

## **A CRITICAL REVIEW ON LICHENS AND ITS MEDICINAL ASPECTS**

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Abstract

A photosynthetic partner [the phyto-biont] & a fungus [the myco-biont] form lichens, which are composite creatures that include a symbiotic relationship. Lichens differ greatly from cultured fungi & algae in terms of form, physiology, & biochemistry. Lichens are found in some of the most severe settings on the planet, & scientists may utilise them for a variety of economic purposes. A resurgence of interest in lichens as a source of pharmaco-logically active bio-molecules, has occurred during last two decades. Traditional medicines & further bio-pharmaceutical applications that are concerned with economic relevance have long been interested in the study of lichens & the bioactive chemicals they contain. Symbiotic & bioactive relationships among several types of algae were examined & summarised, as were the lichen's morphological characteristics & symbiotic & bioactive relationships with a wide range of microorganisms, including fungi, viruses, & cancerous cells. A prime focus was placed on the potential of recent advances in lichen & lichen-forming fungus to speed the commercialization of lichen-based goods.

**Keywords:** fungi, lichens, antimicrobial, anticancer, traditional medicine

### **INTRODUCTION**

As Symbiotismus, Albert Bernhard Frank [1] first used the term biologically to describe the symbiotic relationship between five crustose lichens. De Bary is widely attributed as the creator of the expression "differently named creatures living together" [2] from a speech he delivered in 1878, although he was aware of Frank's work, since he subsequently alludes to it [3]. Schwendener, on the other hand, was the first to recognise lichens as a fungus-alga hybrid in 1867. [4].

Bioactive chemicals with tremendous medicinal potential can be found in lichens, a type of fungus that produces bioactive molecules. They are multicellular creatures made up of fungi & phototrophic cells [algae or cyano-bacteria, or both at similar time]. Bacteria & viruses are also present [5,6]. More over a quarter of the world's fungi are found in the lichen kingdom [7]. For medicinal & culinary purposes, lichens are rich sources of bioactive compounds. A total of 1.050 secondary compounds have been discovered so far. For the most part, they are exclusive to lichen-forming fungus. It is clear that lichen secondary metabolites, such as amino acid compounds & sugar alcohols, aliphatic acids, macrolytic lactones, monocyclic aromatic compounds & quinines, chromones, xanthenes, dibenzofurans & terpenoids, steroids, carotenoids, & diphenyl ethers indicate the great potential of lichens for pharmaceutical use [8,5]. Since these compounds are manufactured in cultures, their sluggish development is a concern [9], as opposed to medicinal mushrooms.

Lichens' high carbohydrate [53.3–79.07 percent] & fibre [5.486–16.26 percent] & content of low fat [1.4–6.6 percent] are the primary indicators of their nutritional significance. Mineral & protein content of lichens ranges from 5.95 to 16.2 percent. Amino acid composition of *Rimelia reticulata* thalli from Africa was found to include isoleucine, leucine, methionine, threonine, phenylalanine, tryptophan, & valine [8]. Fungi & lichens, for example, were utilised as sustenance by people during the conflict in the region of Bosnia & Hercegovina [10]. Cooked mushrooms, like *Tricholoma terreum*, *Ramaria flava* & *Evernia prunastri* [11] can also be used to make lichen's salad or bread, along with other lichens as *Cetraria islandica*.

## **USES OF LEECHES MEDICALLY**

Lichenized fungi [lichens] can be used to make therapeutic agents since their secondary metabolites have anticancer, antibacterial, & antioxidant characteristics [12,13,14,15,16]. Some *Usnea* lichen extracts, for example, demonstrated strong antioxidant capacity, such as a protective effect in human lymphocytes via controlling enzymatic activity. While usnic acid [dibenzofuran] is particularly well-known for its cancer-fighting properties, it has also been shown to have antibacterial & cytoprotective properties [16]. Natural antioxidants such as B.

fuscescen, P. tiliacea&U. decussata might also be found in certain lichen species, such as B. fuscescens&P. tiliacea.

Bio-active compounds&their potential use in conventional medicine were examined. Peltigera, Solorina, Nephroma, Cetraria, Flavocetraria,&Alectoria are only few of the lichens that may generate large concentrations of phenolic chemicals [17,18]. Peltigeralaciniata, Cladoniarappi, Thamnoliavermicularis,&Cora aff. glabrata from the Venezuelan Andes were natural sources of antioxidants–phenols that might be used in human treatment, according to Plaza et al. [19].

One of the best places to get medications&functional meals these days is from specially modified lichens. Lichens have traditionally been eaten as a delicacy in many cultures, including China, Japan, India, Nepal, Africa,&Europe [20,21,10]. Thamnoliabusuliformis&Thamnoliavermicularis are among the edible lichens found in the Himalayas that are consumed as a vegetable, steamed,&even made into soup; Cladoniagracilis, C. stellaris, Dermatocarponminiatum, Lobariapulmonaria, Ramalinafastigiata&R. sinensis, among others, are used to make tea.

#### *Used In traditional medicines*

A few prior studies have looked into lichens' medicinal properties. By Llnao&smith lichens in Europe's traditional applications were examined[22,23]. The first global assessment of lichen usage was produced by Sharnoff&was later supplemented by Crawford[24,25]. It was reported in Upreti&Chatterjee [2007][26] that Sharnoff had created a database on the medical usage of lichens in other countries, which was reprinted in their study. The Chinese usage of lichens as medicine was recently studied by Wang&Qian[27]. The new publication covers all the medical applications described by these earlier writers, as well as numerous additional records. In spite of this, it is the most thorough study to date. For medicinal purposes, Usnea is the most common lichen genus, but it is often used interchangeably with other arboreal hair lichens. According to traditional European practise, Usnea is not one of Europe's most commonly used therapeutic lichens. There are lichen taxonomies&lichen identification procedures that are inseparable. Lichens are often identified by the environment in which they occur. A lot of people believe that

they get their attractive features from the soil they grow on. Alektoroid lichens, for example, are considered better medicine by Nuxalk when growing on alder, whereas Lobariaoregana is seen to be better medicine by the Gitga'at when growing on fir, & Evernia was considered better medicine by the Ancient Greeks when growing on cedar. A lichen's therapeutic effects might shift depending on the environment in which it grows. This, on the other hand, might serve as an ingenious means of identifying. There are several microhabitat preferences for lichens, which means that choosing only one substrate will result in preferring picking specific species. The Quichua people of Saraguro, Ecuador, use an intriguing way of identifying lichens: they've discovered that a potent treatment requires seven different shades of rock lichen. It's likely that the many lichen species work together to enhance one other's effects. Seven species may be more likely to yield the proper specimen.

#### *Antibacterial activities of lichens*

Antibiotic-resistant pathogenic microorganisms are well-known to represent a severe danger to human health, & their frequency in healthcare facilities is rising as a result [Babita et al., 2008]. New methods for preventing antibiotic-resistant microorganisms from spreading infections are needed to keep up with 'super' pathogens. Conventional antibacterial treatment may be replaced with natural alternatives [29]. Scientists are particularly interested in lichen-derived compounds & the antibiotic characteristics of these, as up to 50% of all lichens have been documented to exhibit antibiotic activity [24].

#### *Antifungal activity*

There was a high level of antifungal activity in the acetone & methanol extracts of the Umbilicariaceae plants *Lasalliapustulata* [L.] Méret. [Umbilicariaceae], *Parmeliasulcata* Taylor, & *Umbilicariacrustulosa* [Ach.]. With the help of 5-propylresorcinol & divaricatinic acid, usnic acid was found to be an effective antifungal agent [30]. Extracts of *Parmeliasulcata* containing salazinic acid from acetone, chloroform, diethyl ether, methanol, & petroleum ether were shown to be antifungal against *Aspergillusniger*, *Aspergillusfumigatus*, & *Penicilliumnotatum*. Teloschistaceae] methanol extracts included

antifungal compounds parietin & anthraquinone, which were shown to be highly effective against Caloplacacarina [Ehrh. ex Hedwig] Th.Fr [32]. Researchers found antibacterial activity in the lichen extracts Protousneapoepigii [Nees & Flot.] Vain. [Parmeliaceae] & Usneaflorida var rigida Acharius, which comes from the Andean lichen Protousneapoepigii. Researchers tested the antifungal effectiveness of acetone extracts from three different species of lichen, including Everniaprunastri, Hypogymniaphysodes, & Cladoniaportentosa. Aspergillus flavus, Botrytis cinerea, Colletotrichum lindemuthianum, Fusarium solani, Stagonosporanodorum, Pythium multimum, & Phytophthora infestans, among others Anthraquinones found in Xanthoria lichens have antifungal properties, according to Manojlovic et al [31] It has been shown that lecanoric acid, a fungicide found in Parmotrema inctorum lichens, is highly effective against Cladosporium sphaerospermum. A lichen component called anthraquinone parietin from Caloplacacarina has been shown to exhibit antifungal properties [31], as have a number of acids & 5-propylresorcinol compounds from Andean lichens.

#### *Anticancer activities*

There have been studies on the anticancer effects of several lichen compounds including usnic acid, cristazarin, protolichesterinic acid, polyporic acid, depsidone, & lichenin on tumour cells such as Melanoma B-16, P388 leukaemia, K-562 leukaemia, Ehrlich solid tumour, & lymphocyte cells. It has been shown that in vitro anticancer activity of lichen extracts has been examined using the proliferation assay [33] in three cancer cell lines: human pancreatic cancer cell line PANC-1, prostate cancer cell line DU-145, & breast cancer cell line MCF-7.

Lichen extracts have long been explored for their potential anticancer effects. In the crown gall tumour inhibition test, extracts from the lichen Collema flaccidum demonstrated substantial anticancer efficacy. Colleflaccinosides & bisanthraquinone glycosides were discovered as the pure inhibitors [34]. Inhibiting cell proliferation in human breast, pancreatic, & colon cancer cell lines, Tenuiorin [a tridepside] & methyl orsellinate isolated from Peltigera leucophlaebla were found to be effective [35]. T-47D breast cancer cell line & Capan-2 pancreatic cancer cell line were both inhibited by usnic acid in terms of cell growth & proliferation [36].

CFP-2, a lichen-derived polysaccharide, decreased the survival of HL-60&K562 cells via the apoptotic route&telomerase activity, indicating its potential as a cancer therapy. *Cetraria islandica* L. [Ach.] Protolichesterinic acid suppressed the proliferation of malignant cell lines. Compounds from lichens have been shown to have anti-proliferative effects on human platelets, which is attributed to their inhibition of 12[S]-HETE, which has been linked to cancer&metastasis. Extracts from *C. aculeata* were shown to have genotoxic/antigenotoxic&cytotoxic properties in bacterial&mammalian cell systems. Cell growth&mortality were reduced in prostate cancer DU-145 cells treated with pannarin. The orcinol compounds, tenuiorin&methyl orsellinate, found in *Peltigera leucophlebia* [Nyl.] Gyeln [Peltigeraceae], inhibited soybean 15-lipoxygenase in vitro. As a result, anti-proliferative activity against human breast, colon cancer,&pancreatic cell lines was investigated for tenuiorin&methyl orsellinate.

#### *Anti-oxidantal activities*

A number of lichen&secondary metabolite features have been linked to their ability to protect against oxidative stress. *Melanelia fuliginosa*&*Melanelia subaurifera* lichens were studied for their antioxidant, anticancer,&antibacterial properties. Gyro-phoric acid, anziaic acid, Lecanoric acid, &2'-O-methyl anziaic acid were identified in these lichens, as well as dibenzofurane [usnic acid]. IC50 values varied from 121.52 to 424.51 g/ml for these antioxidants. 2'-O-Methyl anziaic acid had the strongest antibacterial activity, with a MIC of 0.0625 to 1 mg/ml. The strongest anticancer activity was discovered in *M. subaurifera* extract [IC50 = 9.88–31.64 g/ml].

It has been found that methanolic&acetone extracts of the lichens [*P. rampoddense*, *P. praesorrediosum*, *P. reticulatum*,&*P. tinctorum*] have antibacterial&antioxidant properties. Protocetraric acid, praesorediosic acid, -collatolic acid, usnic acid, -alectoronic acid, atranorin,&chloroatranorin have been identified from these lichens. Salazinic acid, atranorin, Norsticticaci, protocetraric acid,&evernic acid were found as secondary metabolites in the 1 species of lichen. Researchers observed that the MIC values were in the range of 1–20 mg/ml&the cytotoxic activity varied from 24–45 micrograms per litre [mg/ml]. Hence, it was determined that the lichen might be produced as raw ingredients in the foodstuff

supplement & pharmaceutical sectors since it has anticancer, antioxidant, & antibacterial potentials. *Stereocaulon strictum* var. *compressum* & *Lobariella pallida*, which are lichen extracts, were also tested for antioxidant capacity. Also evaluated were lobariellin, methyl orsellinate, stereocaulin, methyl haematommate, methyl -orcinol carboxylate, porphyrilic acid, & atranorin, among other chemical elements. The results showed that lobariellin, methyl haematommate, & porphyrilic acid, when separated from other chemical ingredients & extracts, prevented lipid peroxidation, scavenged free radicals, & decreased ferric ions to their maximum levels.

### *Immuno-modulators*

Using immunomodulators, the immune system may be influenced & the body's reaction altered. Immunomodulators are becoming increasingly popular in the medical profession because of their use in a variety of therapies, including transplant rejection, patient recovery, & the stabilisation of the immune system in HIV-positive individuals. It's becoming increasingly popular to use plant-based solutions as an alternative to conventional therapies. Thadhani et al. used chemiluminescence probes based on luminol or lucigenin to investigate immunomodulatory potential of various lichen compounds. Chemiluminescence-based cellular tests were used to investigate the effects of the chemical components on human polymorphonuclear leukocytes, murine macrophages & respiratory burst of human blood phagocytes. Some examined compounds of lichen, viz. methyl orsellinate, orsellinic acid, lecanoric acid, methyl haematomate, & lobaric acid, showed a strong inhibitory impact on phagocytosis response as compared to the standards. Neutrophils isolated from mice were discovered to produce both myeloperoxidase-independent & myeloperoxidase-dependent ROS, which were suppressed by lobaric acid.

Using murine macrophages RAW264.7, researchers examined the immunological effects of *Umbilicaria esculenta* polysaccharide [UEP]. At a concentration of 600 g/ml, UEP was shown to increase phagocytosis & proliferation by 2.5 & 1.4 times, respectively, as compared to the negative group. The stimulation of NO synthase [2.7 times], nitric oxide [25.2 times], tumour necrosis factor-, interleukin factors, & interferon- was carried out in a concentration dependent manner.

Moreover In addition, cyclophosphamide-induced immunodeficiency mice were used to test the effects of tremella polysaccharides.

Tremella polysaccharides exhibited the best outcomes in mice therapy, increasing the spleen&thymus index&relieving pathological features of immunosuppression. The dose of 80 mg/kgBW provided the best results in this situation. It was also observed to increase mRNA expression of IL-12, IL-4,&IL-1 in spleen&liver, as well as suppress mRNA expression of TGF- $\beta$  in same organs. [48] Gynostemma pentaphyllum Makino polysaccharides [GPMPP] were shown to have immunomodulatory properties in another study. In vivo investigations showed that GPMPP dramatically increased thymus&spleen indices&activated macrophage phagocytosis. GPMPP. It also increased CD4+ T cell counts&CD4+/CD8+ ratio, as well as the IL-2 level in the Cy-immune-mice's spleens&sera. The GPMPP also had a significant effect on SOD, T-AC, GSH-Px, CAT,&GSH levels, as well as an inhibitory effect on MDA. GPMPP was shown to be an effective natural immunomodulator [49]. Licorice polysaccharide shown similar efficacy in tumor-bearing mice. Licorice polysaccharide has been shown to decrease tumour development&increase blood levels of antitumor cytokines IL 2, IL 6,&IL 7 while reducing protumor cytokine TNF [37]. It was shown that the polysaccharide UP2 in Umbilicaria esculenta has an immunostimulatory effect on RAW264.7 cells in a dose-dependent manner. The highest phagocytic activity was recorded at 200 g/ml,&NO generation was induced by all samples [20–500 g/ml] [38].

## CONCLUSION

In light of this, we might conclude that lichens have long been important, dating back to traditional Chinese medicine&onwards. Aside from the obvious medicinal use of lichens, it appears that their extracts&their secondary metabolites might play a significant role in the pharmaceutical industry. Anticancer medicines&cell proliferation inhibitors may be produced from these natural compounds, which constitute an exciting new lead chemical. Antiviral drugs, immunomodulators, insecticides,&antibacterial agents can all be used with it.



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