

## REVIEW ARTICLE

## Lichens: Origin, types, secondary metabolites and applications

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### Abstract

Lichen is a symbiotic organism composed of a fungus with a photosynthetic partner usually either a green algae or cyanobacterium. The aqueous extract of lichens produce a number of secondary metabolites with varying biological activities including antibiotic, antimycobacterial, antiviral, anti-inflammatory, analgesic, antipyretic, antiproliferative and cytotoxic effects against various diseases. Secondary metabolites produced by lichens are used to monitor air pollution, food for humans and animals, and also control the biodeterioration problems. It has a potential application in the field of natural dyeing. The drug derived from the secondary metabolites of lichen, usnic acid has a potential effect in cancer therapy due to its antimitotic and antiproliferative action. The antioxidant property of secondary metabolites plays a major role in treatment of various diseases. This review will summarize the origin, types, secondary metabolites and applications of some lichens.

**Keywords:** Lichen, cyanobacterium, secondary metabolites, biodeterioration, cancer therapy.

### Introduction

Lichens are formed through symbiosis between a fungal and a photosynthetic partner such as algae or cyanobacteria. More than 17,000 species and over 800 lichen products are known to be utilized by mankind eg., for dying, pollution monitoring, perfumery, floral decorations, as well as for dietary and medicinal purposes (Ingolfsdottir, 2002). Components such as usnic acid are utilized for perfumery and for medicinal purposes (Huneck, 1999). They do not have roots, leaves or flowers so they take water and nutrients directly from the atmosphere and also other substances from air and other atmospheric pollutants. These ones are not well-spent and are accumulated in their tissues (Wolterbeek, 2002). The fact that lichens produce a thick layer on the stone and protect the surface from environmental factors, suggests a possible role of lichens as a protective coating, especially against an aggressive environment (Lallemant and Deruelle, 1978). Lichens have bio-accumulator capacity and high sensitivity towards specific pollutants. Pollution effects in lichens are shown in the decrease of sorts of lichens number due to the break-up of symbiotic association. Therefore, lichens are used as bio-indicators according to the presence/absence of kinds of lichens in the environment. An aqueous extract of lichen species *Lobaria pulmonaria* is foliose (leaf-like) lichen. It is pale brown when dry and bright green when wet.

Lichens has been used widely in folk medicine for treatment of various diseases, such as eczema, respiratory diseases, pulmonary diseases and arthritis, also used as food and cosmetics (Biswas, 1956; Zeybek and John, 1992) and it also has the function of anti-inflammatory and antiulcerogenic effects. Lichens have been used for medicinal purposes throughout the ages, such as *Cetraria islandica*, (Iceland moss), *Lobaria pulmonaria* and *Cladonia* species were reported to be effective in the treatment of pulmonary tuberculosis (Vartia, 1973). Lichens are important food for many animals, including man (Richardson, 1988). They are used in the production of alcohol, paints, as well as in the perfumes and the pharmaceutical industries. Different bioactive secondary metabolites have been isolated from lichens and some of them are used in pharmaceutical sciences. 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, antitumour, analgesic and antipyretic properties (Vartia, 1973; Lawrey, 1983; Lawrey, 1989; Ingolfsdottir *et al.*, 1997) and also with antiproliferative (Ogmundsdottir *et al.*, 1998), antioxidant (Hidalgo *et al.*, 1994), anti-HIV (Neamati *et al.*, 1997). Some lichen species are used as stomachic and anti-diabetic drug in Turkish folk medicine (Baytop, 1999).

Lichen forming fungi produce antibiotic secondary metabolites that protect many animals from pathogenic microorganisms (Lawrey, 1989). The first study of the antibiotic properties of lichens was carried out by Burkholder *et al.* (1944). Some lichens have ethnopharmacological properties reported from *Cetraria islandica* which is used as a cough remedy (Van Haluwyn and Lerond, 1993). Aliphatic alpha-methylene-gamma-lactone isolated from lichen, *C. islandica* was a potent inhibitor of DNA polymerase activity of human immunodeficiency virus-1 reverse transcriptase (HIV-1 RT) (Pengsuparp *et al.*, 1995).

#### *Lichen symbiosis*

Lichen symbiosis is one of the most successful ways whereby fungi fulfill their requirement for carbohydrates, with nearly one fifth of all known fungal species being obligate lichen-forming species. More than 40% of all known as Ascomycota species are lichenized. They are found nearly in all terrestrial habitats from poles to tropics, ranging from marine (littoral) and fresh water aquatic habitats to xeric environments. Lichens are the dominant life forms occur 8% in the land surface of the earth, including polar, alpine and coastal habitats where fog and water vapor are abundant. Another measure of their ecological success is their nearly ubiquitous ability to colonize various substrates. They can grow on or inside rocks (epilithic or endolithic), on or inside the bark of woody plants as epiphytes, on wood, soil, mosses, leaves of vascular plants (especially in the tropics), on other lichens, as well as on man-made substrates such as concrete, glass, metals and plastics (Joneson and Lutzoni, 2009).

#### *Lichens reproduction*

Lichen reproduction requires the transmission of fungal and photosynthetic partners from one generation to the next. If the mycobiont reproduces sexually, the fungal spores upon germination need to find a compatible photobiont and resynthesize which is called as lichen symbiosis *de novo* (horizontal transmission of the photobiont) (Richardson, 1988). If the mycobiont reproduces asexually, the photobiont is most often transmitted to the next generation with its mycobiont through specialized vegetative propagules (such as soredia or isidia), or through thallus fragments containing both symbionts (vertical transmission of the photobiont). This occurs since sexual reproduction of the fungal partner seems to be the most common mode of reproduction (Wolterbeek, 2002).

#### *Types of lichens*

Lichens have a variety of different growth forms. The simplest lichens are crusts of loosely mixed fungal hyphae and algae. Others are more complex with leafy or shrubby forms like miniature trees having specialized structures attached on them to a surface. Crustose (or Crustaceous) lichens are encrusting forms which spread over and into the surface of their habitat. They cannot be removed from the surface without crumbling away. In all

lichens, the fungus forms a thallus or lichenized stroma that may contain unique secondary compounds. The lichens occupying rocks as their substrates are generally known as saxicolous species which can be divided into three distinct groups: crustose, foliose, and fruticose, basically in the terms of the modes of attachment to the substrate (Carcia-Rowe and Saiz-Jimenez, 1991). Foliose lichens are lichens with leafy lobes, which spread out in a horizontal layer over the surface. They are attached by root-like threads and can be easily removed with a knife. Fruticose lichens are shrubby forms with many branches. They can be removed from the surface by hand. Filamentous (hair-like) lichens are totally different. They consist of chains of algal cells wrapped around with fungal hyphae. Leprose (powdery) lichens are an odd group of lichens which have never been observed to produce fruiting bodies. Because, knowledge of the form of the fruiting bodies is essential for the identification of fungi, these lichens have not yet been identified properly or at least not yet given full scientific names.

These fungi not only lack an inner cortex, but also lack an outer one, i.e. no cortex, only an algal cell layer and sometimes a weakly defined medulla. Squamulose (consisting of small scale-like structures, lacking a lower cortex) lichens have a portion of their thallus lifted off the substrate to form 'squamules'. They are otherwise similar to crustose lichens which possess an upper cortex but not any lower cortex. In gelatinous lichens, cyanobacteria produce polysaccharide which absorbs and retains water. There are many gradations of forms in between these three main groups and lichen may not always fit clearly into one or other of these artificial categories (Culberson *et al.*, 2009).

#### *Secondary metabolites*

Different bioactive secondary metabolites have been isolated from lichens and some of them are used in pharmaceutical sciences. Usnic acid is a natural compound normally found in lichen species belonging to the genus *Usnea*. Usnic acid is a very active lichen substance used in pharmaceutical preparation, active against microorganisms and viruses as well as analgesics and antipyretics (Proksa and Proksova, 1999). This compound inhibits bacterial as well as eukaryotic cell proliferation *in vitro*. Its antimetabolic and antiproliferative action was shown in a variety of biological systems including higher plant cells (Rowe *et al.*, 1991). Also, the pharmacological potential of usnic acid has been evaluated in the control of tumor proliferation (Cardarelli *et al.*, 1997). Its pharmacological potential against hyperproliferative skin diseases, such as psoriasis (Periera *et al.*, 1994) as well as parasitic infestations (Kumar and Muller, 1999) has been evaluated. Evident toxic effects for usnic acid seem to be absent both in pharmacokinetics studies in mouse. Pulvinic acids constitute a group of natural products containing a g-alkylidenebutenolide ring system. They have been isolated from several lichens and higher fungi

and represent bright yellow and orange pigments. A number of regioselective and non-regioselective syntheses of unsymmetrical pulvinic acids have been reported (Fournet *et al.*, 1997). This acid has the antioxidant properties. Boldine are natural products whose medical properties are well-known for many decades. Boldine has been shown to possess antioxidant activity (Brodo *et al.*, 1999, Jang *et al.*, 2000), anti-inflammatory effects as well as photo protector capacity (Hidalgo *et al.*, 1998).

#### Applications of lichens

Lichens have been used widely in folk medicine for treatment of various diseases, such as eczema, respiratory diseases, pulmonary diseases and arthritis, also used as food and cosmetics. The following sections will discuss about the applications of some lichens.

#### Heavy metal stress tolerance and sorption

Many lichens can cope with heavy-metal stress. Some secondary metabolites of lichens such as depsides and depsidones produced by the fungal symbiont and accumulated on the outer surface of its hyphae, are supposed to play an important role in the extracellular immobilization of heavy metals (Purvis and Pawlik-Skowron, 2008). In heavy-metal-polluted areas, lichens accumulate high amounts of heavy metals (e.g. Cu, Zn, Pb, Cd, Mn) indicating it as a strong metal tolerant (Sarret *et al.*, 1998). Copper ion sorption in lichens owing to the ion exchange between the surroundings (aqueous solution) and the lichen cation active layer. The course of sorption of these ions, similarly as in the case of cations of other heavy metals, depends on the concentration and type of cations naturally found in lichen surroundings:  $H^+$ ,  $Na^+$ ,  $K^+$ ,  $Mg^{2+}$  and  $Ca^{2+}$  (Andrzej *et al.*, 2007).

#### Activity on human cancer cell lines

Fruticulous or foliaceous lichen species extracts has the cytotoxic effect on four human cancer cell lines. The four cancer cell lines are: cK- 562: chronic myelogenous leukaemia, the U251: glioblastoma, the DU145: Prostate carcinoma and the MCF7: breast Adenocarcinoma. Among these the extracts from *Cladonia convoluta*, *Cladonia rangiformis*, *Parmelia caperata*, *Platismatia glauca* and *Ramalina cuspidata* demonstrated interesting activities particularly on human cancer cell lines (Bezivin *et al.*, 2003).

#### Antioxidants

Free radicals play an important role in many chemical processes in the cells, but they are also associated with unwanted side effects, causing cell damage. Since synthetic antioxidants are often carcinogenic, finding natural substitutes is of great interest. Lichens have been found to contain a variety of secondary lichen substances, which are strong antioxidant compounds. Antioxidants can interfere with the oxidation process by reacting with free radicals, chelating free catalytic metals and also by acting as oxygen scavengers.

Phenolic antioxidants function as free radical terminators and metal chelators (Shahidi and Wanasundara, 1992). The antioxidants produced by lichens may be used to preserve food quality from oxidative deterioration of lipid. Therefore, antioxidants play a very important role in the food industry. Synthetic antioxidants, such as butylated hydroxyanisole (BHA), butylated hydroxytoluene (BHT), and *tert*-butylhydroquinone (TBHQ) are widely used in the food industry, but BHA and BHT have suspected of being responsible for liver damage and carcinogenesis (Grice, 1986). *Cetraria islandica* is well-known in Turkish folk medicine which is used for treatment of diseases such as hemorrhoids, bronchitis, dysentery and tuberculosis (Sanchez-Moreno *et al.*, 1999).

Protolichesterinic acids, alpha-methylene-gamma-lactone, fumarprotocetric acid and  $\beta$ -orcinol depsidone are considered as major biologically active secondary metabolites of *C. islandica*. The secondary metabolites from *C. islandica* exhibited high antimicrobial activity (Wichi, 1988). All concentrations of aqueous extract of *C. islandica* showed higher antioxidant activities (Gülçin *et al.*, 2002) which increased when increasing the concentration of extracts (from 50 to 500  $\mu$ g) added to linoleic acid emulsion.

#### Bioindicators

Lichens are used as bioindicators and/or bioaccumulations to identify PAHs (Polycyclic aromatic hydrocarbons), phenols and trace metals (Pawlik-Skowron *et al.*, 2008). Combustion processes from road traffic, industrial sector and home heating are the main responsible for the generation of PAHs (Samanta *et al.*, 2002; Gryniewicz *et al.*, 2002). These toxic compounds are present largely in air, water, aerosols, soils and sediments (Kipopoulou *et al.*, 1999; Haawthorne *et al.*, 2000). *Usnea longissima* is one of the lichen species that are most sensitive to air pollution. In some European countries, its health was accepted as an indicator of air pollution. The presence of *U. longissima* indicates clear air, while its absence indicates polluted air. It has been used to strengthen hair and also used in the production of hygienic products for women (Brodo *et al.*, 1999). It has also been used widely as an expectorant, for wound dressing and to stanch nose bleeding, as well as in the treatment of ulcers. It has also been used in the treatment of injuries to the legs and loins, bone fractures, and skin eruptions (Blackwell, 1990; Lal and Upreti, 1995).

#### Conclusion

The review reported about origin, types, secondary metabolites and their applications. The secondary metabolites produced by lichens have vast application in medical, therapeutic, food, and perfumery and also in dyeing purposes. Due to rapid increase in air pollution and global warming issues, environment faces numerous issues which can be overcome only by the environment friendly lichens. So it's our duty to protect the precious lichens and save our mother nature.

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