GSC Biological and Pharmaceutical Sciences

eISSN: 2581-3250 CODEN (USA): GBPSC2

Cross Ref DOI: 10.30574/gscbps

Journal homepage: https://gsconlinepress.com/journals/gscbps/

GSC Biological and Pharmaceutical Sciences

GSC Online Press INDIA

(Review Article)

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An integrative review of the biology and chemistry of lichens and their ecological, ethnopharmacological, pharmaceutical and therapeutic potential

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GSC Biological and Pharmaceutical Sciences, 2023, 23(03), 092–119

Publication history: Received on 29 April 2023; revised on 08 June 2023; accepted on 10 June 2023

Article DOI: https://doi.org/10.30574/gscbps.2023.23.3.0223

Abstract

This purpose of this paper is to review and evaluate published literature on the biology and chemistry of lichens and their ecological, ethnopharmacological, pharmaceutical and therapeutic potential. A systematic method was used to gather literature on "the biology and chemistry of lichens and their ecological, ethnopharmacological, pharmaceutical and therapeutic potential." A total of fifty-five research papers published between the years 1963 to 2022 were selected and utilized for this review. Tables were used to present the results. The subtopics were then chosen using a subjective method: lichens and their benefits/ importance. In this paper, eight (8) ecological functions and fourteen (14) pharmaceutical properties and therapeutic potentials were evaluated and presented. Lichen biology and chemistry and their roles in ethnopharmacological are also discussed. Additionally, lichens as pioneer and keystone species and their role as bioindicators to assess ecosystem health, sustainability and productivity was also addressed in this research. The published papers established that lichens have many benefits and importance, they are capable of synthesizing a range of chemicals that are beneficial to us and they are used in both traditional and pharmaceutical preparation of different treatments to combat many different diseases that affect human beings. More studies to investigate the uses of lichens should be done, especially in neotropics as there is a paucity of data and in this biodiversity rich region.

Keywords: Lichens; Biology; Chemistry; Ecological; Ethnopharmacological; Pharmaceutical; Therapeutic potential

1. Introduction

1.1. Lichens

Lichens are slow-growing organisms that can endure extreme climatic changes for hundreds of years [19], [99]. Theophrastus, the Father of Botany, popularized the term "lichen" for a class of plants in the scientific community around 300 BC [19], [120], [121]. There are between fifteen to twenty thousand (15,000-20,000) species of lichens in the world. According to Peterson and Ikeda (2017), Grimm *et al*. (2017) and Bhagarathi *et al*. 2022, many of them are specialized to particular habitats and seldom across the landscapes.

Over time, lichens have been variously categorized as a single organism, gradually mistaken for bryophytes (mosses), or for seaweeds due to previous descriptions based on their outward appearance. The complex anatomy of lichens was only discovered and documented by scientists after the invention and use of microscopes in the early 1800s [19], [62], [116],[186], [187].

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Lichens are thought to be complex living organisms that are created through symbiotic relationships between a fungus and an alga or cyanobacteria [19], [118], [175], [176], [204]. The mycobiont is a heterotrophic fungus that forms the main body of the lichen and is thought to be the dominant partner that gives the lichen its distinctive features, including the shape of its thallus and the type of fruiting body. The photobiont, which is typically found between the upper and lower fungal cortex, is an autotrophic algae or cyanobacterium [19], [62], [97], [116], [175], [186], [187], [191], [204].

Lichens are sometimes referred to be pioneer species since they invade many settings. The majority of terrestrial habitats, including hot deserts, rocky beaches, and tropical rainforests in the tropics as well as frigid polar regions like the arctic tundra and even high-altitude environments, contain them. Other extreme habitats, such as toxic slag heaps, are also home to lichen species [19], [80], [116]. Ascomycetes make up more than half (50%) of the known species of lichenized fungus, which have an estimated range of thirteen thousand five hundred to twenty thousand (13,500-20,000) species globally [19], [77].

Lichens come in a range of hues, including black, white, orange, grey, yellow, and green, among others, and are grouped according to the many growth forms they exhibit. The majority of lichens, known as crustose lichens, grow in a crust-like fashion (Figure 1). Some are shrub-like and are known as fruticose lichens (Figure 1), while others are leafy and are known as foliose lichen (Figure 1) [19], [38], [62], [116]. [186], [187], [191].

Lichens are also divided into groups based on the variety of substrates they grow on. For example, corticolous lichens grow best on the barks of vascular plants, muscicolous lichens grow on the tops of mosses, saxicolous lichens live on rocks, terricolous lichens use soil for growth, and foliicolous lichens grow on the leaves of vascular plants [19], [118], [186], [187]. The largest group of lichens, corticolous microlichens, is also the least studied by scientists [10], [19], [62], [77], [186], [187].

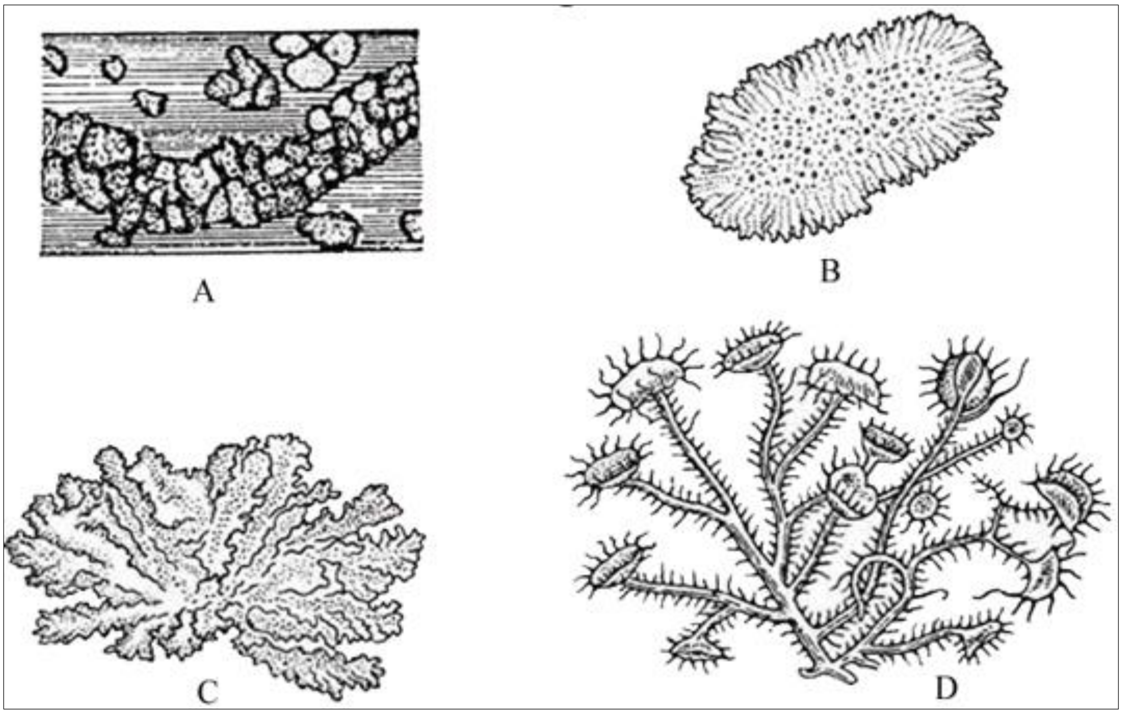

Figure 1 Different growth forms of lichens. (A) Leprose, (B) Crustose, (C)Foliose and (D) Fruticose (Iswary, 2018)

Lichens serve multiple ecosystem roles and are important in many major industries [19], [178], [186], [187]. Lichens have been used as a key biological indicator for tracking anthropogenic disturbance over time, including air pollution, acid rain, nitrogen deposition, and many other environmental conditions [19], [28], [38], [51], [55], [62], [97]. According to Peterson and Ikeda (2017), Grimm *et al*. (2021), and Bhagarathi *et al*. (2022), lichens and their habitats also play an essential role in biodiversity and are also crucial to many organisms.

Moreso, many species, including caribou, reindeer, squirrels, musk ox, etc., which eat reindeer moss (*Cladonia mangifea*) in the tundra, use lichens as a source of food. Lichens are used as food by fish and other aquatic species. People in Iceland, Sweden, and Norway frequently consume Iceland moss (*Certaria islandica*); Jews revere *Lecanora esculenta* as a sacred food; and in Japan, the stone mushroom (*Endocarpon miniatum*) is utilized as a vegetable for making a variety of cuisines [19], [22], [28], [108], [142], [154], [185], [202].

2. Material and methods

The topic of "biology and chemistry of lichens and their ecological, ethnopharmacological, pharmaceutical, and therapeutic potential" was the subject of a systematic review using "Google Scholar," a web-based search engine that offers a quick and simple way to search and access published articles, journals, and books. Particular keywords such as lichens, biology, chemistry, ecological, ethnopharmacological, pharmaceutical, therapeutic potential were utilized in the search.

By reviewing the connected works of literature, a method was applied to choose the subjects that were explored. The publications that were obtained were restricted to the years 2000 to 2022. However, not all of the papers that were received were used in this study since the main goal was to compile data from recent research (past 10 to 20 years) on the biology and chemistry of lichens and their ecological, ethnopharmacological, pharmaceutical, and therapeutic potential. However, papers with pertinent work from as far back as 1963 and the 2000's were also used. This review utilized a total of fifty-five (55) research publications.

3. Results

When searching "Google Scholar" for information on the biology and chemistry of lichens and their ecological, ethnopharmacological, pharmaceutical, and therapeutic potential, a total of 50,900 results were found. Among the results obtained from the search, a total of 16,400 were published within the years 2000 to 2023, 16,200 were published between the years 2010 to 2023 and 16, 300, were published between 2015-2023. 8,530 publications within 2010-2023 reviewed biology and chemistry of lichens and 6,550 publications reviewed lichen ecological, ethnopharmacological, pharmaceutical, and therapeutic potential.

However, not all the results retrieved for this research focused on the biology and chemistry of lichens and their ecological, ethnopharmacological, pharmaceutical, and therapeutic potential together. Some focused solely on lichen biology and ecology, while others focused on lichen chemistry and active biological substances they produced. Others focused on ethnopharmacological and pharmaceutical potential of lichens, whereas, some focused on the therapeutic potential of lichens and their application to traditional medicine and medical science. Additionally, a few papers discussed lichen nutrition and substrates and lichen distribution and habitats.

4. Discussion

4.1. Lichen Biology

4.1.1. Lichen Morphology

The mycobiont is heavily influenced by the morphology of lichens. In a lichenized partnership, the mycobiont creates around 80% of the lichen thalli and the photobiont creates the remaining 20%, but there are exceptions to the thallus development pattern [144]. The phylum Ascomycota, where about forty percent (40%) of species maintain symbiotic interactions, is where the majority of lichenized fungi are found. Approximately 98% (98%) of lichens also associate with an Ascomycota mycobiont [120], [121], [158], [181].

The phylum Deuteromycota contains the second-highest proportion of lichenized fungi in the fungi kingdom. When fungal sexual reproduction has never been seen, they are sometimes referred to as fungi imperfecti [181]. Additionally, roughly twenty (20) of the total species are from the phylum Basidiomycota and are lichenized [181]. Examples include species of agarics like species of *Lichenomphalia*, *corticioid* fungus like species of *Dictyonema*, and clavarioid fungi like species *of Multiclavula*. Lichens adopt the scientific names of their mycobiont in accordance with the International Code of Botanical Nomenclature (ICN) norm for algae, fungi, and plants [118], [121], [158].

Lichens can be distinguished from other organisms by the variety of thallus shapes and morphologies. The fruticose lichens (Figure 2) have a multi-branched, leafless, or mini-shrub growth pattern similar to *Usnea* species. They often stand upright or hang down, and the limbs on their three-dimensional plants either have a circular cross-section or are flattened. The foliose lichens (Figure 2), including *Lobaria pulmonaria* (L.) Hoffm, thrive best in a two-dimensional environment. Like *Pertusaria scaberula*, the crustose lichens (Figure 2) stick firmly to the substrate and tend to resemble a thick layer of paint. Squamulose lichens, such as *Phyllopsora santensis*, have thin scales that resemble leaves and are crustose at their tips and bottoms. As opposed to *Chrysothrix xanthine*, which has a distinct fungal and algal layer, the majority of leprose lichens are powdery, composed of granular particles, and lack an organized thallus [86], [120], [121], [158], [204]. Other lichenized forms are referred to as micro-lichens, whereas members of the foliose and fruticose lichens are categorized as macro-lichens [61].

The degree of necessary synergy for the partners involved gradually changes. Twenty percent (20%) of all lichens contain the green alga *Trebouxia*, which is infrequently encountered as a free-living organism. Some phytobiont genera, such as *Gleocapsa*, *Nostoc*, *Scytonema*, and *Trentepohlia*, can, on the other hand, frequently be found in both their lichenized and their free-living states [105]. In some instances, the lichenized symbionts (*Collema* and *Peltula*) and the free-living populations (*Nostoc* and *Scytonema*) coexist in the same habitat, such as desert soils.

Additionally, because only a few lichen algae have been identified as species and because the systematics of the majority of cyanobacteria and unicellular green algae have not been thoroughly researched and assessed, it is difficult to describe how a single phytobiont species can exist in both a free-living and a lichenized state at the same time [13]. Last but not least, it has been observed that the majority of lichens are very specific with the photobiont selected [14], [146], [158].

Due to competition with other fungi and/or nutrient intake by other living species, the growth of the mycobionts is often quite slow, and they are unlikely to survive well in a free-living form [117]. Later, various thalli of lichens belonging to the same lichen species have also yielded multiple photobiont species, such as *Trebouxia* [47], [70], [158].

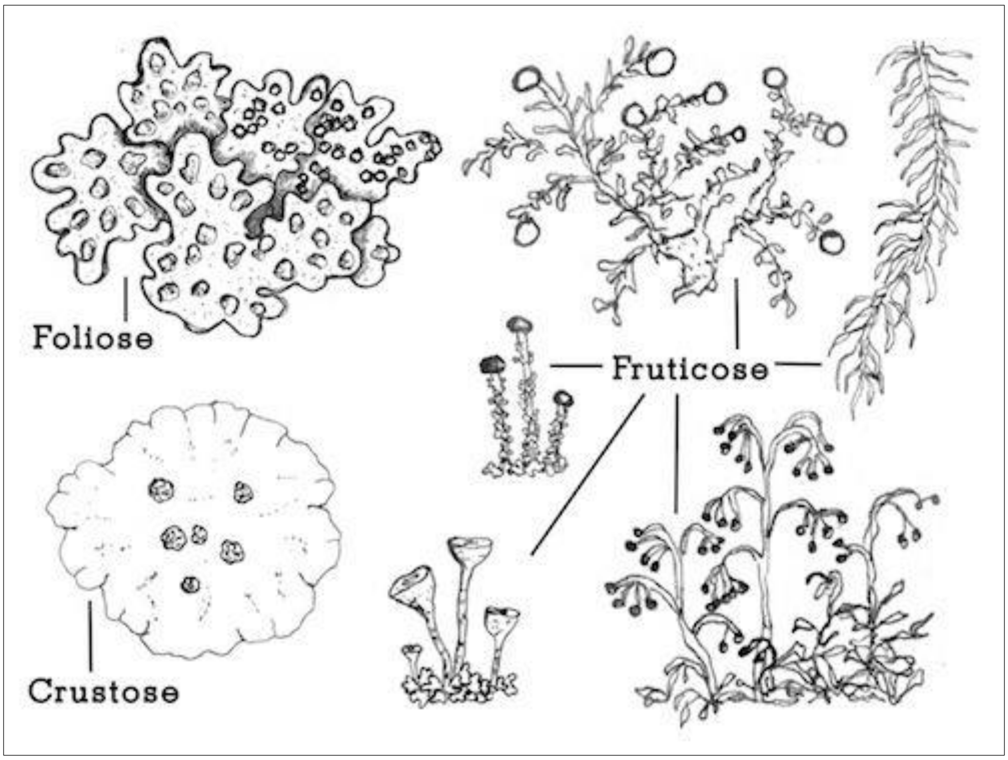

Figure 2 The common lichen morphologies (National Park Service, 2023)

4.1.2. Lichen Thallus Structure

The lichen thallus, which is an alliance of fungus and alga, was originally shown to have a dual nature by Swiss botanist Schwendener in 1867. Fungal hyphae make up the thallus, which is the vegetative tissue that makes up the lichen's body. A mesh, which may be loose or dense, is produced by the filaments branching outward. Normally, the photobiotic cells are surrounded by the fungus's mesh, which keeps them enclosed within its intricate tissues. Studies have shown that the cortex, a layer of fungus hyphae that protects the thallus, can exist or not (Figure 3) [12], [67], [103], [118].

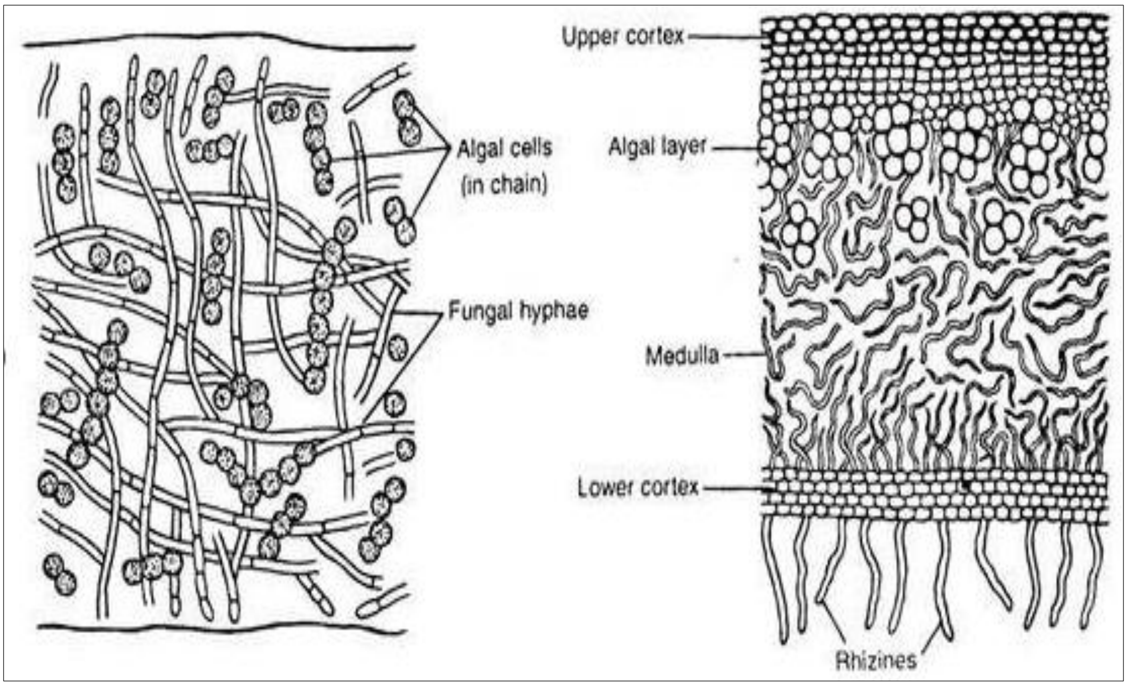

Figure 3 Internal structure of lichen thallus (Chaudary, 2023)

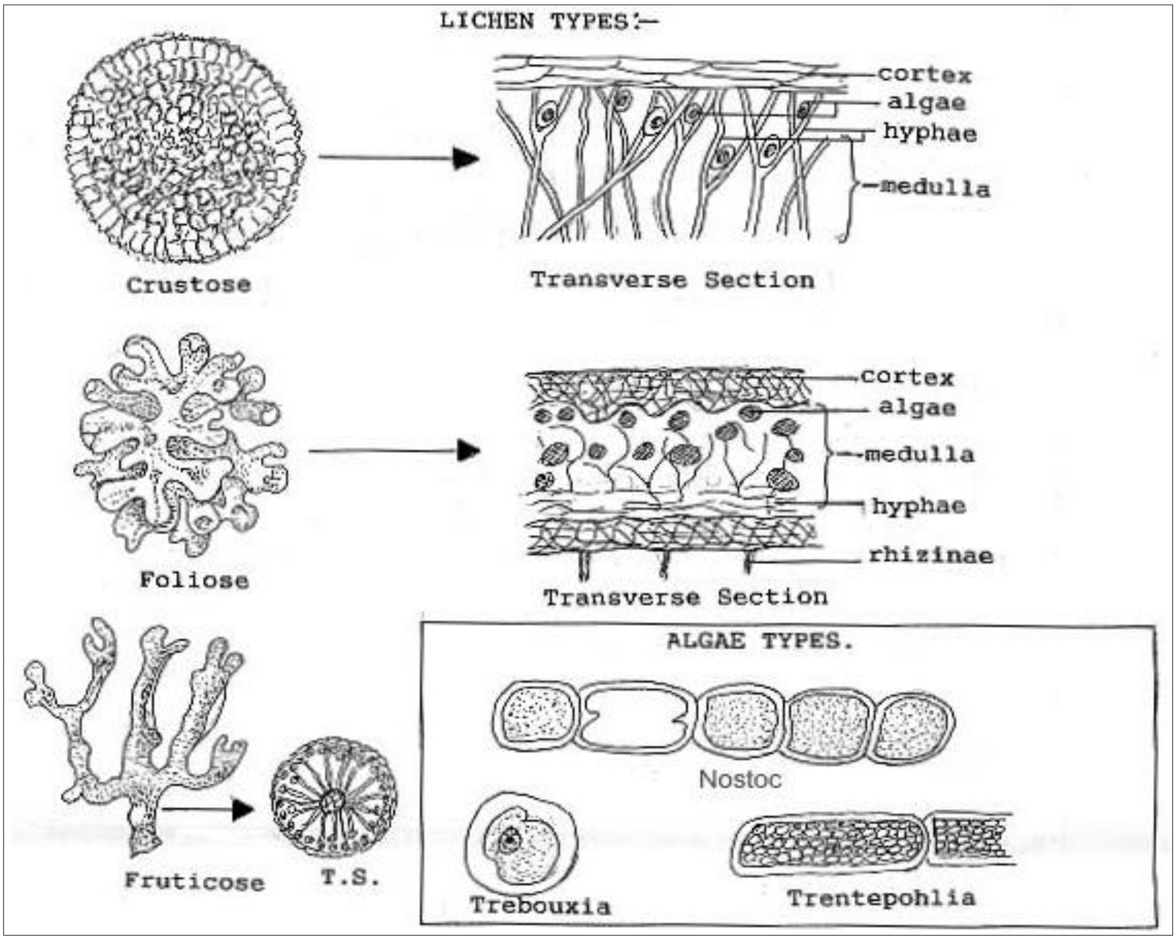

Figure 4 Types of lichens and their internal and external structures. The primary phycobionts also are green algae (*Trebouxia* and *Trentepohlia*) and cyanobacterium (usually *Nostoc*) (Biogeodiversity, 2021)

Only one cortical layer, which wraps around the branches, is present in fruticose lichens (Figure 4). Foliose lichens, on the other hand, have a distinct lower cortex present on the bottom side of their structure and an upper cortex present on the top side (Figure 4). Only the upper cortex is found in the lichens that are crustose and squamulose (Figure 4). The lichen is in intimate contact with the substrate from the interior of its body. There is no cortex in the other lichen body groups of gelatinous, filamentous, leprous, byssoid, etc. This form of lichen is referred to as ecorticate (absence of cortex) [12], [67], [103], [118].

Additionally, the photobiotic layer, which is located underneath the cortex, is less densely packed and contains the photobiotic partner that is embedded inside the fungal filaments (Figure 3). The less dense packing subsequently makes it possible for air to move about during the photosynthesis process. The medulla is located beneath the photobiotic layer (Figure 3). In comparison to the layers above it, the medulla is less densely packed with hyphae. Most crustose and squamulose lichens maintain touch with the lichen substrate through the medulla layer [12], [67], [103], [118].

4.1.3. Lichen Reproduction

Lichens have the ability to reproduce either sexually or asexually, depending on the fungus partner. The majority of the time, the projecting lichen thallus structures found on the surface are crucial for sexual reproduction. Only the fungal partner reproduces sexually in this lichenized connection. Before a functioning lichen symbiosis may develop, fungal spores must be dispersed and come into contact with a suitable photobiont [2], [67], [118], [172].

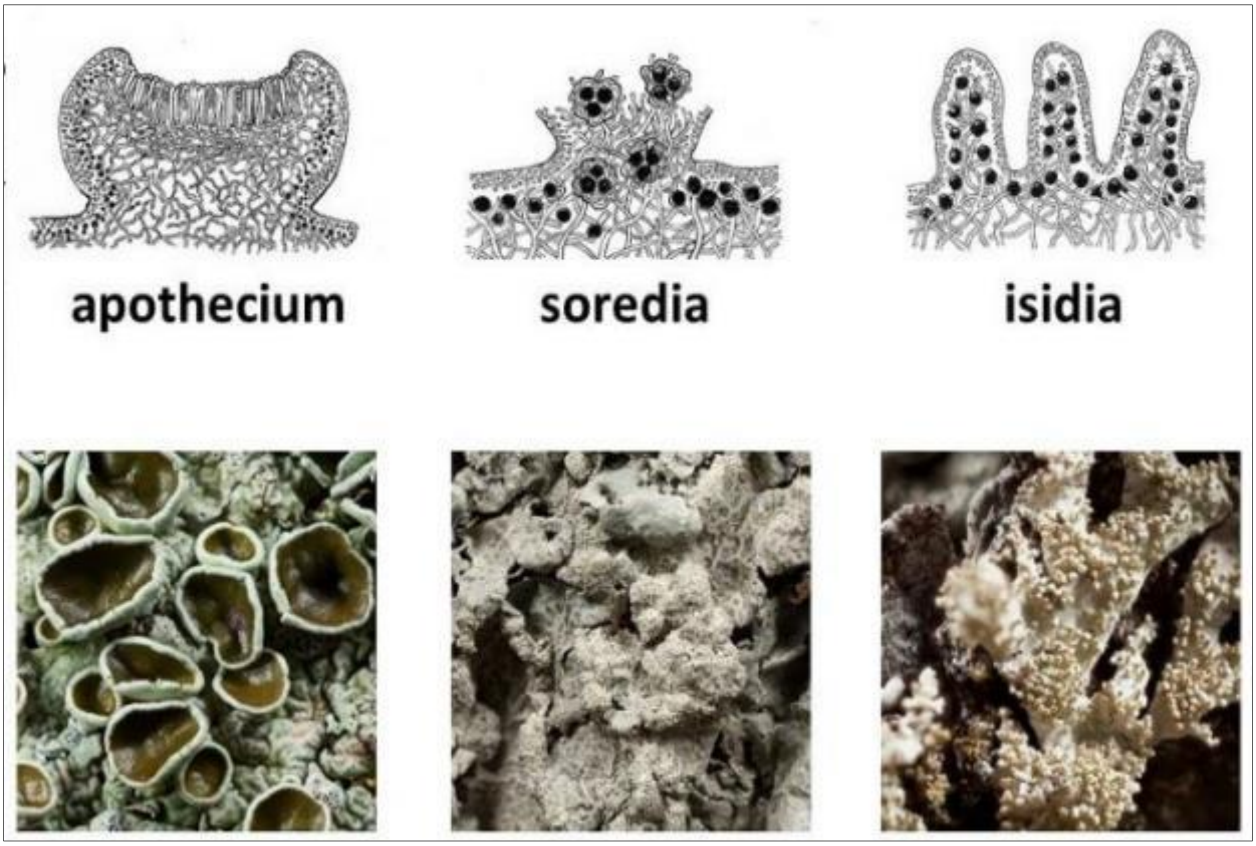

Figure 5 Reproduction strategies utilized by lichens (Beigel, 2023)

Basidiomycete-symbiotic lichens produce mushroom-like reproductive structures that are similar to those of their non-lichenized ancestors. The majority of lichens develop spores in organs referred to as ascomata and are connected with an ascomycete symbiont. The most prevalent varieties of ascomata are apothecia, which are cup- or plate-shaped structures (Figure 5), perithecia, which are immersed structures in the thallus, and pycnidia, which are structured like perithecia but lack asci. The apothecia feature a layer of exposed asci, which are the cells that produce spores. Apothecia typically have a hue that differs from vegetative tissues. Many species of lichen appear to reproduce primarily by their sexual spores, and many are capable of creating large numbers of sexual structures [67], [118], [172].

Lichens that are unable to reproduce sexually do so by using vegetative reproduction, which can either be accomplished by breaking off a portion of their thallus and letting it grow on its own or by dispersing diaspores, which are little spheres of algal cells that are covered by fungal cells. The fruticose lichens are easily broken apart, and the broken pieces can produce new lichens. During dry seasons, a lot of lichens break apart, and the pieces are carried away by the wind. Later, when moisture returns during the wet seasons, they start growing again. Small clusters of algae cells known as soredia (Figure 5) are encircled by fungus hyphae. The soredia are created in the soralia, and the wind also scatters them like shards. According to Hoegger (1993), Sillett *et al*. (2000), and Kirika (2012), isidia (Figure 5) are branched, spiny, elongated outgrowth structures from the thallus that separate for mechanical dissemination.

4.1.4. Nutritional Aspects of Lichens

Lichens are easily found in boreal woodlands and provide a large amount of non-structural carbohydrates. They are also poor in easily digestible fibers. This characteristic also offers adequate energy, and small mammals in the wild frequently consume them. In the winter, herbivorous animals such reindeer, caribou, squirrels, marmots, musk oxen, lemmings, and Eurasian deer devour various portions of the lichen condition. The lichen *Aspilicia esculenta* is also consumed by Libyan sheep that graze in the desert, and saxicolous lichens are occasionally eaten by various mollusc and insect species [34].

Therefore, the majority of lichens contain nutritional components. For instance, *Cladonia stellaris* has 2% water-soluble carbohydrates, 3.1% crude protein, 78.4% hemicellulose, and the remaining 1.7% cellulose [74]. The therapeutic and frequently consumed edible lichen *Bryoria fremontii* is found in North America and is used by many different populations to prevent famine. The three main types of structures produced by lichens are α-glucans, β-glucans, and galactomannans [4], [127]. Lichens also include necessary polysaccharides. It is proposed that the lichen polysaccharides of the β-glucan and galactomannan types have chemotaxonomic significance. It was discovered that the photobiont produced a wide range of polysaccharides, while the mycobiont in the lichenized relationship produced polysaccharides that are identical to the parent lichen [182].

Furthermore, nitrogen may be constrictive and affect lichen development and spread, and as a result, little is known about the sources of nitrogen that are readily available and the rates at which lichens acquire nitrogen in their natural environments. Furthermore, the problem of how various lichens differ in their capacity to absorb various N compounds has been poorly addressed [35], [85]. Along with chlorophylls and phycobilins, which are known to act as light energy receptors and aid to stop chlorophyll from being degraded by molecular oxygen, lichen contains a number of carotenoids that range from 23.25 to 123.5 g/g of dry weight [139].

The products lichens synthesize can protect them from different nutrient deficiencies e.g., dibenzofuran Usnic acid. This acts as an extensive secondary cortical metabolite produced by lichen forming fungi that promotes intracellular absorption of cupric ions ($Cu2+$) in epiphytic lichens. As a result, lichen generates divaric acid depside and usnic acid hence, indicating that this depside facilitates the absorption of $Cu2+$ in order to survive in habitats where nutrients are low [65].

4.1.5. Lichen Substrate Preference

Lichens are well known for thriving in practically every type of terrestrial habitat, including aquatic habitats [37], [132], 148]. Lichens are widely known for their capacity to colonize a wide range of man-made and organic substrates. Peat mosses, tree bark, rocks, wood, soil, and even other lichens, the backs of sloths, some insects, and broad evergreen leaves are examples of natural lichen substrates. Plastic, glass, metal, concrete, and cloth are examples of artificial substrates where lichens can be discovered [26], [148].

Lichens can grow on practically any firm surface, and some stray or tumbleweed lichens float over parched soils while others grow unattached. Epiphytic lichens include those that develop on wood, bark, or even organic fence materials [37], [132], [148]. Lichenologists classified lichens based on the type of substrate they grew on, such as foliicolous lichens that grew on vascular plants' leaves or corticolous lichens that grew on living plants' bark [26], [148], [163]. The saxicolous lichens live on rocks and can be divided into two (2) separate groups: siliceous lichens, which live on acidic rocks, and calcareous lichens, which live on basic calcium-rich rocks like limestone, cement, and even pavements. According to Davis (1999); Brodo *et al*. (2001); Peterson (2010); Resl *et al*. (2018), the terricolous lichens thrive on soil. Biocrusts, also known as biological soil crusts or simply biocrusts, are essential soil enhancers and even function as stabilizers in many desert habitats [37], [132], [148]. Terricolous lichens that grow alongside moss and free-living cyanobacteria help to generate biocrusts. Lücking coined the word "plasticolous" in 1988 to describe the lichens that develop on plastics.

4.1.6. Lichens and Host Plant Specificity

Lichens often display preferences for particular tree species when choosing where to live. This can be affected by the bark's characteristics, as well as its microclimate and chemical circumstances [191]. Understanding host specificity is crucial when examining the ecology and distribution of lichens, and having a solid understanding of the degree of specificity can be helpful for calculating and tracking lichen diversity and conservation. For instance, depending on areas, forest types, and different species of phorophyte (host), the substrate factors can affect the lichen distributions [191].

According to Rosabal *et al*. (2013), the texture, water interactions, and chemical composition of plant bark, including pH, are crucial substrate characteristics that control the dispersion of lichens like corticolous lichens. In 2003, Gradstein *et al*. reported that the bark's roughness has a significant role in the development of lichenized symbionts. When investigating substrate ecology, the diameter of the trunk is considered as relates to the age of the tree. Another element that affects the distribution of lichen is bark moisture, however even on the same tree, this parameter can change frequently because microhabitats and microclimates differ depending on tree height [152], [191]. As a result, due to the chemistry of the bark, certain inorganic and organic chemicals, ash content, and pH may have an impact on where lichens are distributed. Although phorophytes are significant, there is no evidence that lichen-phorophyte specialization exists in some tropical forests [152]. Despite this, there are still a number of factors that can alter the spread of lichens.

4.1.7. Lichen Distribution and Habitats

Numerous abiotic elements, such as the availability of moisture, light, wind velocity, and temperature, can have an impact on lichen formation. Lichens have a variety of habitats and can thrive in various environments [18], [19], [51]. There are resilient lichen species that can endure in frigid tundra and scorching deserts. Their ability to survive drying and their complex chemistry are the two (2) primary traits that are claimed to have had a substantial role in their formation [19], [79], [117], [158].

Globally, lichens are found in a variety of environments, including the freezing Antarctic continent's most southerly rocks, tropical rain forests, and even deserts with no predictable annual precipitation. Rock shorelines, freshwater lakes, and mountain streams are examples of semi-aquatic locations in marine tidal zones where certain lichen species can be found. Formerly known as the western populations of *Peltigera hydrothyria* (or *Hydrothyria venosa*), the *Peltigera gowardii* is a species of lichen that even thrives permanently submerged in places like spring-fed mountain streams [19], [37], [132].

Many lichens and mosses, which are prevalent in many terrestrial ecosystems, tend to create a gradient, with mosses predominating regions that remain the wettest throughout the year (though some lichens are present) and even lichens predominating areas that remain the driest. In the lichens themselves, several slopes are frequently visible. The Pacific Northwest and the mountains and conifer forests of northern California are among the regions where the chlorolichen species can be found. They have common mossy zone that are close to the ground; as they mature and long fruticose lichens known as alectorioid lichens (generally *Alectoria* and *Bryoria*) colonize the mid-canopy of trees; then as the old-growth conditions develop, cyanolichens will start to colonize a specific zone in the lower canopy of the tree, just above a mossy understory [19].

Some lichens have evolved to inhabit more compact microhabitats. Around a tree trunk, gradients may be present. Mosses may predominate in the areas that receive the most moisture from the canopy drip, followed by larger fruticose and foliose lichens. Researchers may locate a variety of powdered crustose leprarioid lichens and tiny pin-lichens with tiny stalked fruiting bodies when they move to protected locations without direct liquid water. The best development of these protected microhabitats occurs in very old-growth forests. A single enormous rock's face is another location where extremely similar gradients are frequently encountered [19], [82], [131].

There is extremely little vegetation and a harsh environment in the icy Antarctica. The most prevalent types of creatures in this area are lichens, of which roughly 350 species have been identified in the Antarctic region [19], [79], [151]. The prominent fruticose lichen of the *Usnea* and *Umbilicaria* genera, which can grow to a height of about twenty centimeters (20 cm), is thought to be the largest primary producer in these Antarctic biomes. The shape and size of some crustose lichen thalli on the sandstone varies greatly [19], [48]. According to Kappen (1988) and Bhagarathi *et al*. (2002), lichens can quickly and easily desiccate up to 97% of their water content to develop into an anabiotic illness. *Psoroma antarcticum* was recently discovered by Park *et al*., 2018, in the South Maritime Shetland and the South Orkney Islands of Antarctica. The cup-shaped apothecia, smaller ascospores, and thalli with gray to black melanin are some of the distinctive characteristics of this new species, which is closely related to the lichen *Psoroma hypnorum* [19], [129].

Poikilohydric lichens are lichens that can withstand water deficiency for an extended period of time and resume physiological functions when the conditions are right [9], [19], [92], [197]. When a gene from lichens is transferred to other organisms that battle water scarcity everywhere in the world, its role can be understood [8], [19], [50], [204]. Different studies later shown that lichens' ability to endure drought was largely attributed to their antioxidant capability [19], [76], [196]. Further investigation found that the redox status of reduced glutathione and oxidized glutathione during drying and rehydration is sedated when three (3) lichens with the ability to endure drought are exposed to heat stress [19], [91]. For instance, the lichen species *Endocarpon pusillum* discovered that the antioxidant capacity under twenty percent (20%) of PEG-induced dehydration stress was associated to the up-regulation of the antioxidant enzyme, glutathione and thioredox in gene [19], [196]. The *Endocarpon pusillum* mycobiont region is characterized by a single Trx protein with the ability to function as a disulfide reductase and a chaperone in transgenic yeasts. As a result, the mycobiont is more resistant to drought than the phycobiont [19], 98].

4.2. Lichen Chemistry

According to estimates, lichens create 600 secondary metabolites, commonly referred to as lichen compounds [120], [121], [193]. Additionally, out of all these lichens, roughly 550 of these chemicals are only found in lichens and cannot be found in any other plant groupings. Additionally, the most crucial factor in the identification of lichen is chemotaxonomy. By using a color spot test, thin layer chromatography, or even high-performance liquid chromatography (HPLC), the compounds that lichen synthesizes can be detected [120], [121], [193].

4.2.1. Lichen Metabolites

Lichens can produce a vast variety of secondary metabolites, the most of which are unique. The various lichen chemical compounds will assemble on the external surfaces of the fungal hyphae where they are present. According to Lauterwein *et al*. (1995), lichens are capable of creating a wide range of physiologically active primary (intracellular) and secondary (extracellular) metabolites.

Bioactive Metabolites from Mycobionts

Usnic acid was identified by Ingolfsdottir in 2002 as having significant therapeutic potential among the common metabolites present in lichen. Usnic acid has been incorporated into various weight reduction solutions since it is a powerful stimulant for the metabolism of cellular energy. The lichen-derived substance Methyl-orcinol carboxylate is patented and used to treat methicillin-resistant *Staphylococcus aureus*. It also has the potential to treat pathogenic human fungi that are resistant to polyene and the antibiotic azole [83].

According to Carlin (1987) and Vráblková *et al*. (2006), lichens have an abundance of pigmentation that can change depending on the amount of irradiance during the course of the year. The pigments allow for the screening of ultraviolet B for melanin and parietin; *Collema* cyanobacterial lichen patent offers about 80% UVB irradiation protection [192]. Because anthraquinones are present in some lichen species, such as *Heterodermia obscurata* and *Nephroma laevigatum*, they can be used as colors. Additionally, in the paper industry, they serve as catalysts in the production of wood pulp [32], [115].

Bioactive Metabolites from Photobionts

According to Burja *et al*. (2001), certain cyanobacteria from both marine and freshwater ecosystems produce a wide range of peptides and are a plentiful supply of blended peptide polyketides. The *Nostoc spp*. strain IO-102I, which is associated with lichens, produces microcystins, one of the most often identified bioactive substances [126]. Carotenoids, another biologically active substance, are naturally occurring, economically important pigments that are frequently found in free-living green algae *Trentepohlia* and algal lichen symbionts [117]. In addition, cyanobacteria and green algae derived from lichens are an important source of beneficial qualities, particularly medicines [155].

4.3. Ecological Functions of Lichens

Like coral reefs, lichens also tend to create a variety of habitats for other kinds of creatures and boost the productivity of ecosystems in a variety of environments, from hot deserts to tropical forests [111], [131].

Table 1 List of ecological functions of lichens

Ecological Function	Description of Ecological Functions	Author(s)
Promote Primary Productivity	Lichens use solar energy to fix carbon and add organic materials to the biological ecosystems in a lichenized partnership where the fungi are housing a photosynthetic partner. Lichens are generally thought to be slow-growing organisms, yet epiphytic lichens in damp forests have been found to commonly increase their biomass by ten to thirty percent (10-30%) year, and in rare cases by as much as one hundred percent (100%) annually. When the air is clear and the humidity is high, it is discovered that California's oak woodlands have high lichen biomass in the winter. Specifically, *Usnea* spp. and *Ramalina menziesii* (the California State Lichen) were found to have high lichen biomass, which was noted to rival the biomass of leaves accessible in the summer.	(Keon & Muir 2002), (Peterson & Ikeda, 2017), (Mark et al., 2020)
Promote Primary Succession	When the weather is particularly hot, the Usnea lichen can potentially start forest fires. Some lichens grow on concrete, window panes, and stonework in high-humidity environments, and over time, they can erode buildings and cause damage and degeneration. Lichens are the early colonizers in situations where primary succession is encouraged, such as dry, naked rocks, cliffs, mountains, etc. Lichens contribute to the erosion of cliffs and rocks throughout the growth and development stage by secreting unique acids that are able to penetrate the rocks with their hyphae. Because of this, it creates tiny gaps where organic matter gathers, allowing for the development of additional organisms. Petrologists and geologists can therefore investigate and ascertain the age and other characteristics of surfaces and rocks by measuring the size of lichens.	(Goyal, 2017), (Manisha, 2018), (BYJU'S, 2022), (Bhagarathi et al., 2022)
Promote Nitrogen Fixation	Nitrogen is thought to be a limiting element that helps many ecosystems produce successfully. The cyanobacteria in the cyanolichens contribute to nitrogen fixation by transforming atmospheric nitrogen into a form that plants can utilise. In the Pacific Northwest, the nitrogen-fixing lichen *Lobaria oregana* is widely known for its contributions to the ecosystems of old growth forests. In the Andrews Experimental Forest in Washington state, nitrogen fixing rates for *L. oregana*, which occupies several forests in California's northern coastal ranges, have been estimated to be as high as 16.5 kg/ha/year. Lichens have an important role as a supply of nitrogen for healthy desert ecosystems as part of biocrusts. For some species of vascular plants, biocrusts also help to boost the availability of nutrients in the soil.	(Pike, 1978), (Rhoades, 1983), (Belnap et al. 2001), (Harper & Belnap 2001), (Antoine 2004), (Mark et al., 2020)
Influencing Climate and the Global Water Cycle	Non-vascular plants like lichens and mosses may store a significant amount of precipitation. By increasing the evaporation of freely flowing water by around 61%, they can affect the climate and the global water cycle. Additionally, because of the algal symbiont, they are crucial in the fixation of nitrogen. When it rains, certain nitrates are leached from the lichens and used by various soil-based plants, helping lichens to aid in the conversion of atmospheric nitrogen into nitrate	(Porada et al., 2018), (Goyal, 2017), (Bhagarathi et al., 2022)
Promote Seed Germination	Biocrusts have been documented as changing seed germination and subsequently influencing the composition of vascular plant communities by physical soil binding or chemical leachates. It has been documented that biocrusts in the western dry habitats prevent the germination of invasive annual grasses, and this may be the mechanism for the reciprocal exclusion of biocrusts and annual grasses. Many initiatives have started to create ways to spread biocrusts for restoring dry lands.	(Serpe et al. 2006), (Peterson, 2013), (Doherty et al., 2015), (Mark et al., 2020).
Provide Microhabitat for Microfauna	Large colonies of arthropods and other tiny organisms like tardigrades can find a variety of habitats in lichens, notably in their foliose and fruticose forms. It has been discovered and proven that these communities have an impact on the bird populations that eat those arthropods. Numerous spiders, lizards, and	(Richardson 1974), (Pettersson et al. 1995), (Young &

	insects have developed ways to blend in with the lichens. The peppered moth in England, which changed into a light form and became rare when it was subjected to predation, is considered the most renowned instance of lichen mimicry that has been recorded. Lichens were widely eliminated from populous areas during the industrial revolution as a result of air pollution.	Clifton 2016), (Mark et al., 2020)
Provie Habitat for Macrofauna	Lichens are used as nesting material by many different bird species. Lichens have also been shown to be used by Northern flying squirrels to line their nests.	(Richardson & Young, 1977), (Rosentreter et al., 1997), (Mark et al., 2020)
Lichens in Biomonitoring and Pollution	Lichens are integral in the environmental monitoring of various circumstances affecting natural resources. In 2010, Fenn et al. used lichens as a great resource for studies and evaluations of air pollution, and their ability to accumulate metals makes them important for minerology. Lichens absorb various chemicals to which they are exposed. The composition of the lichen community can be used to infer pollution levels in the environment because many distinct lichen species exhibit varying levels of tolerance to air pollution. Additionally, additional environmental elements like the legacy of old-growth conditions found in forests can be inferred due to the presence or lack of specific species. Since lichens require clean, fresh air to properly support their growth, another significant characteristic of lichens is that they cannot tolerate pollution. Because of this, lichens are able to take in carbon dioxide and heavy metals from the atmosphere. As a result, lichens contribute significantly to biodegradation by dissolving contaminants such as polyester, lead, copper, radionuclides, etc. that are harmful to the environment. Lichens are also utilized to break down a variety of viruses and other environmental reservoirs that have the potential to infect humans, animals, and plants with severe infectious diseases. Sulfurous and nitrogenous oxides in some agroecosystems can harm delicate lichens. By observing and measuring the levels of pollutants in a specific lichen species, environmental scientists and researchers can use this property of lichen to estimate the degree of pollution in a given ecosystem. Because of this, lichens are regarded as superior biomonitors of healthy ecosystems. The abundance of epiphytic lichens and the build-up of heavy metals in the thalli of one species of corticolous lichen, *Parmerlia caperata*, were used by Loppi & Corsini, 2003, as indicators of air pollution in Pistoia, central Italy.	(Stole et al., 1993), (Selva, 1994), (Purvis & Halls 1996), (Jovan & McCune, 2004), (BYJU's, 2007), (Ardelean et al., 2015), (Goyal, 2017), (Giordani, 2019), ((Mark et al., 2020), (Bhagarathi et al., 2022)

4.4. Ethnopharmacological Aspects of Lichens

Since the beginning of time, humans have been dependent on different plant species for many reasons, with health being the most important. Traditional knowledge (TK) incorporates the skills, practices, and cutting-edge technology of local and indigenous cultures from all over the world. Indigenous communities pass on their traditional knowledge verbally from generation to generation. Since its development, TK has been useful and usable in a variety of fields, including forestry, agriculture, horticulture, fisheries, and even health [134].

The most common sources of medicine are plants, and they have been carefully described in various traditional medical systems, including Tibetan medicine, Indian Ayurveda, Traditional Chinese Medicine (TCM), Western Medical Herbalism, and Indian Ayurveda [107]. 11,146 types of medicinal plants are used in Traditional Chinese Medicine. Ayurvedic pharmacopeia in the Indian subcontinent has between twelve and fifteen hundred (1200-1500) plant species, of which an estimated ten thousand (10,000) species are used for therapeutic purposes [166].

The ethnic applications of plants found in many parts of the world have been acknowledged in several literary works throughout the years, but because the ethnic uses of lichens are not widely recorded, they were disregarded. In the course of history and even in the modern world, many ethnobotanists have disregarded cryptogams. However, a number of temperate nations around the world, including those in Asia, Africa, Europe, and the United States, have been conducting in-depth research on lichens. Additionally, various Asian nations, such as India, China, Nepal, and Tibet examined and documented the ethnic features of lichens [33], [39], [93], [187], [195].

According to Crawford, 2019, there are sixty (60) different lichen genera that are frequently used in conventional medicine. Some of the most common genera of lichens used in the medicinal world are *Cetraria islandica*, *C. nivafis* (Parmeliaceae), *Cladonia coccifera*, *C. pyxidate* (Cladoniaceae), *Usnea plicata*, (Usneaceae), *Peltigera canina*, *P. Venosa*, *P. horizontalis*, *P. polydactyla* (Peltigeraceae), *Lobaria pulmonaria* (Stictaceae), Xanthoria parietina and *Evernia prunastri* (Usneaceae) [187]. Traditional medicine frequently uses lichens to treat a variety of ailments, including respiratory, gynecological, and obstetric problems, wounds, skin disorders, and skin cancer [33], [155], [164]. There are several exceptions to the rule that most lichen species are not dangerous. For instance, there are certain poisonous lichen species, such as *Bryoria fremontii*, *B. tortuosa*, *Cetraria pinastri*, and *Letharia vulpine*. Because they contain secondary metabolites as vulpinic acid or pinastrinic acid, they are well known as dangerous lichens [39].

Studies on lichens have also shown that they are widely used as traditional foods, medicines, and sacred sacrifice fires known as "HAVAN" or "HOMA" in religion. They also serve a critical role in healthy ecosystems and human welfare. Lichens were then widely used by medical professionals during the medieval ages [39]. In an Egyptian vase from the 18th Dynasty (1700-1600 BC), the lichen *Evernia furfuracea* was employed as a medicine. Due to their wide availability and high nutritional content, lichens were predominantly employed as a food source in Europe. In the Atharveda (1500 B.C.), Shipal was the first to document the use of lichen as medicine [187]. Additionally, charrila, a crude medicine derived from *Parmelia*, is widely available in Indian marketplaces and is used to treat a variety of illnesses [30].

There are numerous reports of lichens being used extensively by different ethnic groups in India. *Heterodermia diademata* (Physciaceae) was used in the treatment of cuts and injuries, *Parmelia cirrhata* (Parmeliaceae) was used as a kitchen vegetable, *Peltigera polydactyla* (Peltigeraceae) was used to stop the bleeding, *Stereocaulon himalayense* (Stereocaulaceae) was found to be effective in the treatment of urinary trouble and blisters of the tongue. In 2016, Pathak *et al*. reported that villagers in Sikkim and Tamil Nadu, India, used the lichens *Hypotrachyna cirrhata* and *Flavoparmelia caperata* to treat various wound infections, burns, and bites. Shah documented the use of three (3) lichen species, primarily *Parmotrema nilgherrense*, *Everniastrum nepalense*, and *Everniastrum cirrhatum*, for domestic pharmaceutical purposes between the years 1998 and 2014. In addition, *Buellia cf subsoriroides*, which is useful as a substitute for "henna" in the Garhwal region of India, and *Parmeli asancti-angeli*, which is used by the Gond and Oraon tribes of Central India to treat white patches around the throat that result in a skin condition similar to ringworm [188].

Furthermore, the Bhotia tribe and other inhabitants of the Garhwal Himalaya use *Usnea plicata* as stuffing for pillows and cushions. The treatment of bone fractures by the Madhya Pradeshi Baiga tribe with the lichen *Usnea plicata* was documented by Lal in 1988. Over fifty (50) different lichen taxas' global distribution of ethnomedicinal data were evaluated by Upreti and Chatterjee (2007). Similar to this, Upreti *et al*. (2005) mentioned fifteen (15) species of lichen that are used by various ethnic groups in India and Nepal as food, medicine, or ornaments in daily life. *Thamnolia vermicularis* is predominantly utilized by the Bhotias tribes to eradicate milk worms that typically cause spoiling, according to Upreti and Negi's 1996 paper on its ethnobotanical use. The medicinal efficacy of the lichen *Parmelia impson* was described by Kaushal and Upreti (2001), and later Rai *et al*. (2014) reported using *Heterodermia diademata* on wounds for protection against infection and water retention.

In 2012, Vinayaka and Krishnamurthy recorded the ethnobotanical uses of six (6) lichen species from separate tribal communities in southern India, *Parmotrema reticulatum*, *P. tinctorum*, *Ramalina pacifica* which are widely utilized as food, *Heterdermia diademata* and *P. cristiferum* which as strong medicinal potentials, and last but not least, *Usnea galbinifera* used for pillow stuffing and decorative purposes. According to Kala (2002), the Bhotiya tribal group in Uttaranchal, India's high-altitude Garhwal Himalaya, employs lichens as a source for natural dye. In 2017, Devkota *et al*. listed seven (7) species of lichen that are used by nine distinct Nepalese populations, including *Everniastrum cirrhatum, Parmotrema cetratum* and *E. nepalense* that are used in food preparation, *Heterodermia diademata* and *Ramalina* species utilized for its therapeutic purposes, *Usnea plicata* which is used as a part of rituals, esthetic and bedding products, and *Thamnolia vermicularis* utilized as spiritual and esthetic.

Heterodermia diademata and *Eupatorium odoratum* were both utilized by the Limbu community of eastern Nepal to treat cuts and wounds, according to Limbu and Rai (2013). According to Kunwar *et al*. (2010), lichen decoction and extract can be used to cure moles in Nepal. Ahmadjian and Nilsson (1963) documented the lichen *Cetraria islandica* and it is widely advertised in Swedish apothecaries and is effective in treating lung disease, diabetes, and catarrh. Three (3) lichen species, *Parmelinella salacinifera*, *Heterodermia galactophylla*, and *Parmotrema wrightii*, were identified by Londono-Castaneda *et al*. in 2017 as being used as a source of medicine by the Pankararu indigenous community in Brazil. These species are used to treat issues with the human digestive system, such as vomiting and diarrhea. These three-lichen species aqueous extracts are used as a treatment for epilepsy and other smoking-related illnesses. In addition, Wang *et al*. (2001) reported on the ethnic groups of Yunnan Province, China, and they mentioned the usage of five lichen species as a food source: *L. kurokawae*, *Lobaria isidiophora*, *Ramalina conduplicans*, *L. yoshimurae*, and *R.*

sinensis. They also identified five lichen species that are used to make medicinal teas: *Lethariella cashmeriana*, *L. semanderi*, *L. sinensis*, *Thamnolia vermicularis*, and *T. subulifor*.

Similar to this, Song and Gang (2013) reported a large number of lichen species that are utilized by Chinese indigenous populations. Headaches and vertigo are treated by the lichen *Cladonia amaurocraea*. When someone is coughing up blood or has cuts or scalds, *Cladonia cervicornis* lichen is applied. *Cladonia pyxidata* extracts were used to treat bacterial skin infections, and *Cladonia fenestralis* is used to make a medicinal tea. Additionally, they list *Rhizoplaca chrysoleuca*, which is used to treat intestinal blockage, pain alleviation, burns and scalds, tuberculosis, and skin diseases. The lichen *Bryoria asiatica* is used to treat kidney disease, vertigo, heart palpitations, and problems urinating. Additionally, headaches, coughs, infections, pulmonary TB, and irritated lymphatic vessels are treated with *Usnea ceratina*. *Usnea plicata* can also be used to halt bleeding, relieve pain, and stop bloody feces. Drinking *Cetraria islandica*'s decoction helps digestion and fortifies the stomach's walls. Other lichens, such as *Parmotrema tinctorum*, are used to treat swelling, ulcers, bleeding from wounds on the outside, and hazy eyesight. Contrarily, *Punctelia borreri* lichens are also used to treat exterior wounds, uterine bleeding, and blurred vision.

Usnea barbata is a lichen that African countries utilize to cure cattle mammary infections, according to a 2002 article by Afolayan *et al*. The ethnobotanical uses of lichens by indigenous peoples as a source of food, fodder, medicine, and beauty have been reported in several European countries. Many important lichen species used by indigenous people in European countries are *Cladonia pyxidata, Cladonia cornuta, Cladonia coccifera, Cetraria islandica, Evernia prunastri, Hypogymnia physodes, Lobaria pulmonaria, Peltigera canina, Peltigera aphthosa, Usnea plicata, Usnea hirta, Usnea florida, Usnea barbata*, and *Xanthoria parietina* [33], [164].

4.5. Pharmaceutical Properties, Therapeutic Potential and Biological Activities of Lichens

Lichens can live in some of the harshest environments on Earth, and many of their medical uses can be advantageous to academics and researchers. Lichen acids are the name given to the secondary metabolites that lichens manufacture. Lichen acids are formed by mycobionts and are dispersed over the surface of lichens as amorphous or crystals [165], [197]. Lichen acids have a variety of biological potential which includes antioxidant, anticancer [197], enzyme inhibitory [121], antiviral [43], antifungal [124], antidiabetic [49], allelopathy [59], antipyretic, crop growth inhibitory, cytotoxic, anti-hepatotoxic [168] and antiproliferative properties [52]. In the pharmaceutical industry, several lichens are also frequently employed as anti-infectives to create anti-mycobacterial, antiviral, and other anti-inflammatory drugs [19], [28].

Table 2 Integrated list of pharmaceutical properties and therapeutic potential of lichens

Pharmaceutical Properties and Therapeutic Potential	**Description of Properties and Therapeutic Potential**	**Author(s)**
Antifungal Activities	Secondary metabolite called aspergyllone that was isolated from the endolichenic fungus *Aspergillus niger.* Tiegh that was found in the Indian lichen *Parmotrema ravum* Serus. The substance was tested against infections that damage plants, people, and food, and it was discovered to have potent anti-fungal activity against *Candida parapsilosis*. Further investigation demonstrated that the Himalayan lichen *Bulbothrix setschwanensis* possesses both antibacterial potential against *S. aureus* and anti-fungal potential (*Cryptococcus neoformans*) capabilities. Antimicrobial activity has been often found in lichens. The ethanol extract obtained from four (4) specie of lichens *Parmotrema reticulatum, Everniastrum cf. vexans, Peltigera laciniate* and *Parmotrema blanquetianun* has antifungal activity against six different microbes viz *Listeria monocytogenes, Staphylococcus aureus, Proteus vulgaris, Pseudomonas aeruginosa, Escherichia coli,* and *Klebsiella pneumonia*. Clinical strains of *T. rubrum, E. floccosum*, and *M. canis* are resistant to the antifungal effects of the active xanthone derivatives found in lichens. The usnic acid derivatives usone and isousone have been shown to have dose-dependent fungal inhibitory efficacy against *Trichophyton rubrum spp*.	(Kosanic et *al.*, 2014), Yu *et al.* (2016), (Maurya *et al.*, 2018), (Plaza *et al.*, 2018), (Resende *et al.*, 2018), (Padhi *et al.*, 2019)

Anti-Bacterial Activities	Some lichens, such as *Usnea* and *Cladonia*, which produce usnic acid and are used in the pharmaceutical manufacturing of ointments to treat burns and wounds, are employed for their antibacterial characteristics. Four ethanolic extracts produced by lichens that have strong antibacterial activity against *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Proteus vulgaris*, *Escherichia coli*, *Klebsiella pneumonia* and *Listeria monocytogenes*. The active compounds xanthones derivatives of lichens have antibacterial activity against multi-drug resistant pathogenic microbes such as *Enterococcus faecalis* and *Staphylococcus aureus*. Recent research revealed that the synthesis of eco-friendly biogenic manufacturing of silver nanoparticles from the lichen *Usnea longissimi*. These synthetic nanoparticles, is more cost-effective and can avoid pollution from the atmosphere. The size of each synthetic nanoparticle between the 9.40-11.23 nm range are involved in the function of usnic acids, amines, phenols, aldehydes and ketones in reducing silver into a silver nanoparticle. The active nanoparticles possess gram-positive antimicrobial activity (*Streptococcus pyrogenes*, *Streptococcus mutans*, *Corynebacterium diphtheriae* and *Corynebacterium xerosis*) and gram-negative antimicrobial activity against strains (*Escherichia coli*, *Pseudomonas aeruginosa* and *Klebsiella pneuomoniae*). The lichen extract showed significant antibacterial activity against burn wound-associated MRSA clinical isolates. *P. furfuracea* and *E. prunastri* acetone extracts shown significant activity with MICs ranging from 0.039 to 0.15 mg/mL and a bacteriostatic effect. Additionally, one MRSA was bactericidally destroyed by *R. farinacea* extract, with MIC values for all MRSA strains ranging from 0.078 to 0.625 mg/mL. Usnic acid, which was *R. farinacea* main antibacterial ingredient, might cause this activity. Atranorin and fumarprotocetraric acid had much less effectiveness against MRSA strains than usnic acid. Usnic acid disrupted the bacterial membrane, exhibiting excellent antibacterial activity against clinical isolates of MRSA with MIC values between 25 and 50 μg/mL. Several lichenic compounds, including lobar acid, physodic acid, rhizocarpic acid, 3-hydroxyphysodic acid, hybocarpone, and (R)-(+)-usnic acid, were found to be effective against methicillin- and multidrug-resistant *Staphylococcus aureus*. These compounds were isolated from the lichen species *Sterocaulon dactylophyllum, Hypogymnia physodes, Psilolechia lucida, Hypogymnia physodes, Lecanora conizaeoides,* and *Lecanora albescens*. Despite the fact that the antibacterial activity of lichens has been extensively studied, whether in the form of raw extracts or purified compounds, the mechanism of action of these substances has not been thoroughly evaluated.	(Kokubun *et al*., 2007), (Zambare and Christopher, 2012), (Gupta *et al*., 2012), (Manojlovic *et al*., 2012), (Pompilio *et al*., 2013), (Kosanic e*t al.*, 2014), (Manisha, 2018), (Plaza *et al*. 2018), (Resende *et al*., 2018), (Siddiqi *et al*., 2018), (Aoussar *et al*., 2020), (Es-sadeqy *et al*., 2020), (Bhagarathi *et al*., 2022)
Antiviral Activities	Chromatographic methods are used to purify usnic acid and parietin from the extract of the lichen *Teloschistes chrysophthalmus*. Use usnic acid and parietin purified products for their antiviral activity and virucidal effects (against Junin and Tacaribe arenaviruses, respectively) when appropriate. This experiment, known as a "virucidal assay," was carried out directly on the virus cell nuclei to check the effectiveness of the activities against the viral cell-inactivating traits. As a potential bioterrorism agent, the arenavirus JUNV (Junin virus) has been studied as a model system because it is known to induce hemorrhagic Argentine fever in humans. Usnic acid may reliably reduce the amount of JUNV produced by infected Vero cells by a dose of 9.9 and 20.6 micrometers, respectively. It is possible to use usnic acid in a dose-dependent manner to lower the output of JUNV from infected Vero cells (9.9 m and 20.6 m, respectively).	(Damonte & Cote, 2002), (Rotz *et al*., 2002), (Fazio *et al*., 2007), (Zambare & Christopher, 2012), (Kosanic e*t al*., 2014)
Anti-Insecticidal Activities	Over time, killing mosquito larvae has proven to be an effective method of reducing the mosquito population in various breeding grounds before they mature into adults. The most extensively used insecticides are based on	(Bonning & Hammock, 1992), (Khanuja *et al*.,

	synthetic chemicals, but because of their frequent usage, chemical resistance has developed widely and there are now broad public concerns about food safety and environmental health issues. Numerous bioactive components found in phytochemicals provide an alternate source and agent for controlling insects while having little to no negative effects on unintended targets and the environment. Furthermore, it was shown that the methanol extract of *R. conduplicans* was effective against mosquito larvae. Additionally, *Spodoptera ornithogalli* and *S. littoralis* were well controlled by extracts from the lichen *Letharia vulpine*. The LC_{50} values for various bioassays using (−) and (+) usnic acids against the mosquito larvae of *Culex pipiens* were 0.8 and 0.9 ppm, respectively.	2007), (Cetin *et al.*, 2008), (Vinayaka *et al.*, 2009)
Anti-Drug Resistance Bacteria	Investigations were done on the antibacterial activity of six lichen species' methanol extracts against nine clinical bacteria isolates that were multidrug resistant. Additionally, *Usnea articulata* and *Usnea florida* have the highest activity of all the lichen species, with minimum inhibitory concentrations of 4–10 mg/mL. In the most recent study, the secondary spreading metabolite was isolated and purified from *Evernia mesomorpha* and identified using LCMS, 1H-, 13C-, and DEPT-NMR. The divaricate chemical has potent antibacterial properties against Methicillin-resistant *Staphylococcus aureus* (3A048; an MRSA), and it can be used to treat infections caused by MRSA or by germs resistant to common antibiotics. Usnic acid, a compound derived from the lichen *Usnea steineri*, has synergistic effects against four different strains of resistant bacteria, including *Staphylococcus epidermidis*, which has a MIC of 3.12 g/mL, *Staphylococcus aureus*, and *Staphylococcus haemolyticus*, which has a MIC of 12.5 g/mL. Usnic acid was discovered to have no synergistic antibacterial properties when combined with penicillin and tetracycline.	(Zambare & Christopher, 2012), (Tozatti *et al.*, 2016), (Oh *et al.*, 2018), (Aoussar *et al.*, 2020), (Bate *et al.*, 2020)
Tyrosinase-Inhibitory Actions	Tyrosinase is considered to be a key enzyme in various mammalian cells and it helps to avoid excessive melanin pigment production. Melanin possesses the property of absorbing ultraviolet radiation in order to safeguard the skin and also removing reactive oxygen species (ROS) in the skin of mammals. It therefore plays an integral role and widely utilized in the cosmetics and the medicinal sectors. The inhibition of the surplus of tyrosinase enzyme manufacturing is therefore necessary. Some species of lichens has the potential property to prevent the activity of tyrosinase. In some lichen species such as *Graphis assamensis*, *Graphina multistriata*, *Graphis Phaeographopsisindica*, and *Graphis nakanishiana*, are capable of tyrosinase inhibitory activity which occur considerably. Additionally, some edible and medicinal lichen species disclosed tyrosinase inhibition property (*Usnea plicata* and *Umbilicaria esculenta*).	(Briganti *et al.*, 2003), (Behera *et al.*, 2006) (Kim & Cho, 2007), (Nguyen *et al.*, 2016), (Zambare & Christopher, 2012).
Allelopathy Activities	Allelopathy is thought to be a natural process where one organism produces allelochemicals, secondary metabolites, that can have either positive or negative effects on another organism. Due to the presence of secondary usnic acid metabolites, the lichen extract has adverse allelopathic effects on bryophytes (moss *Physcomitrella*) by suppressing protonemic and gametophore development. *Parmelia reticulate*, a Himalayan lichen with allelopathic potential, can prevent the growth of weeds like *Phalaris minor*, which grows among wheat and barley plants. The effects of the secondary metabolites of saxicolous lichen usnic acid, parietin, and norstic acid as biocides to prevent ecotoxicity against the following micro-colonial bacteria *Coniosporium perforans, Coniosporium apollinis*, green algae *Scenedesmus ecornis*, and coccoid cyanobacteria *Chroocococcus minutus* were examined in a different study.	(Stamp, 2003), (Macias *et al.*, 2007) (Zambare & Christopher, 2012), (Gazzano *et al.*, 2013), (Goel *et al.*, 2014), (Goga *et al.*, 2017)
Photo-Protective Activities	Overexposure to UV radiation (UV-A and UV-B) can cause a number of skin diseases, including skin cancer, immune system suppression, and premature aging, which is becoming a major problem in the world. The industry offers a wide variety of sunscreen creams as one of the ways to	(Heber *et al.*, 2011), (Zambare & Christopher, 2012), (Pierfrancesco, *et al.*,

	shield yourself from radiation. There are many different kinds of sunscreen, including those for skin care, eyes, lips, and hair. Some higher plant species, mosses, and the majority of lichens can withstand desiccation. The photobiont component of the lichen contributes to the reduction of load segregation in Photosystem II (PSII) reaction centers, which helps to inhibit fluorescence emission. For instance, *Parmelia sulcate, Peltigera neckeri*, and *Lobaria pulmonaria* are three lichens that can block UV rays.	2013), (Clark & Hessler, 2015)
Anti-Hepatotoxic, Cytotoxic and Anticancer Activities	Alcohol use can increase the levels of NADH/NADP in hepatocytes, which can stop the mitochondrial -oxidation of fatty acids. It can also increase the transit of lipids from the small intestine to the liver, which results in abnormal fat deposition in the body. The reindeer lichen, also known as *Cladonia rangiferina*, has been reported and studied for the treatment of fever, liver conditions, arthritis, convulsions, tuberculosis (TB), and constipation. Alcohol-related liver and tissue toxicity can be reduced by using the reindeer lichen extract. The pharmaceutical industry has recently placed a significant deal of emphasis on the anticancer potential of secondary lichen metabolites. Additionally, it is considered feasible to treat cervical cancer after receiving a pre-treatment of usnic acid ($C_{18}H_{16}O_7$) and zinc sulfate ($ZnSO_4$). Other varieties of lichen, such as *Alectoria ochroleuca* and *Nephroma expallidum*, are found in the Himalayas and Nepal and act as chemo preventives for cancer. The extract of *Cetraria aculeata* was discovered to have antigenotoxic potential in contrast to *Salmonella typhimurium*. In addition, certain lichens, such *Collema flaccidum* in particular, are members of the Collemataceae family and contain the active compounds bianthraquinone, colleflaccinosides, and glycosides, which have anticancer properties. With IC50 values of 12.72 and 15.66 µg/mL, the acetone extract of the *Usnea barbata* (usnic acid) lichen showed significant anti-cancer activity against human melanoma and human colon carcinoma cell lines. HepG2 cells can undergo apoptosis when exposed to the active ingredient usnic acid and its different derivatives (usenamines), which are taken from the lichen *Usnea longissimi*. The maximum cytotoxicity for the cell lines HCT-116 and SW480 was found in the ethyl acetate and acetone extracts from the lichens *Pseudevernia furacea* and *Platismatia glauca*, respectively IC50=21.2 ± 1.3 µg/mL and 51.3 ± 0.8 µg/mL. Subsequently, the lichen *Stereocaulon alpnum* gathered from the Antarctic region exhibit anticancer activities against human cervix adenocarcinoma (HeLa cells) and human colon carcinoma (HCT116 cells) cell lines because of the existence of lobaric acid and secondary metabolites of lobarstin. These secondary metabolites aid to improve the arresting of the cell cycle thus, causing important dose- and time-dependent reduction in the development of carcinogenic cells. *P. furfuracea* extract, when applied for 72 hours, was found to have the most impact on all cancer cell lines examined, particularly human prostate cancer (22RV1) cell lines. This outcome is consistent with that of the earlier work, which shown that *E. prunastri* and *P. furfuracea* extracts had cytotoxic effects on human melanoma (FemX) and human colon carcinoma (LS174), with IC50 values that are comparable to 55.09-120.89 µg/mL. Moreover, *P. furfuracea* demonstrated the most potent cytotoxic action. It was also shown that these extracts triggered cell death in LS174 and FemX cells by strongly arresting the cell cycle in the sub-G1 phase. Even at low concentrations, unprocessed lichen extracts or their constituent parts showed activity against many cancer cell lines. The IC50 values of three lichen extracts did not indicate strong cytotoxic activity IC50 > 30 µg/mL, while the physodic acid isolated from *P. furfuracea* vs. FemX and LS174	(Barona & Lieber, 1979), (Huneck & Yoshimura, 1996), (Scirpa *et al*., 1999), (Ingólfsdóttir *et al*., 2000), (Ezanka & Dembitsky, 2006), (Zeytinoglu *et al*., 2008), (O'Shea *et al*., 2010), (Manojlović *et al*., 2012), (Ranković *et al*., 2012), (Zambare & Christopher, 2012), (Kosanić *et al*., 2013), (Shrestha & St. Clair, 2013), (Kosanic *et al*., 2014), (Yu *et al*., 2016), (Hong *et al*., 2018), (Kosanić, 2018), (Šeklić *et al*., 2018), (Shukla *et al*., 2019), (Studzińska-Sroka & Zarabska-Bożjewicz, 2019), (Tomović, J. 2019), (Aoussar *et al*., 2020)

	cancer cells with IC50 of 19.52 and 17.89 μg/mL demonstrated strong cytotoxic effect.	
Antidiabetic Activities	Diabetes is a well-known physiological condition that is spreading throughout the world and causing a number of health-related difficulties. Currently, there are no medications available to treat diabetes. The most common type of diabetes, diabetes mellitus, accounts for 90% of cases and is characterized by chronic enzymatic hyperglycaemia. In the future, the field of lichens will be unbeatable for treating diabetes. The lichen *Parmotremaha babianum* contains anti-diabetic compounds that drastically lower blood glucose levels. Orally administered *Cladonia humilis* lichen extract significantly decreased blood glucose levels in rats with alloxan-induced hyperglycaemia. The natural substances in *Ramalina sinensis* are efficient against a variety of enzymes that participate in inhibitory processes. This particular lichen species has the potential to inhibit the activity of the -amylase enzyme resulting in a decrease in blood glucose level and prevent it from noninsulin dependent diabetes-type-2. The breakdown of starch by the -amylase enzyme leads to hyperglycaemia and this cause an increase in the blood glucose level. This lichen can suppress the -amylase enzyme activity leading in a drop in the blood glucose levels and prevent non-insulin dependent type-2 diabetes. When starch is broken down by the -amylase enzyme, the effect is an increase in blood glucose levels caused by hyperglycaemia.	(Zambare & Christopher, 2012), (Zhang *et al*., 2012), (Ganesan *et al*., 2016), (Hengameh *et al*., 2016), (Bhutkar *et al*., 2018)
Immuno-Modulatory Activities	Immunity can be activated or suppressed by a variety of modifications to the body's immune system and with the help of biological agents. *Cetraria islandica*, a lichen, has been employed in medicine to treat inflammatory conditions. Protolichesterinic and fumarprotocetraric, two chemicals, are produced, purified, and tested against dendritic cell maturation as determined by IL-10 and IL-12p40 secretion. When arthritis is treated with an aqueous lichen extract, the upregulated secretion results in the anti-inflammatory action.	(Freysdottir *et al*., 2008), (Zambare & Christopher, 2012)
Antioxidant Activities	Lichens have taken part in numerous investigations exploring for novel natural antioxidants and their potential anti-chronic illness protective properties. The number of total phenols in the studied extracts demonstrated a strong in vitro antioxidant effect. This outcome was consistent with previously published research that shown a favorable relationship between the phenolic content and the antioxidant activity. Furthermore, there was no evidence of a connection between the lichen extract's flavonoid level and its antioxidant effects. Depsides, depsidones, and dibenzofurans are the main components of lichen that are in charge of the antioxidant properties. According to previous studies using acetone extracts of *P. furfuracea* and *E.* prunastri harvested in Serbia and Turkey, *P. furfuracea* extract had a larger antioxidant activity and the highest quantity of phenols than *E. prunastri* extract. Of the tested extracts, *P. furfuracea* extract demonstrated the best antioxidant power with the greatest concentration of polyphenolic compounds. The *R. farinacea* extract exhibited the highest ferric reducing power, but the least number of phenols, indicating that the presence of nonphenolic chemicals may be the cause of this extract's activity.	(Sökmen *et al*., 2012), (Fernández-Moriano *et al*., 2015), (Nguyen *et al*., 2019), (Aoussar *et al*., 2020)
Production of Laboratory Materials	In order to create orcein, a biological stain, the lichen *Rocella tinctoria* is employed. Before litmus was made synthetically, the *Rocella tinctoria* could be used as a source of the pH indicator. Numerous colours used in laboratories, such as pH indicators, litmus tests, and other dyes, are derived from various lichen species.	(Manisha, 2018), (BYJU'S, 2022), (Bhagarathi *et al*., 2022).
Cosmetology	Some lichen species, such *Ramalina* and *Evemia*, are used to make incense sticks and as fragrant incense. Different types of scent are made using other lichen species, such as *Lobularia pulmonaria* and *Evemia prunastri*. The	(Manisha, 2018), (BYJU'S, 2022),

	cosmetic industries use lichens as a natural medicine to cure a variety of rashes and skin conditions. Lichens were also acknowledged for their significant role in cosmetology.	(Bhagarathi *et al*., 2022).

5. Conclusion

This review emphasizes the biology and chemistry of lichens and their ecological, ethnopharmacy, medicine pharmacy. Lichens have many roles, importance and benefits in the areas of food preparation, cosmetology, biological and ecological processes, pharmacological synthesis of drugs to treat different ailments and disorders of the human body; the full potential of lichens are not yet fully researched and documented in the scientific world. Lichens also play important roles in ecological process that contributes to the health and sustainability of ecosystems. Lichens play key roles in primary productivity as well as nitrogen fixation and promotes seed germination. Additionally, lichens serve as a suitable habitat for many microfauna (such as arachnids, insects and small reptiles like lizards) and macrofauna (like warm-blooded animals e.g., birds and squirrels). Lichens are considered as both pioneer and keystone species and they are very important in biomonitoring to detect air quality and pollution. Therefore, they can be used as indicator species by biomonitoring agencies, companies, other stakeholders to make strategic plans for environmental assessment. More research should be done when it comes to lichen biology and chemistry and their ecological, ethnopharmacological, pharmaceutical and therapeutic potential; especially in neotropical countries.

Compliance with ethical standards

Acknowledgement

The authors would like to thank the University of Guyana, Division of Natural Sciences, Department of Biology for giving this tremendous opportunity and supporting the successful completion of this research. The author would like to express his sincerest gratitude to the following individuals who have assisted and provided supervisory insights throughout this research: Mr. Rahaman Balkarran, Prof. Gomathinayagam Subramanian, Mr. Phillip Da Silva, Dr. Gyanpriya Maharaj, Ms. Sushmita Kalika-Singh, Ms. Ferial Pestano, Ms. Zenesia Phillips-Henry and Ms. Chalasa Cossiah.

Disclosure of conflict of interest

The authors hereby declare that this manuscript does not have any conflict of interest.

Statement of informed consent

All authors declare that informed consent was obtained from all individual participants included in the study.

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