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Potential of Lichens: A Review of Bioactive Compounds with Biological Activities

Monika Thakur and Hem Chander
Division Botany, Department of Bio-Sciences,
Career Point University, Hamirpur 176041, (H.P.), India

(Corresponding author: Monika Thakur)
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ABSTRACT: Lichens are entities that are formed by the interaction of mycobiont as well as photobiont or blue-green algae through symbiosis. Lichen utilizes a wide range of bioactive molecules with several biological properties like antifungal, antibacterial, antitumor, antioxidant, antiherbivore, insecticidal, allelochemical, and antigenic action. These metabolites play a significant role in photoprotection towards extreme emission and it might be a promising antipyretic and analgesic drug applicant. The assets of lichens bioactive components make them worthy as well as possible therapeutic mediator. Lichen compounds play a key role in metal homeostasis as well as contamination resistance. During this domain, there seems to be a great need for research to explore the significance of lichens, which are a valuable substitute for many active substances with tremendous therapeutic value. The biological activities of bioactive molecules derived from lichens are described in this review.

Keywords: Lichen, Secondary Metabolites, medicinal value, antioxidant.

INTRODUCTION

Lichen is a viable, ecologically obligatory, symbiosis with an exhibiting the mycobiont or one or more unicellular as well as filament-able photoautotrophic partners situated inside an outer membrane region (photobiont). Ascomycota is mainly fungal partners (98%) and several others adhere to the Basidiomycota (Gilbert, 2000; Honegger, 1991). Probably 21% of all fungi are capable of functioning as mycobionts (Honegger, 1991); rendering lichens the highest cooperative community of fungi. As photosynthetic partners throughout the synthesis of lichens, only 40 genera remain associated: 25 photobionts as well as 15 blue-green algae (Kirk *et al.*, 2008). Photobionts are not recognized at the species level in about 98 percent of lichens (Honegger, 2001). In such a wide variety of habitats, lichen exists: from Polar Regions to tropical areas, from plains to hills and mountains (Müller, 2001), and from marine to xeric settings. Lichens have been located on or inside stones, on soil, on stems as well as shrubs or trees, on the surface of growing foliage, on exoskeletons of animals, uninterrupted substrate created by man, like timber, leather, bone, metal, concrete, and plastic (Brightman and Seaward, 1977; Seaward, 2008). In different weather conditions, lichens can thrive; they must lead to high heat, drought, floods, alkalinity, increased levels of air pollutants as well as extremely nitrified nutrient-poor ecosystems (Nash, 2008), that are the first colonizers of terrestrial habitats (pioneers) (Nash, 2008). Both lichen thallus fungal or algal cells are characterized by their ability to survive in space (Sancho *et al.*, 2007). This remarkable efficiency of lichens in rare habitats is partly explained by associations between the mutualistic partners (Backor and Fahselt, 2008). However, several lichens are quite resistant to different contaminants, particularly substances relying on nitrogen, sulfur, or heavy metals, and are thus extensively used as biomonitors (Fernández-Salegui *et al.*, 2007; Glavich and Geiser, 2008). Lichens are important plant resources that are being used all over the globe for medicine, fodder, perfume, spice, dyes, and other purposes. Lichens seem to be well for producing a wide range of bioactive compounds. Lichens are used for a variety of purposes in folk medicine, including astringents, laxatives, anticonvulsants, antiemetics, antiasthmatics, anti-inflammatories, antibiotics, as well as the diagnosis of cardiovascular, respiratory, or gastric disorders (Shukla *et al.*, 2010). Furthermore, Pharmaceutical, as well as biotechnological research, has been performed to assess and grow biomaterials including lichen-isolated natural compounds for human usages (Nunes *et al.*, 2010; 2011).

Harikrishnan *et al.* (2020) exhibited the anticancer activity of *Parmotrema rampoddense* lichens which prohibited the Akt activity through stimulating the mitochondria triggered apoptotic pathway. Abdullah *et al.*, (2020) performed the biosynthesis of $ZnO@TiO_2@SiO_2$ and $Fe_3O_4@SiO_2$ nanocomposites using the bioactive potential of *Lecanora muralis* (LM)

lichen which showed the antibacterial and antifungal activities of nanostructures or demonstrated that green synthesized nanostructures have a very good antibacterial ability against *Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas* spp. and *Candida* spp. pathogenic bacteria, and fungi but no antifungal activity toward the *Aspergillus flavus*, *Aspergillus niger*, and *Aspergillus terrus* fungi species. Gökalsın *et al.*, (2020) displayed the inhibitory potentials of *Ramalina farinacea* and *Platismatia glauca* extracts were tested against QS systems of *P. aeruginosa* using biosensor strains (lasB-gfp, rhlA-gfp, and pqsA-gfp). Aoussar *et al.*, (2020) demonstrated the cytotoxic, antioxidant, and antimicrobial activities of acetone extracts of *Evernia prunastri*, *Ramalina farinacea*, and *Pseudevernia furfuracea*, illustrating that the lichens analyzed include notable active substances including physodalic acid, evernic acid, and usnic acid, as well as protocetraric acid, that the tests reported that all *P. furfuracea* extract had the highest free-radical-scavenging potential (IC50 = 498.40 g/mL) when it came to antioxidant capacity. The most potent antibacterial extract was recorded for *P. furfuracea* extract with a minimum inhibitory concentration (MIC) ranging from 0.039 to 0.31 mg/mL. The isolation of two known substances, atranorin and ribenone, from the ethyl acetate extract as well as hydroalcoholic extract of *Graphis ajarekari*, displayed fibrinolytic, anti-inflammatory, and cytotoxic effects (Tatipamula and Vedula, 2020). Ingelfinger *et al.*, (2020) explored the pharmacological activity of six lichen extracts (*Evernia prunastri*, *Pseudevernia furfuracea*, *Umbilicaria pustulata*, *Umbilicaria crustulosa*, *Flavoparmelia caperata*, *Platismatia glauca*) these lichen extracts tested in this study exhibit significant pharmacological activity in the context of inflammation and/or cancer, indicating that the group lichen-forming fungi includes promising members for further testing. Extract of mushroom *Ganoderma applanatum* and the lichen *Candelariella vitellina* exhibited the antioxidant, antirotavirus, and anticolon cancer activities (Elkhateeb *et al.*, 2020).

A. Bioactive Compounds

A wide range of bioactive compounds are produced by lichens, and several of them are particular to lichen-forming fungi. These chemically diverse lichen compounds (aliphatic and aromatic) are of very low molecular weight (Türk *et al.*, 2003). They are created by mycobionts (Elix, 1996; Huneck, 1999) which absorb as outer membrane small crystals on the external surface of the mycelium within the cortex and in the medullary surface. The photobiont could also affect the mycobiont's bioactive compounds (Brunauer *et al.*, 2007; Yamamoto *et al.*, 1993; Yoshimura *et al.*, 1994). The majority of lichen compounds are phenolic acids (derivatives of orcinol and b-orcinol), dibenzofurans (usnic acid), depsides (barbatic acid), depsidones (salazinic acid), depsons (picrolichenic acid), lactones (protolichesteric acid, nephrosteric acid), quinones (parietin) as well as metabolites of pulvic acid from their organic compounds (vulpinic acid). Lichens naturally included numerous biochemical pathways to generate the number of aspects (Fig. 1) primarily polymalonate, shikimic acid as well as mevalonic acid processes. Biosynthetic pathways were responsible for the formation of lichen metabolites (Boustie and Grube, 2005).

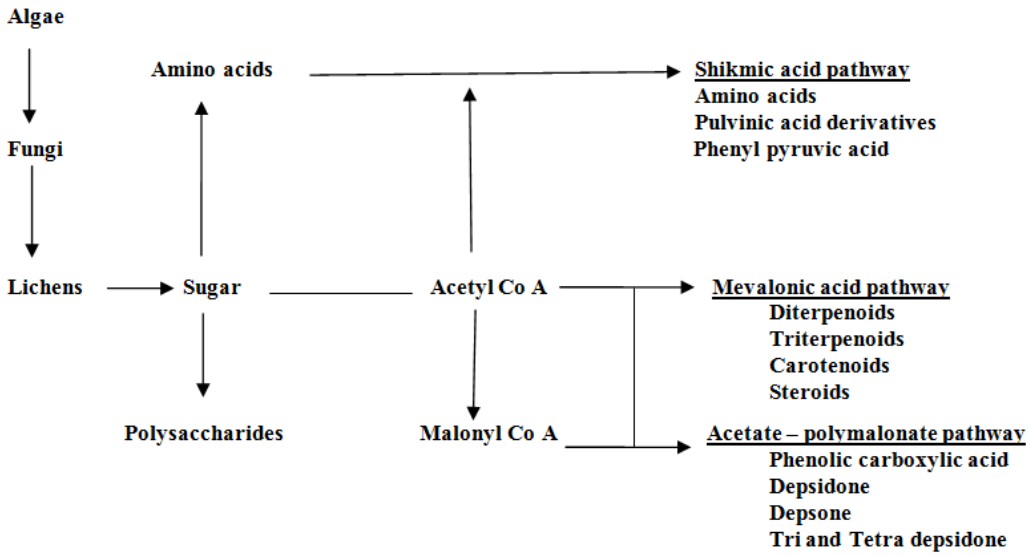

Fig. 1. Diagrammatic representation of secondary metabolites synthesized by lichens (Brahma *et al.*, 2016).

Polymalonate mechanism: The bioactive compounds of lichen produced by the polymalonyl mechanism adhere primarily to the single class of compounds, depsides as well as depsidones. Fungal partners produce these substances only when they are paired with algae (lichen symbiosis). The active mutualistic interaction of lichens plays a major role in these metabolites. Shikimic acid mechanism: Pulvinic acid as well as terphenylquinone are primarily lichen compounds produced through the shikimate pathway. These substances are generated through the merger of different components of phenylpyruvate. These substances are commonly present in the Stictaceae family of lichens. Mevalonic mechanism: The

synthesis of mevalonic acid primarily results throughout terpene metabolism. Sesquiterpenes in lichens have not been documented since. Even rare are Diterpenes. Triterpenes are found within lichens and twenty different triterpenes are being extracted from lichens of various organisms. In various organisms of lichens, Zeorin seems to be the principal terpene (Boustie and Grube, 2005).

B. Biological activities

Bioactive compounds from lichens, particularly polymalonyl generated polyketides, are being demonstrated to display numerous biological functions in different screenings (Huneck, 1999; 2001; Muller, 2001). Crude solvent extracts or isolated substances from lichens display biological properties including antimicrobial, immunomodulatory, antibacterial, antiviral function enzyme inhibitory, anticancer, antioxidant as well as an anti-inflammatory. Species of lichens are protective against various diseases (Table 1).

C. Antioxidant Activity

In many metabolic pathways within cells, free radicals (reactive oxygen species or reactive nitrogen species) having an essential function, but they are also connected with adverse side effects, inducing damage to the cells. In a cellular membrane, these target proteins as well as biomolecules, and also essential fatty acids. Reactive oxygen species can be associated with food degradation, neurodegenerative diseases, and several severe human disorders, like Alzheimer's disease, atherosclerosis, emphysema, hemochromatosis, several types of cancer, Parkinson's disease, as well as schizophrenia. Lichen thalli also have a plethora of generation of reactive oxygen species, as well as the bioactive substance that provides resistance towards reactive oxygen species created through ultraviolet rays (Marante *et al.,* 2003). Russo *et al.,* (2008) showed that superoxide anion synthesis was prevented in vitro by sphaerophorin (depside) or pannarin (depsidone), pannarin becoming more effective, confirming (Hidalgo *et al.,* 1994). *Lobaria pulmonaria* methanol extract decreased the over-accumulation of free radicals induced through indomethacin in rat stomachs, raising superoxide dismutase as well as glutathione peroxidase concentrations in rats (Karakus *et al.,* 2009). The usnic compound has also been shown to be a gastroprotective agent since it decreases oxidative damage as well as prevents neutrophil invasion in indomethacin-induced gastric ulcers in rats (Odabasoglu *et al.,* 2006). *Dolichousnea longissima* as well as *Lobaria pulmonaria* methanol extracts are used to provide substantial in vitro antioxidant effects (Odabasoglu *et al.,* 2004). According to Luo *et al.,* (2009), over accumulation of free radical's oxidative stress is intensified by harsh circumstances within the Antarctic (like low temperatures, drought, winter darkness, ultra Violet or light intensity); therefore, Antarctic lichens absorb greater quantities of antioxidant substances and have greater antioxidant capacity than polar regions lichens. In reactive oxygen species as well as superoxide anion scavenging, and also in decreasing energy assays between screened lichen species collected from King George Island, Antarctica, an acetone extract of *Umbilicaria* Antarctica being shown to be the most efficient antioxidant. As the main bioactive components, Lecanoric acid was described. Methanol-water extracts of five lichens have been tested for their antioxidant effects through *Caloplaca regalis*, *Caloplaca* sp., *Lecanora* sp., *Ramalina terebrata*, *Stereocaulon alpinum* from Antarctica (Bhattarai *et al.,* 2008).

Table 1: Lichens sp. involved in various biological activities.

Lichens species	Compounds	Mechanisms	Bioactivities	References
Parmotrema grayana	Divaricatic acid, Atranorin acid or Usnic acid	Prevented glycation activity	Antidiabetic	Thadhani *et al.* (2013)
Parmotrema chinense	Stictic acid	Inhibited α-amylase enzyme functioning		Valadebeigi and Shaddel (2016)
Hypogymnia physodes	-	By using acetone extract, increased cytotoxicity of MCF-7 (IC50 72.4 µg/mL), T47D (IC50 75.4 IC50 µg/mL), MDA-MB-231 (IC50 93.9 µg/mL)	Anticancer	Studzińska-Sroka *et al.* (2016)
P. rampoddense	Atranorin	Prevented the Akt activity through stimulating the mitochondria triggered apoptotic pathway		Harikrishnan *et al.* (2020)
Usnea meridionalis	Usnic acid	Induced greatest release of NO in peritoneal macrophages.	Immunostimulatory	Santos *et al.* (2004)
Cladonia lepidophora		Anti-proliferative effect against MCF-7, HeLa, HCT-116	Anticarcinogenic	Brisdelli *et al.* (2013)
Usnea complanata	Psoromic acid (depsidone)	Moderate to strong antioxidant activity, concentration-dependent manner, on the FRSA, NOR and in LPO. Poor fibrinolytic potential	Cardioprotective	Behera *et al.* (2012)

Hypogymnia physodes	Physodalic acid (depsidone)	Induced thymocytes toxicity mainly through increased ROS levels and decreased MMP	Immunoprotective	Pavlović *et al.* (2013)
Cladonia macilenta	Biruloquinone (quinone)	Improved viability the H_2O_2 and β-amyloid injured PC12 cells. Classified as a a mixed-II inhibitor	Neuroprotective	Luo *et al.* (2013)
Parmelia caperata	Protocetraric acid (depsidone)	Highly antibacterial active and presented strong anticancer activity toward FemX and LS174 cell lines. These activities could be due to its higher phenol content.	Antibacterial and anticarcinogenic	Manojlović *et al.* (2012)
Stereocaulon alpinum	Lobastin (depsidone)	Active against Gram-positive bacteria, *B. subtilis* and *S. aureus*. Moderate antioxidant activity compared with the synthetic commercial standard BHT	Antibacterial and Antioxidant	Bhattarai *et al.* (2013)
Lethariella canariensis	Methyl β-orsellinate (Benzoic acid derivative)	Activity against *Staphilococcus aureus*	Antibacterial	Marante *et al.* (2003)
Usnea longissimi	Usnic acid	Increased SOD, GPx, GSH and cNOS activities and reduced CAT, GR, LPO, iNOS and MPx activities	Gastroprotective	Odabasoglu *et al.* (2006)
Usnea longissma	Usnic acid	Dose-dependent inhibitory effect on LPS-induced TNF-α and NO production in macrophages RAW 264.7, associated with decreased synthesis of TNF-α mRNA and iNOS protein	Anti-inflammatory	Jin, Li and He (2008)
Cladina kalbi	Atranorim	Superoxide dismutase-like and scavenging activity of peroxyl radicals. Induce cytoprotection in the presence of toxic concentrations of H_2O_2 on the SH-SY5Y cells. Conversely, it presented a pro-oxidant capacity in a lipid-rich system, enhancing TBARS and also enhanced production of NO and H_2O_2 in higher concentrations	Antioxidant, cytoprotective and pro-oxidative	Melo *et al.* (2011)

D. Antimicrobial Activity

Solvent, ethanol, and ethyl acetate extracts of *Alectoria sarmentosa*, as well as *Cladonia rangiferina*, were shown to have modest antifungal efficacy towards various species of fungi, particularly human pathogens (Rankovic 'and Mišic', 2007), the most active ethanol extracts. Halama and Van Haluwin, (2004) showed a strong ability to inhibit the growth of certain plant pathogenic fungi, i.e. *Phytophthora infestans*, *Pythium ultimum*, and *Ustilago maydis*, in acetone extracts of *Evernia prunastri* and *Hypogymnia physodes*. *Caloplaca regalis*, *Caloplaca* sp., *Lecanora* sp., *Ramalina terebrata*, *Stereocaulon alpinum* illustrated target-specific antibacterial activity, particularly good towards Gram-positive bacteria, contrasted with the previously stated lichen substances (Paudel *et al.*, 2008). Dichloromethane as well as methanol extracts from *Protousnea poeppigii* had good antifungal effects against the fungal pathogens *Microsporum gypseum*, *Trichophyton mentagrophytes*, and *T. rubrum*, according to (Schmeda-Hirschmann *et al.*, 2008). Extracts were also successful towards *Candida albicans*, *C. yeast*, *Tropicalis*, *Saccharomyces cerevisiae* as well as *Aspergillus niger* filamentous fungi, *A. flavus* or *A. fumigatus*, but with much greater ability. Isodivaricatic acid, divaricatinic acid, and usnic acid, the main lichen substances in *Protousnea poeppigii*, as well exhibited antifungal action toward *Microsporum gypseum*, *Trichophyton mentagrophytes*, and *T. rubrum*, usnic acid to be less effective. In the same tests, crude extract of *Usnea florida* also exhibited great antifungal properties.

E. Cytotoxic, antitumor, and antiviral activity

Russo *et al.*, (2008) observed that sphaerophorin isolated from *Sphaerophorus globosus* as well as depsidone pannarin isolated from *Psoroma pholidotoides*, *P. pulchrum*, and *P. pallidum* regulates the expression of human melanoma cells in M14, causing the cell death. In the diagnosis of this hostile, therapy-resistant skin tumor, the anti-cancer acts of these lichen compounds are beneficial. A wide-ranging antiviral factor towards RNA (respiratory syncytial virus and HIV1), as well as DNA (adenovirus or herpes simplex virus type 1) viruses, has been reported being an ethyl acetate-soluble fraction (ET4) of the crude methanolic extract of *Ramalina farinacea* (Esimone *et al.*, 2009). Usnic acid isolated from *Ramalina celastri's* aposymbiotic mycobionts demonstrated particular antiviral activity against the Junin virus (Arenaviridae), and that is the cause of human hemorrhagic fever in Argentina, and against the non-pathogenic arenavirus, Tacaribe virus (Fazio *et al.*, 2007). Parietin isolated from the aposymbiotic *Teloschistes chrysophthalmus* mycobionts) demonstrated a virucidal impact against the same viruses. Usnic acid, owing to its capacity to detach or prevent the electron transport chain in mitochondria as

well as cause oxidative stress in cells, was shown to be a potent hepatotoxic factor towards monogastric murine hepatocytes (Han *et al.*, 2004). Usnic acid isolated from *Cladonia convoluta* enantiomer mediated cell death in murine lymphocytic cancer cells and was moderately cytotoxic to several cancer cells, including murine Lewis lung carcinoma, human chronic myelogenous leukemia, human prostate carcinoma metastasis, human breast adenocarcinoma, or human glioblastoma (Bézivin *et al.*, 2004). Usnic acid has also reduced the progression without DNA damage of human lung carcinoma cellsas well as human mammary carcinoma cells (Mayer *et al.*, 2005).

F. Antihervivore and insecticidal activity

Insects, mites, snails, slugs, lepidopteran larvae, caribou, and reindeer are among the herbivores that graze on lichens (Molnár and Farkas, 2010). Herbivory on lichens appears to be uncommon, owing to their poor nutritional content, structural characteristics (for instance, the gelatinous sheath in Collemataceae, thick cortex), and resistance substance development. Lichens can be protected from herbivory by active metabolites (Asplund and Gauslaa, 2007, 2008; Gauslaa, 2005; Nimis and Skert, 2006). Insects, snails, and nematodes are contaminated through lichen compounds.Lichen compounds may be particularly suitable for potential pesticides because natural plant-derived products have a lower environmental effect than synthetic chemicals (Dayan and Romagni, 2001). Lichen compounds are also poisonous to vertebrate herbivores. Cook *et al*., (2007) and Dailey *et al.,* (2008) registered toxicity and death of an estimated 400–500 elk (*Cervus canadensis*) in Wyoming during the winter of 2004 due to lichen *Xanthoparmelia chlorochroa* ingestion. Red urine, ataxia, and muscle fatigue were the first symptoms, followed by recumbency and myodegradation. Both enantiomers of usnic acid had high larvicidal activity against the third and fourth instar larvae of the house mosquito (*Culex pipiens*), according to Cetin *et al.,* (2008), and larval mortality was dose-dependent. Caperatic acid and extracts from the lichens *Flavoparmelia baltimorensis* and *Xanthoparmelia cumberlandia* have antiherbivore properties against the snail *Pallifera varia*, according to (Lawrey, 1983). Methyl b-orcinolcarboxylate, ethyl hematommate and 5chlorohematommate are the lichen metabolites that showed nematocidic activity on larvae of *Toxocara canis*. Giez *et al.,* (1994) and Emmerich *et al.,* (1993) studied the effect of some lichen substances i.e atranorin, pulvinic acid dilactone, calycin, parietin, evernic, psoromic, physodic, 3hydroxyphysodic, fumarprotocetraric, stictic, norstictic, salazinic, vulpinic, rhizocarpic, and usnic acids on the growth and development of the polyphageous insect *Spodoptera littoralis* but did not affect their survival.

G. Allelopathy

Bioactive compounds from lichens stimulate the development and growth of associated lichens, mosses, algae, and vascular plants, and also microorganisms, or may act as allelopathic agents known as allelochemicals (Macias *et al*., 2007; Bhattacharyya *et al.,* 2016). Allelopathic substances are emitted into the atmosphere, according to Macias *et al.,* (2007), and can affect photosynthesis, respiration, transpiration, protein and nucleic acid synthesis, membrane ion transport, and permeability in other species. Moss and lichen populations often coexist on rocks, soil, and trees, competing for light, surface, minerals, as well as moisture. Lichen thalli compete for resources as well as illumination on a wide range of substrates, according to Armstrong and Welch (2007), and play a significant role in assessing the composition of lichen populations and the distribution of individual species, with lichen secondary chemistry possibly having a role in this competition. The crustose lichens *Graphis scripta* and *Caloplaca citrine* had their ascospore germination strongly inhibited by vulpinic and evernic acids. The green alga *Chlamydomonas reinhardii* is inhibited by usnic acid. The lichen *Porpidia albocaerulescens* was discovered to inhibit the growth of the mosses *Hedwigia ciliata* and *Anomodon attenuatum*, as well as the liverwort *Porella platyphylla* (Bhattacharyya *et al.,* 2016). The 4-O-methylated depsides evernic and squamatic acids inhibited spore germination and protonemal growth in three common moss species, *Ceratodon purpureus*, *Funaria hygrometrica*, and *Mnium cuspidatum* (Armstrong and Welch, 2007). Higher plants have long been considered to be inhibited or significantly slowed by lichens. Barbatic acid, diffractaic acid, evernic acid, lecanoric acid, b-Orcinolcarboxylic acids, osrsellinic acids, and 4-ODemethylbarbatic acid are some of the lichen derivatives that have heavy allelochemical activity against higher plants (Nishitoba *et al.,* 1987). Usnic acid inhibits mitosis in Allium. Twelve lichen substances identified in "Letharal," the phenolic fraction of *Lethariella canariensis* showed allelopathic activity against the seeds of common garden plants, and inhibited the germination process of cabbage, lettuce, pepper.

H. Photoprotection

Lichens use a repertoire of techniques to protect light-sensitive algal symbionts from strong thermal levels and Ultraviolet rays' exposure, including the xanthophyll cycle in algal thylakoid membranes, and also light screening and UV-B protection through lichen derivatives (Molnar and Farkas, 2010). Lichen compounds contained in the cortical area improve the visibility of the upper cortex, reducing high event irradiance affecting the algal layer, according to the light-screening method. Some lichen derivatives, such as parietin, usnic acid, and vulpinic acid, serve as light-screening pigments, regulating the solar irradiance entering the algal layer through trapping most of the incident light and shielding the photosynthetic partner from excessive radiation (Bhattacharyya et al., 2016). Many lichen bioactive compounds (including atranorin, calycin, pinastric acid, pulvinic acid, rhizocarpic acid, usnic acid, vulpinic acid) have high UV absorption properties and therefore can act as filters for excessive UV-B irradiation, according to Solhaug and Gauslaa (1996). Since the fluorescence spectrum of the cortical depside atranorin matches the

emission spectra of algal chlorophyll, atranorin's light must be used in photosynthesis (Bhattacharyya *et al.*, 2016).

I. Effect on metal homeostasis and pollution tolerance

Lichen derivatives regulate metal homeostasis in lichens by maximizing lichen resistance to heavy metals in contaminated environments by stimulating the absorption of some metal cations while decreasing the accumulation of others (Molnar and Farkas, 2010). According to Jayanthi *et al.,* (2012), lichen bioactive compounds including depsides and depsidones, which are formed by the fungal symbiont as well as absorb on the outer surface of its hyphae, are thought to play a significant role in heavy metal extracellular immobilization. In heavy metal-polluted areas, lichens produce high levels of heavy metals (e.g. Cu, Zn, Pb, Cd, Mn), showing that they are a strong metal resistant species.In lichen *Hypogymnia physodes* transplanted to areas saturated with heavy metals and acidic inorganic sulfur compounds, Biaonska and Dayan (2005) find significant improvement in the concentrations of active metabolites. Thalli transplanted near a chemical plant manufacturing chromium, phosphorous, and sulfur compounds, for example, showed a substantial reduction in atranorin, physodic acid, and hydroxyphysodic acid levels. The level of physodalic acid, on the other side, risen exponentially, indicating that this substance might be effective in combating emissions stress. Hauck and Huneck (2007) had to use a new mechanism to simulate lichen cell walls, which include several hydroxy and carboxy categories as binding sites for metal cations and illustrated the ion-specific increase or decrease of heavy metal adsorption at cation exchange sites (hydroxy groups) on cellulose filters coated with four *Hypogymnia physodes* lichen compounds (atranorin, physodic acid, physodalic acid, and protocetraric acid). The alkali metal ion Na+, the alkaline earth metal ions Ca^{2+} and Mg^{2+}, and the transition metal ions Cu^{2+}, Fe^{2+}, Fe^{3+}, and Mn^{2+} adsorption was examined. The adsorption of Na+, Ca^{2+}, Mg^{2+}, Cu^{2+}, and Mn^{2+} was strongly suppressed by lichen substances, while the concentration of Fe3+ was increased significantly. Among the four compounds tested, depsidone physodalic acid is considered as being the most effective.

J. Allergenic activity

In people who are allergic to lichens, lichen derivatives might have been a contact allergen. Which may cause occupational allergic contact dermatitis in forestry and horticultural workers ("woodcutter's eczema"), and also non-occupational allergic dermatitis in people who cut as well as manage to kindle, pick berries, hunt, or use cosmetics (perfumes, after-shave lotions, deodorants, and sunscreen products) that contain lichen metabolites (Aalto-Korte *et al.,* 2005). Atranorin, barbatic, diffractaic, evernic, fumarprotocetraric, lobaric, perlatolic, physodic, physodalic, protolichesterinic, salazinic, stictic, and usnic acids are lichen metabolites that induce exposure allergic in sensitive people. According to Thune and Solberg (1980), certain lichen substances (such as atranorin and stictic acid) may photosensitize human skin, resulting in photo contact dermatitis, a condition in which susceptibility to illumination aggravates effects.

CONCLUSIONS

Lichens, with different biological activities, represent an important source of bioactive compounds. There are currently over tens of thousands of bioactive derivatives found in lichens. Lichens are mycobiont as well as photobiont or blue green algae that are mutualistic species. A wide diversity of bioactive compounds is synthesized by lichen-forming fungi, some of which are different. A vast number of noteworthy biological properties such as antibacterial, antioxidant, antimicrobial, cytotoxic, inhibitory enzymes, anti-inflammatory, antiviral, immunomodulatory, are demonstrated by lichen bioactive compounds. In addition, the effects of lichen compounds make pharmaceuticals feasible for them. At the same moment, individuals must be assured that lichens are slow-growing species, as well as their existence might be threatened by the exploitation of their organic compounds. Nevertheless, advanced culture methods, as well as diverse growing conditions within aposymbiotically, generated mycobionts may have a beneficial impact on the production of secondary metabolites without harvesting as well as placing the destruction of natural communities at risk.

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