weaker cytotoxic activity. Finally concluded positive control (CIS-DDP) had slightly compared better cytotoxic activity compared to tested lichen extracts. (Rankovic *et al.,* 2011). Similarly acetone extract of three lichens was examined *P. saxatilis>P. caperata>P. sulcata*

In this study also CIS-DDP had higher cytotoxic activity compared to tested lichen extracts. (Marijana, M. *et al.,* 2011).

The cytotoxic activity of the lichen extract *Parmelia arseneana*, have good results against the target cell lines such as LS174, K562, FemX (Kosanic *et al.,* 2014).

Conclusion

Chemical structure of most of the lichen substances is simple which facilitates synthesis of these compounds in the laboratory. This practice would provide large amounts of material without affecting ecosystem. In addition, many of these compounds can be used as precursors based on their particular mechanism of action and can then be optimized in the laboratory to fit specific applications.

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Conflict of interest

The authors declare no conflicts of interest.

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