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Edible lichens and its unique bioactives: A review of its pharmacological and food applications

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ABSTRACT

Edible lichens are nutritious sources of health-promoting bioactive compounds utilized as ethnic foods and traditional medicine for ages and documented across universal pharmacopoeia. The nutritional, pharmacological and organoleptic features of lichen research are increasing, and new perspectives on its applications allow the development of novel functional foods and drugs. This review highlights the secondary metabolites of edible lichen, biological activities, and major applications in the pharma and food sectors. The potential of lichen as a natural factory for nanomaterial fabrication is discussed with prospective biological mechanisms. The food processing techniques reduce the native acerbity and bitterness in lichens and enhance the volatile flavour ingredients to support the development of new food formulations. Future research should envisage the edibility of lichens and in-depth molecular pharmacological mechanisms using multidisciplinary approaches and techniques that can potentially resolve the challenges in lichen consumption.

1. Introduction

Lichens are composite organisms arising from the symbiotic association of fungi (mycobiont) and algae (photobiont) that can persist in extreme environments. The survivability of lichens in harsh conditions can be directly correlated with the production of unique extracellular metabolites. With the increasing demand for novel human-friendly bioactives in food and pharmacological applications, lichens remain an untapped reservoir of secondary metabolites, which could boost life-saving drug leads. Further, considering that more than 50% of the next-generation medicines are of natural product origin, these super-resistant lichens offer promising means for their applicability as templates for future drug discoveries. Research on the potential use of lichens explored many biological applications, primarily antibacterial (Zorrilla et al., 2022), antioxidant (Elečko et al., 2022), antiviral (Loeanurit et al., 2023), antigenotoxic (Elečko et al., 2022), anti-inflammatory (Mariem Ben Salah & Mohamed Mendili, 2022), anticancer (Kocovic et al., 2022), and antipyretic (Adenubi et al., 2022) activities.

Edible lichens, a nutrition-rich precious resource, have a long history of consumption practice as folk food and medicines widely used in countries such as India, Japan, China, and other European countries. In China, *Umbilicaria esculenta* is one of the main ingredients in culinary preparations after minimal processing (Huang et al., 2018), whereas, in Finland and Switzerland, the salt of usnic acid from *Lobaria spp* is majorly used (Kosanić et al., 2014). Remarkably, the edible macro-lichens found on trees are harvested and taken as major side-dish after frying, stewing and other primary processing techniques. Many of the lichens are edible, having the protein content (5.95 – 16.2%), carbohydrate content (53.2 – 79.08%), fat content (1.3 – 6.5%), crude fibre (5.38 – 16.36%) and ash (4.00 – 12.1%) which are safe to eat (Zhao et al., 2021). A few lichens have significant toxic chemicals, such as vulpinic acid, which should be identified to avoid consumption. More specifically, the essential amino acid compositions (phenylalanine 140%, leucine 109%, tryptophan 291% and valine 183%) in lichens are more than the “ideal protein” standard (Perez-llano, 2020). Comparably, the mineral content such as potassium (800 – 5497 ppm), iron

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(311 – 19579 ppm) and calcium (2130 – 17190 ppm) was relatively high than many stable food commodities and low in sodium content (Bokhorst et al., 2015).

Lichens are increasingly exploited as bionanofactories, where both the live and dead organisms are employed to synthesize metallic and oxide nanoparticles. The nanomaterials are most synthesized from plant extracts, enzymes, fungi, and bacteria. Surprisingly, there is an emerging trend in the biogenic fabrication of multifunctional nanoparticles using lichens, owing to their potential reducing and capping properties. Meanwhile, lichens are sensitive to external environments such as smoke, dust, fluoride, and hydrocarbons, are excellent metal bio absorbers and accumulate heavy metals in their structure (Kosanić et al., 2018). Moreover, lichens are widely employed as indicators for monitoring environmental quality and air pollution. The ecological utility aspects of lichens have been sufficiently reviewed and attracted many scientific communities (Boonpeng et al., 2017; Conti et al., 2012; González-Burgos et al., 2019). However, a review of the edible aspects and nutritional advantages of lichens for functional food formulations is still lacking. Likewise, with the advancement of high-tech instrumentation methods and the discovery of novel bioactive components, this review highlights the key biological significance and details the ethnomedical applications of edible lichens.

This contribution summarizes the applicability of edible lichens in food formulations and their nutritional advantages. Key aspects reviewed herein include (1) secondary metabolites of lichens with pharmaceutical applications; (2) biological therapeutic properties with relevant ethnomedical practices; (3) edible lichens as future food sources and their nutritional advantages; (4) production and use of lichen nanoparticles and its utility in various sectors; and (5) lichen polysaccharides and their functional roles in immune systems.

2. Lichens: habitat, classification, and physiology

Lichens are highly diverse organisms characterized by a stable structure partly from fungus and algae. A wide variety of lichens worldwide have different colors, shapes, and sizes, and nearly 13500 – 30000 species are estimated to be on earth (Zhao et al., 2021). Lichen usually has three types of growth forms based on the thallus structure - fruticose (shrub-like), a three-dimensional structure, crustose (crust-like), a two-dimensional structural lichen which has unseen under the surface and foliose (leaf-like) which occurs between the fruticose and crustose. It has a markedly three-dimensional structure, where the upper and lower surfaces can be seen in this type of lichen (Bokhorst et al., 2015). The lichen was further classified into asco lichens found in ascomycetes, and basidiolichens belong to basidiomycetes based on fungal partners.

It was recently specified that the lichen could live in space and quickly adapt to extreme environments such as the Mars climate (Onofri et al., 2012). Generally, lichens can survive in various environmental conditions such as grassland, seaside, plateau, desert, forest and polar regions. Additionally, lichens are resilient in harsh environments in areas that are hostile to living, like tundra zone, alpine zone, polar regions, and some drought regions, where they are the predominant flora. Further, they mostly grow on tree bark, leaves, mosses, rock, walls, or branches and are divided into three categories concerning lichen habitat. Saxicolous, found in rocks or stones; corticolous, seen in barks of trees; and terricolous, which grows in soil (Bokhorst et al., 2015).

Calcium oxalate synthesis helps the lichen to grow in extreme conditions, whereas polysaccharides are present in the upper side of the lichen. Lichen can grow slowly, less than an mm per year but has a long lifespan and low molecular weight (Dale et al., 1989). It can reproduce both asexually and sexually. Many lichens can reproduce asexually by dispersal of the fragments. Interestingly, fruticose lichen can be easily fragmented, and a new lichen can be produced from that fragment. Likewise, fragmentation is essential for the production of soredia, whereas sexual reproduction can be done only by fungal partners. Discs can appear in sexually reproduced lichen (Ilondu, 2019). Most of the lichens are edible, and very few are recognised as poisonous. Lichen polysaccharides are undigested by humans and are used as bioindicators. They have high nutritional values, and the role of lichen in the medicinal field is to treat various illnesses, including skin diseases, whooping cough, tuberculosis, respiratory, and diabetes mellitus, and also used as food, feed, perfumery, and cosmetics (Perez-llano, 2020). More importantly, lichen polysaccharides have multifunctional properties such as antioxidant, antimicrobial, anticancer, anti-inflammatory, and antiulcerogenic effects (Periasamy et al., 2023).

3. Bioactive metabolites in edible lichen

Lichens are rich sources of both primary and secondary metabolites (Table 1). The primary metabolites of edible lichens include amino acids, amines, proteins, peptides, vitamins, polyols and carotenoids in the cell wall and protoplast (Dawes, 2017). The primary metabolites are intracellular and play an essential role in cellular metabolism (Stocker-Wörgötter, 2002). The amount of free amino acids that lichens excrete is similar to that of other plants, and lichen thallus contains 1.5–24 mg/g of carotenoids, 1.6–11.4% dry weight of nitrogen compounds and 3–5% dry weight of polysaccharides (Hale, 1983). Many vitamins, including ascorbic acid, pantothenic acid, folic acid, nicotinic acid, riboflavin, biotin, thiamine, and -tocopherol, are generated by lichens (Ranković, 2015). The major secondary metabolites of edible lichens are dibenzofurans (usnic acid), lactones (nephrosterinicacid, protolichesterinic acid), depsides (barbatic acid), quinones (parietin), depsidones (salazinic acid), depsones (picrolichenic acid) and pulvinic acid derivatives (vulpinic acid) (Shukla et al., 2010). Most metabolite compounds are water-insoluble and typically deposited on the surface layer of mycelium cells (González-Burgos et al., 2019). Secondary metabolites typically make from 0.1% to 10% of the dry weight of the thallus, but they can occasionally be up to 30% (Solhaug et al., 2009).

The production of secondary metabolites in lichens is influenced by environmental factors such as light, temperature, UV, seasonality and elevation. In addition, the age of the lichens has a major impact on the lichen compounds production and their distribution in the thallus (Ranković, 2015b). The mycobiont and photobiont interaction is vital for producing secondary metabolites, whereas the mycobiont builds up substances such as atranorin, usnic acid, parietin and fungal melanin in the cortex or the medullary layer of the hyphae. The photobiont also impacts the mycobiont's secondary metabolism (Yamamoto et al., 1993). Some of the lichens are yellow in color, and the yellow pigment is the secondary metabolite of the fungal partner, and it has two enantiomers (+) and (-). Such two enantiomers are selective against various gram-positive bacteria (Cocchietto et al., 2002).

Many secondary metabolites are produced from edible lichens and obtained from three pathways: acetyl polymalonyl, mevalonic acid, and shikimic acid (Fahselt, 1994). Orcinol series, β-orcinol series, dibenzofurans, usnic acid, diquinone are the aromatic compounds arising from the intermolecular esterification and mixture of oxides. Lichens monoaryl derivatives and xanthones are products from the single polyacetyl chain of acetyl polymalonyl pathway (Ankith et al., 2017). Metabolites such as terpenes, steroids, and carotenes are most commonly derived from the mevalonic pathenes. Terphenyl quinones and pulvinic acid are the products of the shikimic pathway (Crittenden & Porter, 1991).

Usnic acid is a natural lichen compound and an active antimicrobial agent in pharmacology (Ingólfsdóttr, 2002). The significant product of *Bryoria fuscescens, Cetraria nivalis, Evernia prunastri, Usnea barbata, Usnea pictoides, Ramalina condupulicans,* and *Ramalina farinaceae* is usnic acid, a derivative of acetyl polymanlony pathway (Cocchietto et al., 2002). Further, it can be used against many diseases and absorb and preserve UV light (Shukla et al., 2010). Some depsides include atranorin, sphaerophorin, diffractaic acid, divaricatic acid and gyrophoric acid while the depsidones include salazinic acid, stictic acid, pannarin,

Table 1
Secondary metabolites of edible lichens.

Lichen species	Family	Secondary metabolites	Application	References
Cladonia rangiferina	*Cladoniaceae*	Atranorin Fumarprotocetraric acid	Consume as tea or juice	(González-Burgos et al., 2019)
Lobaria pulmonaria	*Lobariaceae*	Gyrophoric acid Stictic acid Norstictic acid	Food and cosmetics	(Süleyman et al., 2003)
Bryoria fremontii	*Parmeliaceae*	Vulpinic acid	Making cake or cookies	(Turner, 1977)
Bryoria fuscescens	*Parmeliaceae*	Usnic acid Protocetraric acid	Making bread	(Culberson, 2002; Kaitera et al., 1996)
Cetraria islandica	*Parmeliaceae*	Depsidone Fumarprotocetraric acid Protolichesterinic acid	Salads	(Shrestha, 2015)
Cetraria nivalis	*Parmeliaceae*	Usnic acid	Bread making	(Boustie et al., 2011; Perez-llano, 2020)
Everniastrum cirrhatum	*Parmeliaceae*	Atranorin, salazinic acid, protolichensterinic acid	Spices and flavouring agent in meat and vegetables.	(Anil Kumar et al., 2011; Perez-llano, 2020)
Evernia prunastri	*Parmeliaceae*	Orcinol, orsellic acid, monomethyl ether, evernimic acid, everynyl 3,5-dimethoxy toluence, atranorin, and usnic acid	Perfumery	(Ach et al., 2012)
Everniastrum nepalense	*Parmeliaceae*	Atranorin, salazinic acid, protolichensterinic acid, galbinic acid, and protocetraric acid.	Used for sausage and soup	(Jiang & Wei, 1993) (Devkota et al., 2017)
Parmotrema cetratum	*Parmeliaceae*	Atranorin, chloroatranorin, and salazinic acid.	Food product like pickle, soup, and sausage	(Devkota et al., 2017; Hale & Fletcher, 1990)
Parmotrema perlatum	*Parmeliaceae*	Orsinol, atranorin	Aromatic agent in food product and antioxidant	(Hawksworth, 2004)
Parmotrema tinctorum	*Parmeliaceae*	Atranorin, lecanoric acid, methyl orsenillate, and orsenillic acid	Used as flavouring compound in food and used in nutraceutical	(Jayaprakasha et al., 1998) (Tram et al., 2018)
Pseudevernia furfuracea	*Parmeliaceae*	Atraric acid, methyl chloro hematommate, and methyl hematommate	Antimicrobial, Anti-inflammatory	(Güvenç et al., 2012)
Rimelia reticulata	*Parmeliaceae*	Atranorin, chloroatranorin, and consalazinic	Bone growth and neurological functions	(Din et al., 1999; Huang et al., 2018; Kosanić et al., 2013)
		Physodic acid, physodalic acid, chloroatanorin, and 3-hydroxiphysodic	Antioxidant	
Usnea barbata	*Parmeliaceae*	Norstictic acid, usnic acid, atranorin, and chloroatranorin	Used in porridge	(Fernández-Moriano et al., 2016)
Usnea pictoides	*Parmeliaceae*	Usnic acid	Used as a mineral- rich compound in food.	(Rakesh & Dileep, 2013)
Heterodermia tremulans	*Physciaceae*	Atranorin and zeorin	Flavouring agent for meat and vegetables	(Kekuda et al., 2018)
Ramalina condupulicans	*Ramalinaceae*	Sekikaic acid Usnic acid and salazinic acid	Antioxidant Treatment for bacterial diseases and fungal disease of plants	(Luo et al., 2010) (Wiederhold & Riva, 2014)
Ramalina farinaceae	*Ramalinaceae*	Usnic acid, stictic acid, protocetraric acid, and norstictic acid.	Making breads	(Zhao et al., 2021) (Redzic et al., 2010)
Umbilicaria esculenta	*Umbilicariaceae*	Gyrothroris derivatives Patranorin and vulpinic acid Orcinol and methyl orsellinic acid Lecanoric acid	Cholesterol synthesis inhibition Insect growth inhibition Anti-inflammation Phospholipase A_2 Inhibition	(Xu et al., 2011) (Xu et al., 2011) (González-Burgos et al., 2019) (Anjali et al., 2016)
Umbilicaria mammulata	*Umbilicariaceae*	Gyrophoric acid	Food product and anti-inflammatory	(Shrestha et al., 2014)

1-chloropannarin, fumarprotocetraric acid, vicanicin, psoromic acid, variolaric acid and lobaric acid (Crawford, 2019b). Atranorin is one of the leading secondary metabolites obtained from the edible lichen, and it is a para-depsides derivative of the β-orcinol series from the acetyl polymalonyl pathway (Ranković, 2015). Lecanoric acid is also a para-depsides derived from orcinol series from the acetyl polymalonyl pathway and protocetraric acid is a compound of depsidone from β-orcinol series (Tay et al., 2004).

Salazinic acid is a compound under the β-orcinol series having an antimycobacterial activity present in *Everniastrum cirrhatum, Everniastrum nepalense*, *Parmotrema cetratum*, and *Ramalina condupulicans* (Honda et al., 2010). Anthraquinones are a broad family of compounds with a variety of biological activities. A naturally occurring anthraquinone called emodin (1,3,8-trihydroxy-6-methylanthraquinone) is found in many lichens, and parietin is formed from polyaromatic ring polyketides is found in *Xanthoria* sp. (Cohen & Towers, 2004). Protolichestrinic acid is a highly aliphatic compound obtained from *Cetraria islandica, Everniastrum cirrhatum* and *Everniastrum nepalense,* having antimicrobial and also as anti-proliferation on several cancer cells (Bessadóttir et al., 2014). Pulvinic acids are the pigments responsible for lichens' striking yellow and orange colours (Knight & Pattenden, 1976). The secondary metabolites of lichens play a main role in self-protection (including antimicrobial, antioxidant, photoprotective and herbivore resistance) and niche competition. Moreover, they also contribute to the steady state of metal compounds and resist pollution (Yashwant et al., 2021).

4. Biological activities of edible lichens

4.1. Antimicrobial activity

Most edible lichens have antimicrobial activity, which includes *Cladonia rangiferina, Cetraria nivalis, Everniastrum cirrhatum, Everniastrum nepalense, Parmotrema cetratum, Parmotrema perlatum, P. tinctorum, Pseudevernia furfuracea, Usnea barbata, Usnea pictoides, Ramalina conduplicans,* and *R. farinaceae*. The acetone extract of the lichens *C. subulata, C. foliacea and C. rangiferina* showed MIC value between 1.25 and 20 mg/ml (Kosanić et al., 2018). The acetone extract of *Cladonia fimbriata* has higher antimicrobial activity against *Bacillus cereus, B. subtilis, Staphylococcus aureus, E. coli, Proteus mirabilis, Aspergillus flavus, A. niger, Candida albicans, Mucor mucedo, Trichoderma viride, Cladosporium cladosporioides, Fusarium oxysporum, Alternaria alternata, Penicillium expansum,* and *P. chrysogenum* (Kosanić et al., 2018). The acetone extract of *Cladonia rangiferina* found active against *Bacillus mycoides,* *Staphylococcus aureus, Bacillus subtilis, E. coli, Klebsiella pneumoniae, Aspergillus flavus, Aspergillus fumigatus, Candida albicans, Penicillium purpurascens, and Penicillium verrucosum* with MIC value ranged between 0.78 and 12.5 mg/ml (Kosanić et al., 2014). It has also been reported that *C. rangiferina* has high antimicrobial activity against *Staphylococcus aureus* and *E. fuecium.* The ethanol extract of *C. rangiferina* possess good antifungal activity (Dülger et al., 1998). The acetone and chloroform extract of *B. fuscescens* has high antimicrobial activity against *Pseudomonas aeruginosa, Escherichia coli,* and *Acinetobacter sp.* (Çobanoğlu et al., 2010). The ethyl acetate extract of *C. islandica* has higher antimicrobial activity against *B. subtilis,* while the acetone extract and chloroform extract showed higher activity against *B. thurigiensis* and *B. sphaericus* respectively (Dülger et al., 1998).

The edible lichens such as *Bryoria fuscescens, Everniastrum nepalense,* and *Ramalina fasinaceae* produces protocetraric acid, which is a metabolite involves in antimicrobial activity (Tay et al., 2004). Orcinol is a phenolic compound obtained from edible lichens such as *Evernia prunastri, Parmotrema perlatum and Umbilicaria esculenta* having antibacterial and antifungal activities (Millanes et al., 2003). The secondary metabolite protolichesterinic obtained from *C. islandica* acid showed antimycobacterial activity against *Mycobacterium aurum* and had the MIC value of 250 μg/ml (Ingólfsdóttir et al., 1998). *E. prunastri* has antimicrobial activity against some pathogens such as *Bacillus mycoides, Staphylococcus aureus, Bacillus subtilis, Escherichia coli, Aspergillus flavus, Klebsiella pneumoniae, Aspergillus fumigatus, Penicillium purpurescens, Penicillium verrucosum* and *Candida albicans.* Studies proved from the methanolic extract of *E. prunastri* was effective against *E.coli* (MIC value 15.62 mg/ml), *Pseudomonas syringae* (MIC value 31.25 mg/ml), *Streptococcus pyrogenes* (MIC value 15.62 mg/ml), *Xanthomonas campestris* (MIC value 31.25 mg/ml), *Aspergillus niger* (MIC value 62.50 mg/ml), *Pencillium sp.* (MIC value 62.50 mg/ml) and *Sclorotinia sclerotiorum* (MIC value 31.25 mg/ml) and the ethanol extract of *E. prunastri* has high antifungal activity (Aslan et al., 2006; Karabulut & Ozturk, 2015).

The hexane extract of *P.perlatum* has higher antibacterial activity against *B. subtilis* and high antifungal activity against *A. fumigatus* (Hoda & Vijayaraghavan, 2015). The chloroform extract *Rimelia reticulata* has higher antimicrobial activity against *Bacillus subtilis, Escherichia coli, Staphylococcus aureus, Salmonella typhi, Micrococcus luteus and Pseudomonas aeruginosa* than the acetone extract, has a higher antifungal activity of 42.61 ± 1.87 (Meera et al., 2009). *Usnea sp.* has good antimicrobial activity against *Bacillus subtilis, Staphylococcus aureus, Enterococcus faecalis, Escherichia coli, Micrococcus viradans, Citrobacter freundii, Enterobacter cloaceae, Proteus vulgaris, Serratia marcescens* and *Pseudomonas aeruginosa* (Madamombe & Afolayan, 2003). *Usnea barbata* has antimicrobial activity against *B. subtilis* (20 ± 0.01) and *B. megaterium* (22 ± 0.02) (Cansaran et al., 2006). Solvent extract of *R. conduplicans* showed high antimicrobial activity against *E. coli* (1.43 ± 0.05), *P. aeruginosa* (2.00 ± 0.00), *B. subtilis* (1.50 ± 0.00), *B. cereus* (2.60 ± 0.10) *Alternaria sp.* (1.30 ± 0.00), *Curvularia sp.* (2.13 ± 0.05), and *Fusarium sp.* (2.20 ± 0.10) (Srinivasan & Kumaravel, 2015; Sundararaj et al., 2015). The methanol extract of *R. conduplicans* has higher antimicrobial activity against *S. typhimurium* (16.66 ± 1.6) and *P. aeruginosa* (16.0 ± 1.15) (Anjali et al., 2016). The biological activities of edible lichen are listed in Table 2.

Table 2
Biological activities of edible lichens.

Lichen species	Biological activity of lichen	References
Cetraria islandica	Antimycobacterial Antioxidant Anti-inflammation Inhibit HIV-1 reverse transcriptase	(Shukla et al., 2010)
Cetraria nivalis	Antimicrobial activity Chemotaxonomy	(Xu et al., 2016)
Cladonia rangiferina	Antioxidant Antimicrobial Anticancer Anti-inflammation	(Kosanić et al., 2014)
Cladonia subulata	Antimicrobial	(Kosanić et al., 2014)
Cladonia fimbriata	Antimicrobial	(Kosanić et al., 2014)
Bryoria fuscescens	Antioxidant Antimicrobial	(Çobanoğlu et al., 2010)
Bryoria fremontii	Antioxidant	(Turner, 1977)
Everniastrum cirrhatum	Anti-mycobacterial Anticancer Anti-obesity	(V. K.Gupta et al., 2008; Kekuda, 2012)
Evernia prunastri	Antioxidant Antimicrobial Anticancer	(Emsen et al., 2018; Shrestha et al., 2015)
Everniastrum nepalense	Antibacterial	(Yonghang et al., 2019)
Lobaria pulmonaria	Anti-inflammation Anti-ulcerogenic	(Redzic et al., 2010)
Parmotrema cetratum	Antimicrobial	(Nugraha et al., 2021)
Parmotrema perlatum	Antimicrobial and Antioxidant	(Balaji & Hariharan, 2007)
Parmotrema tinctorum	Antimicrobial	(Anjali, 2015)
Pseudevernia furfuracea	Anti-inflammation Antimicrobial Anti-nociceptive	(Güvenç et al., 2012)
Rimelia reticulata	Antimicrobial Antioxidant Anti-inflammation	(Meera et al., 2009)
Usnea barbata	Antimicrobial	(Redzic et al., 2010)
Usnea pictoides	Antimicrobial	(Abuzaid et al., 2020)
Ramalina conduplicans	Antioxidant Antimicrobial	(Wiederhold & Riva, 2014)
Ramalina farinaceae	Antitumor Antimicrobial	(Shukla et al., 2010)
Umbilicaria esculenta	Antithrombotic Anticancerogenic	(Redzic et al., 2010)
Umbilicaria mammulata	Anti-inflammation	(Shrestha et al., 2014)

4.2. Antioxidant Activity

Lichens seem to be an excellent material in the search for natural products with antioxidant activity due to phenolic compounds, which play an important role in free radical scavenging activity (Fernández--Moriano et al., 2016). *Cladonia rangiferina, Umbilicaria esculenta, Bryoria fuscescens, Bryonia fremontii, Cetraria islandica, Evernia prunastri, Parmotrema tinctorum, Pseudevernia furfuracea, Rimelia reticulata,* and *Ramalina conduplicans* are the edible lichens which are having antioxidant activity (Kosanić et al., 2018). Studies have shown that the main metabolites, such as evernic acid and physodic acid of the acetone extract of *Pseudoevernia furfuraceae* and *Evernia prunastri* have strong antioxidant activity, is proved through in vitro experiments of 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical scavenging, reducing power, and superoxide anion free radical scavenging. Physodic showed higher DPPH radical scavenging activity with an IC50 value of 322.44 μg/ml than evernic acid of 69.110 μg/ml (Kosanić et al., 2013). The free radical scavenging and ferrous ion chelating activity of polysaccharide extracts from Umbilicaria esculenta demonstrated strong antioxidant activity. Additionally, the antioxidant potential of the lichen was related to higher polysaccharides content. (Wang, Shu et al., 2018). *Parmotrema tinctorum* and *Umbilicaria esculenta* have lecanoric acid with good antioxidant activities like phospholipase A2 inhibitor and tumor inhibitor (Ranković, 2015a).

Stictic acid, a depsidone compound which is a vital metabolite, has many activities, such as antioxidant activity, and toxicity and can inhibit the cell growth of the human carcinoma cell line (Pejin et al., 2017). Pulvinic acid extracted from several lichens represents bright yellow and orange pigments with antioxidant properties; protocetraric acid is consumed as soup or sausage and is an ingredient in bread. The polysaccharides of *Cladina rangiferina* improved the antioxidant activity of Pb2 + damaged alveolar epithelial cells A549 (GPx, SOD, catalase, reduced glutathione) and reduced the lipid peroxidation and reactive oxygen species (ROS) accumulation in the cells (Tahidul & Kumar, 2019). The secondary metabolites usnic acid and diffractaic acid isolated from Usnea sp. proved to possess antioxidant activity, while usnic acid *Ramalina conduplicans* also has antioxidant activity, and its methanolic extract showed higher scavenging activity of 85.41% (Prashith Kekuda et al., 2009).

4.3. Anti-inflammatory activity

The anti-inflammatory activity can inhibit the inflammation of the disease. The ether extract of *Rimelia reticulata* has higher anti-inflammatory activity (Meera et al., 2009). *Aqueous Lobaria pulmonaria* extract has anti-inflammation activity, which was proved by carrageenan-induced paw edema test (Süleyman et al., 2003). On the carrageenan-induced mouse model of hind paw edema, the ethyl acetate and dichloromethane extracts of *Pseudevernia furfuracea* demonstrated anti-inflammatory action, with the methanol extract having the most pronounced anti-inflammatory inhibitory effect (Güvenç et al., 2012). Without causing DNA damage, usnic acid reduces the proliferative capacity of human lung cancer and breast cancer cells. This could become a brand-new source for a naturally occurring, non-genotoxic anticancer drug. Usnic acid can be a potent hepatotoxic agent against monogastric murine hepatocytes because it blocks the electron transport chain in mitochondria and generates oxidative stress in cells (Mayer et al., 2005). Usnic acid had anti-proliferative effects on endometrial carcinoma (HEC-50) and human leukaemia cells (K562), thus proving it to have anti-inflammatory activity (Ingólfsdóttr, 2002). Also, usnic acid is an antipyretic against lipopolysaccharide-induced fever (Okuyama et al., 1995). Another compound, depsidone pannarin, isolated from lichen, inhibited cell development and led to apoptosis of human prostate cancer and human melanoma M14 cells (Russo et al., 2008).

Lichen is the source of anticancer drugs, and lichen metabolites are potentially used for anticancer activity either as a crude extract or purified form of different lichen compounds and applied in pharmaceutical applications (Fig. 1) (Nugraha et al., 2021). Additionally, lichen extracts may reduce inflammation by limiting the number and migration of white blood cells (Jain et al., 2016). Protolichestrinic acid is a highly aliphatic compound derived from the poly acetyl chain obtained by *Cetraria islandica*, *Everniastrum cirrhatum* and *Everniastrum nepalense* having anti-proliferation activity on several cancer cells (Bessadóttir et al., 2014).

5. Ethnomedicinal uses of lichen

Lichens alone or their derived components are applied in the medical treatment of various diseases and are frequently used externally on wound dressings as a disinfectant or to halt bleeding. The edible lichens are widely used as a medicine for various diseases such as fever, cold, lung trouble, cancer, tuberculosis, etc. Edible lichen has been considered a medicine since the ancient period, and each edible lichen species has specific medicinal properties (Malhotra et al., 2012). The list of ethnomedical applications is listed in Table 3. They are often employed for treating mouth sores as well as skin infections and sores. Lichens are commonly consumed as a decoction to treat digestive or pulmonary disorders. Other lichen applications include obstetrics, gynaecological problems, and treating urinary tract disorders (Crawford, 2019a). *Cetraria islandica* treats acute respiratory diseases of the upper respiratory tract, throat and oral cavity inflammation, gastric and duodenal ulcers, stomach diseases, reduced acidity, general emaciation and weakness, and poor digestion and absorption after severe illnesses or operations. It also treats catarrhal infections and influenza (El-Darier & Nasser, 2021). Lichens such as *Parmelia sulcata* and *Lobaria pulmonaria* have been used to treat cranial and pulmonary disorders. Similarly, *Xanthoria parietina* treats jaundice (Bown, 1995).

E. cirrhatum is one of the familiar lichens used in Ayurveda and Unani medicine as 'Chharila' as aphrodisiac and carminative and is useful in dyspepsia, amenorrhoea, spermatorrhoea, calculi, stomach disorders, enlarged spleen, bleeding piles, diseases of blood and heart, soreness of throat, tooth-ache, scabies, excess salivation, leprosy, bronchitis and general pain (Chandra & Singh, 1971). Several lichen species are reported to efficiently treat various blood and heart ailments and dyspepsia, bronchitis, bleeding piles, scabies, and stomach disorders in many traditional medical systems worldwide, including the Indian system of medicine (V. K. Gupta et al., 2008). *C.* rangiferina treats colds, coughs, fever, jaundice, convulsion, constipation, arthritis and tuberculosis. They were also employed as a poultice to relieve arthritic joint pain (Perez-llano, 2020). Also, the lichens *Cladonia, Cetraria islandica* and *Lobaria pulmonaria* were known for treating pulmonary tuberculosis (Vartia, 1973). *Usnea longissima* was widely used as a dermatological aid for dressing wounds and treating gastric ulcers (Elečko et al., 2022).

Table 3
Ethnomedicinal uses of edible lichens.

Lichen species	Medicinal uses	References
Cladonia rangiferina	Treatment for colds, cough, fever, jaundice, convulsion, constipation, arthritis, and tuberculosis.	(Perez-llano, 2020)
Lobaria pulmonaria	Treatment for lung trouble and cranial disorder	(Perez-llano, 2020)
Bryoria fremontii	Used for antibacterial diseases	(Kaitera et al., 1996)
Bryoria fuscescens	Treatment for anti-inflammatory diseases	(Kaitera et al., 1996)
Cetraria islandica	To treat respiratory diseases, stomach disorders, ulcer, catarrhal illnesses and influenza	(El-Darier & Nasser, 2021)
Cetraria nivalis	Treatment for diabetes	(Perez-llano, 2020)
Everniastrum cirrhatum	Treatment for stomach disorders, enlarged spleen, bleeding piles, scabies, leprosy,bronchitis and tooth-ache	(Chandra & Singh, 1971)
Evernia prunastri	A remedy in folk medicine and cosmetic preservative	(Müller, 2001)
Everniastrum nepalense	To treat against diabetes, cough and tuberculosis	(Yonghang et al., 2019)
Parmotrema cetratum	Treatment for tuberculosis, skin diseases and diabetes.	(Yonghang et al., 2019)
Parmotrema perlatum	For lung and digestive ailments treatments	(Crawford, 2019b)
Parmotrema tinctorum	Used as a folk medicine	(Anjali, 2015)
	Treatment related to pulmonary and cranial disorders	(Bown, 1995)
Pseudevernia furfuracea	To treat respiratory problems and Wound healing	(Malhotra et al., 2012)
Rimelia reticulata	Treatment for lung disease, diabetes and jaundice	(Meera et al., 2009)
Usnea barbata	Strengthening of hair	(Perez-llano, 2020)
Usnea longissima	To treat gastric ulcer and wound dressing	(Odabasoglu et al., 2006; Thippeswamy et al., 2011)
Usnea pictoides	Healing wounds	(Abuzaid et al., 2020)
Ramalina condupulicans	Antiseptic	(Devkota et al., 2017)
Ramalina farinaceae	Antiseptic	(Devkota et al., 2017)
Umbilicaria esculenta	Inhibit phospholipase A2	(Zhao et al., 2021)
Xanthoria parietina	To treat jaundice	(Bown, 1995)

6. Lichen as food, feed and ingredient

The edible lichens are used in the food industry based on their purpose as food/feed/ingredient (Fig. 1). Lichens were considered food during World War II and used to treat the wounds of the affected people in the war. Lichen was the cheapest food readily available then, and *Cetraria islandica* was the first used for food purposes (Perez-llano,

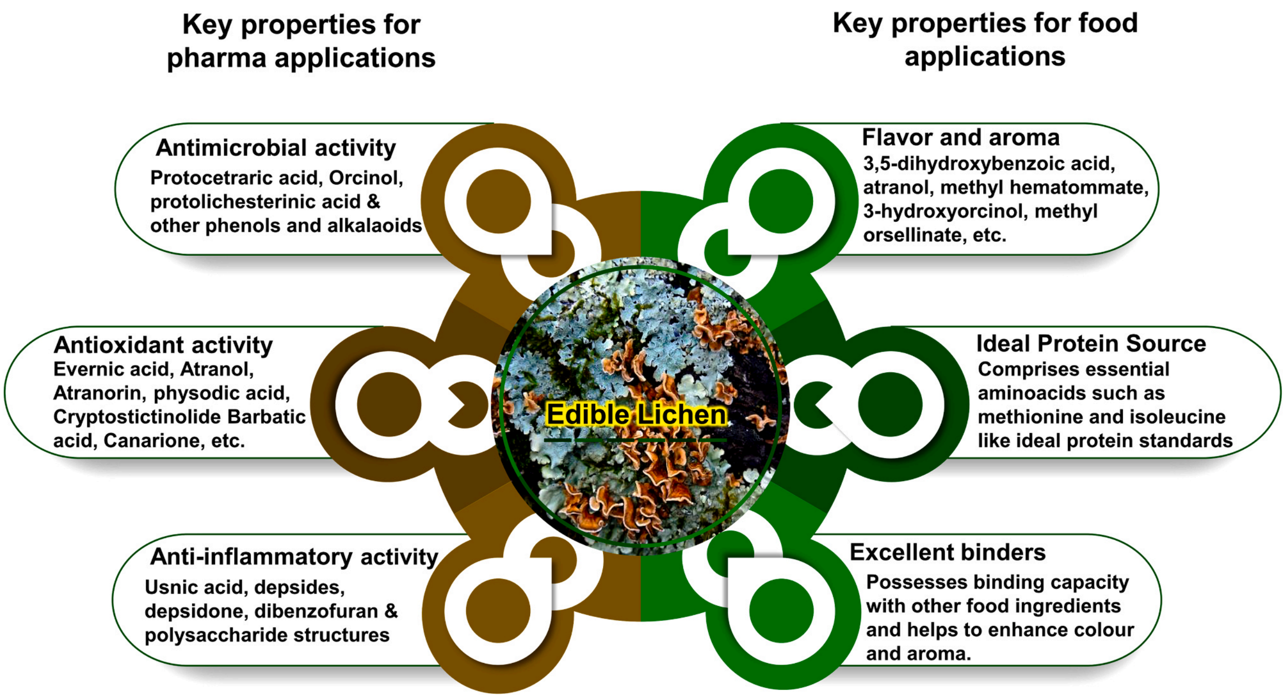

Figure 1. Major pharma and food applications of edible lichens.

2020). Some edible lichens, like sausage, soup, and salads, are directly taken as food. The edible lichens have glucans which increase nutritional values and have high carbohydrate and energy sources (Stuelp et al., 1999). Some edible lichens are highly digestive, which will be a good source of food in the winter season (Redzic et al., 2010). *C. islandica* is used as an emergency food after removing the toxic ingredients by boiling or by adding to the solution containing sodium carbonate base. *B. fremontii* is consumed as cooked thallus with berries, fish eggs, soups with other edible components, cookies and cakes, and Species of the Ramalinaceae family has high nutrition and trace element, which can be used with meat or pork. At the same time, *Umbilicaria esculenta* is regarded as a delicacy and sold as "iwa-take" or "rock mushroom" (Luo et al., 2010).

Usnea genus includes numerous fruticose-type lichens with tufted, filamentous appearance and flaccid nature. *Lobaria pulmonaria* is an edible lichen that can be consumed as a tea, aromatic drink, and laxative cream (Zhao et al., 2021). The secondary metabolite atranorin from several lichen species can be consumed as a tea, juice, sausage, porridge, soup, pickle, spice, and flavouring agent in food protocetraric acid is consumed as soup or sausage and ingredient in bread (Tay et al., 2004). *Dermatocarpon miniatum* and *Cladina rangiferina* are added to soups and salads, and *Everniastrum nepalense* is cooked with meat (Huang et al., 2018). *Cetraria islandica* and *Cetraria nivalis* are mixed with grain, boiled with a surplus of water to produce a broth, and consumed as porridge (Yusuf, 2020). *Cetraria islandica* is usually soaked in lye water or ash water for several days after removing the lower parts and then boiled, rinsed, dried, ground, and mixed with the flour to make bread, gruel and jelly (Ivanova & Yaneva, 2020). *Cladina rangiferina* and *C. islandica* are employed in bread making, and *Evernia prunastri* are used as fermentative agents (Perez-llano, 2020). *U. florida* is the most prevalent species of the genus Usnea possessing sufficient nutrients, including highly rated vitamin C and is also used to make tea mixture. Another important aspect of edible lichen application is its suitability for fermentation to produce alcohol. Reports were available on the alcoholic fermentation of lichen powder (*Cetraria islandica*) comparable to plants (Upreti et al., 2005). *Ramalina fraxiea, Cetraria islandica, Bryoria spp.,Cladonia rangiferina, Anaptychia ciliaris* and *Usnea florida* are used in brandy making, and *Lobaria pulmonaria* is used as hops in beer making (Ivanova & Ivanov, 2009). The purpose material of edible lichen with their application is listed in Table 4.

Cladonia rangiferina is a member of the Cladoniaceae family that thrives in both hot and cold climatic conditions, and it is a light-coloured fruticose form. It can be used as feed for animals, particularly for reindeer, and is also known as deer moss, reindeer lichen, caribou moss, or grey reindeer moss. *Cetraria islandica* is fodder for cattle and pony, and *Evernia prunastri is* used as food for the rabbits. The Bryoria genus includes about 23 species, including *Bryoria fremontii,* also known as "wila," a dark brown, hair-like, hanging lichen (Esslinger Theodore, 2004). *B. fremontii* is an alternate food source for cattle and other pet mammals.

Similarly, most edible lichens are used in food products to enhance flavor and aroma. In the food industry, it has also been observed that *C. islandica* is used as a spice and food decorative ingredient (Yusuf, 2020). Parmeliaceae species is a foliose type of lichen and are primarily used as an ingredient in food like spice or flavoring compound having sufficient minerals for high nutritional properties (Rakesh & Dileep, 2013). The lichen species *Parmotrema tinctorum* and *Platismatia glauca* is widely used as spice and flavouring agent, and *Parmotrema perlatum* is used as an aromatic agent to enhance the sensory attributes of food (Hawksworth, 2004). *Pseudevernia furfuracea* is a well-known foliose lichen used commercially as a preservative in food and herbal preparations, spice blends, and culinary preparations like curries (Aoussar et al., 2017). *Ramalina subcomplanata* and *Rimelia reticulata* is commercially used as spice and flavouring agent for meat and vegetables in different states of India (Upreti et al., 2005). *Cetraria ericetorum* is a flavouring agent in many soups (Ivanova & Ivanov, 2009).

7. Other major applications

7.1. Allelopathic effects

Lichens can potentially prevent or significantly slow the growth of higher plants. Lichen secondary metabolites can act as allelopathic agents called allelochemicals, affecting the growth and development of nearby algae, lichens, mosses, vascular plants and microbes (Goga et al., 2017). Vulpinic and evernic acids have been found to significantly

Table 4
Application of edible lichens.

Lichen species	Food	Feed	Ingredient	Application	References
Cladonia rangiferina	-	+	-	Food for animals	(Perez-llano, 2020)
Lobaria pulmonaria	+	-	+	Tea or aromatic drink	(Odabasoglu et al., 2004)
Bryoria fuscescens	-	-	+	Making bread	(Culberson, 2002)
Bryoria fremontii	+	+	-	Cookies and cakes, cooked thallus, fish eggs, soup and porridge	(Kirkpatrick et al., 2001)
Cetraria islandica	+	+	-	Feed for cattle and ponies, spice and food decorative	(Yusuf, 2020)
Cetraria nivalis	-	-	+	Porridge	(Llano, 1948)
Everniastrum cirrhatum	-	-	+	Bread making or mix with wheat flour	(Devkota et al., 2017)
Evernia prunastri	-	+	+	Feed for rabbit and bread making	(Perez-llano, 2020)
Everniastrum nepalense	-	-	+	Pickles, curry, soup and sausages	(Devkota et al., 2017)
Parmotrema cetratum	-	-	+	Mixed with wheat flour and barley	(Devkota et al., 2017)
Parmotrema perlatum	-	-	+	Aromatic agent in food	(Hawksworth, 2004)
Parmotrema tinctorum	-	-	+	Flavoring agent and spice for food	(Ekka, 2011)
Rimelia reticulata	-	-	+	Flavoring agent	(Upreti et al., 2005)
Usnea pictoides	-	-	+	Spices	(Emsen et al., 2018)
Usnea florida	+	-	+	Tea mixture	(Yusuf, 2020)
Heterodermia tremulans	-	-	+	Spices and flavoring agent in meat and vegetables	(Upreti et al., 2005)
Ramalina condupulicans	+	-	-	Stir fried pork dish	(Luo et al., 2010)
Ramalina farinaceae	+	-	-	Cook and mixed with various food	(Hanuš et al., 2008)
Umbilicaria esculenta	+	-	+	Chocolate and pastry, mushroom	(Upreti et al., 2005)
Umbilicaria mammulata	+	-	-	Porridge, salad and bread	(Upreti et al., 2005)

suppress the ascospore germination of the crustose lichens *Caloplaca citrine* and *Graphis scripta*, while (−) usnic acid inhibits the green alga Chlamydomonas growth (Whiton & Lawrey, 1984). Evernic and squamatic acids, and 4-O-methylated depsides inhibited spore germination and protonemal growth in three common moss species like *Ceratodon purpureus*, *Funaria hygrometrica*, and *Mnium cuspidatum* (Armstrong & Welch, 2007). Some lichen metabolites, including barbatic acid, diffractaic acid, evernic acid, lecanoric acid, b-Orcinolcarboxylic acids, osrsellinic acids, and 4-ODemethylbarbatic acid, have potent allelochemical effects on higher plants (Pyatt, 2009).

7.2. Pollution tolerance and effect on metals

Air pollution is a major problem in today's technological world because of the population, which can cause diseases. The air quality of the environment may vary based on the surrounding and climatic conditions. Bio monitors generally use an organism to check environmental conditions and factors. Interestingly, lichen can be used as a bioindicator to determine the air quality in the environment (S. Gupta et al., 2016). Lichens monitor environmental factors in many countries because `they can easily adsorb heavy metals in the air (Vijay et al., 2021). *Usnea* sp. is a good air-quality biomonitor that can effectively accumulate heavy metals. Arsenic can be efficiently accumulated by *Usnea barbata* and mulate fluorides, which can inactivate the pigments (Conti et al., 2012). The lichens can be used to evaluate the air quality in the environment (S. Gupta et al., 2016). *Parmotrema tinctorum* is one of the edible lichens which has the activity of reducing air pollutants like SO_2, and NO_2 (González-Burgos et al., 2019).

The behaviour of methyl, inorganic, and elemental mercury in terms of sorption and desorption on *Parmelia sulcata* indicates that this lichen can also be employed as a sorbent material for the removal of inorganic and methyl mercury from aqueous solutions (Balarama Krishna et al., 2004). *Lobaria pulmonaria* is a major lichen that can be used as a bioindicator of air quality, and it can maintain monitoring for an extended period (Nascimbene et al., 2010). These lichens can also determine the pollution in the air and environment of forest areas (Loppi & De Dominicis, 1996). Each lichen species has different adaptability; some species can grow under pollution (S. Gupta et al., 2016). Lichen growth will adversely affect if the air's sulphur dioxide concentration exceeds 30 µg/m3 (Casale et al., 2015). *Lobaria pulmonaria, Usnea* sp., and *Parmelia* sp. can grow clean, whereas *Cladnia* sp. can also survive in a polluted area (Nascimbene et al., 2010). *P. reticulatum* is a biomonitoring air pollutant by extending the elemental composition of pollutant sources and can act as a biomonitor to detect the contaminant occurring in the environment (Boonpeng et al., 2017). These lichens can be used predominantly and replaced by detectors or other equipment to evaluate the changes in the locality. Thus, the pollution of air and emission of chemicals from industries can be determined by lichen species.

7.3. Lichen nano particles

Studies have shown that various lichen species can create distinctive nanoparticles with different forms, sizes, and physicochemical and biological activity (Table 5) & (Fig 2). *P. tinctorum* was able to produce Ag nanoparticles from silver nitrate in an efficient and environmentally benign manner. These nanoparticles are notable for their spherical form, excellent stability and average diameter of 15.14 nm (Khandel et al., 2018). *Usnea longissima* used for synthesis of Ag nanoparticles showed good antimicrobial activity against *Streptococcus mutans, Streptococcus viridans, Streptococcus pyrogenes, Staphylococcus aureus, Corynebacterium xerosis* and *Corynebacterium diphtheria* and *Escherichia coli, Pseudomonas aeruginosa* and *Klebsiella pneuomoniae* (Yashwant et al., 2023). *Cetraria islandica* extract was used as a stabilizing and reducing agent to prepare Ag monometallic and Ag-Au bimetallic nanoparticles (Çlplak et al., 2018). Silver nanoparticles were biosynthesized from AgNO3 using the lichen extract *Cetraria islandica,* with the nanoparticle's diameter ranging from 5 nm to 29 nm. Response surface methodology showed that as reaction time and the $AgNO_3$/lichen ratio increased, particle size decreased while temperature increased, resulting in larger particles (Yildiz et al., 2014). Another study proved that silver nanoparticles synthesized from *Cetraria islandica* showed good antibacterial activities (Baláž et al., 2020). According to studies, iron oxide nanoparticles with particle sizes ranging from 31.74 to 53.91 nm and spherical in form were synthesised from the extract of *Ramalina sinensis* using the co-precipitation method. The visible UV spectra for the iron oxide nanoparticles showed a peak in the range of 280–320 nm and the nanoparticles were efficient antibacterial agents against *Pseudomonas aeruginosa* and *Staphylococcus aureus* (Safarkar et al., 2020).

Goga et al., 2021 carried out extracellular reduction of ferric chloride salts into Fe_3O_4 nanoparticles using *R. sinensis* and a sharp absorption peak was seen in the 300 and 350 nm range. The biomolecules in *R. sinensis* prevent the agglomeration of nanoparticles, and the polysaccharide sulphate functions as a potent reducing agent, where sulphate groups play important roles in the extracellular synthesis of Fe_3O_4 nanoparticles by oxidising the aldehyde group into carboxylic acids (Arjaghi et al., 2021). Using *Lobaria pulmonaria* and *Pseudevernia furfuracea*, silver nanoparticles were synthesized with an average size of

Table 5
Lichen as nanoparticles.

Lichen species	Nanoparticle	Activities	References
Cetraria islandica	Ag and Au	Catalytic activity	(Çlplak et al., 2018)
Cetraria islandica	Ag	Antibacterial actions	(Baláž et al., 2020)
Cladonia rangiferina	Ag	Antibacterial activity	(Rai & Gupta, 2019)
Evernia prunastri *Lobaria pulmonaria* *Ramalina farinacea*	Ag	Antioxidant, Antibacterial and Anti acetylcholinesterase activities	(Mariem Ben Salah et al., 2022)
Lobaria pulmonaria	Ag	Antioxidant and Antibacterial activity	(Goga et al., 2021)
Parmelia perlata	Ag	Antioxidant, Antimicrobial, Antidiabetic and Antitumour agents	(Manojlović et al., 2021)
Parmelia sulcata	Ag	Anticancer activity	(Dhanesh et al., 2021)
Parmotrema tinctorum	Ag	Antimicrobial agent	(Khandel et al., 2018)
Pseudevernia furfuracea	Ag	Antioxidant and Antibacterial activity	(Goga et al., 2021)
Pseudevernia furfuracea *Usnea florida*	Ag and Zno	Neuroprotection	(Koca et al., 2022)
Ramalina dumeticola	Ag	Antibacterial activity	(Biomimetik et al., 2015)
Ramalina fraxinea	ZnO	Protection against neuropsychiatric diseases	(Koca et al., 2019)
Ramalina sinensis	Fe_3O_4	Prevent the agglomeration of nanoparticles, polysaccharide sulphate functions as a strong reducing agent and antibacterial agent	(Arjaghi et al., 2021)
Ramalina sinensis	Fe_3O_4	Antibacterial activity	(Safarkar et al., 2020)
Usnea longissima	Se	Antioxidant activities	(Kosanić et al., 2018)
	Ag	Antibacterial activity	(Yashwant et al., 2018)

10 nm using solid-state mechanochemical synthesis (Goga et al., 2021). *Ramalina fraxinea* extract synthesized ZnO nanoparticles, and it has been shown effective in treating neuropsychiatric disorders, particularly neurodegenerative disorders (Koca et al., 2019).

Nano silver was synthesized from the extract *Parmelia sulcata* and was toxic against cancer cells (MCF-7) but not normal cells (NIH3T3). *Ramalina dumeticola* with silver nanoparticles efficiently suppressed the growth of Gram-negative bacteria. Moreover, the downregulation of cell cycle genes (PCNA and Cyclin-D1), as well as inflammatory genes (TNF-alpha and IL-6), promoted the intrinsic apoptotic pathway (Dhanesh et al., 2021). According to the findings, silver nanoparticles from *Parmelia sulcata* can effectively destroy cancer cells and serve as a different medicinal agent for cancer treatment (Dhanesh et al., 2021). Lichens have been proven to be an effective capping and reducing agent for nanoparticles due to their immense abundance, rapid development, and capacity to persist in the environment. The functional groups of the secondary metabolites derived from lichen extracts are crucial in avoiding nanoparticle aggregation and enhancing nanoparticle production and stabilisation (Çlplak et al., 2018).

7.4. Lichen polysaccharides

Generally, it is assumed that lichen polysaccharides of high production, such as α-glucans, β-glucans and galactomannans, are of fungal origin. Studies on the polysaccharide content of various lichen mycobionts and phycobionts revealed that the mycobiont produced polysaccharides identical to those of the parent lichen phycobiont had distinct polysaccharides (Olafsdottir & Ingólfsdottir, 2001). A combination of lichenan and isolichenan was derived from *Cetraria islandica,* and it was the first polysaccharide fraction from a lichen species. *Umbilicaria esculenta* produces two different kinds of polysaccharides, one composed of mannose, glucose, rhamnose and galactose with a molecular weight of 124.7 kD, while the other consisting of mannose and glucose of 249.4 kD and both polysaccharides have a significant preventive effect on thrombosis (Wang, Shu et al., 2018). Also, three main polysaccharides were isolated from the lichenized fungus *Umbilicaria mammulata*: laminaran, pustulan and galactofuranomannan (Carbonero et al., 2006).

Galactoglucomannans with a (1−6)-linked main chain were isolated from the mycobiont of several Parmotrema species, including *Parmotrema tinctorum*, *Rimelia cetrata* and *Rimelia reticulate* (Carbonero et al., 2005). A neutral rhamnose-containing glucogalactomannan polysaccharide with a molecular weight of 7.86×10^4 Da was isolated from *Usnea longissima,* and it boosted the antioxidant levels in the mice's liver and intestine by 20–50% after intragastric injection (Wang et al., 2021). When extracted using the Fehling precipitation method, *E. prunastri* has been found to have a galactomannan that contains galacturonic acid (Teixeira et al., 1994). An immunologically active complex polysaccharide called thamnolan consisting of rhamnopyranosyl and galactofuranosyl units have found to be present in the water extract of the lichen *Thamnolia subuliformis* and can be isolated using ethanol fractionation, ion-exchange chromatography, preparative GP-HPLC, dialysis and gel filtration (Olafsdottir et al., 1999). Thus, polysaccharides from many other lichen species have been isolated and characterized, the majority of the lichen species that have been studied so far produce significant amounts of polysaccharides, up to 57%, and many of them have been found to have a biological activity such as antitumor, immunostimulant, antiviral etc. (Gorin et al., 1991).

8. Challenges and the way forward

Evidence-based knowledge of edible lichens for food applications may total 15 – 40 (Yang et al., 2021; Zhao et al., 2021). However, because lichens are already part of the human diet in many countries, the selection of lichen species, processing methods, and safety aspects of lichens need careful interventions and strategies. Moreover, the in-vitro and clinical studies supporting the health benefits and mechanism of action of lichen substances are insufficient, and more focus is required on accurately identifying their biological activities. Furthermore, attention to lichen polysaccharides and their nanoparticle applications holds great promise for new food and pharma applications, constituting a valuable future resource.

Practising edible lichen as a regular diet is beneficial for the health and the planet as a sustainable resource. Moreover, since the price projections of conventional animal proteins increase and plant food resources are depleting, innovations that exploit and validate lichens' safety will pave the way for its role as a future food source. With increasing urban populations, one daunting challenge for food scientists would be consumer acceptability. Observing the global demand for vegan protein-rich food and rising health consciousness, it is necessary to create market awareness of the benefits of consuming lichens from nutritional and environmental perspectives. Meanwhile, mass-rearing techniques that produce safe and stable lichen biomass must be developed. Regulatory frameworks and interdisciplinary collaborations of ecology, taxonomy, pharmacology, and biology are required for the cost-effective, reliable production of high-quality edible lichens.

9. Conclusions

Edible lichens are increasingly becoming a popular research topic in food and pharma applications, particularly recognizing their abundant nutrients and unique biochemical substances. This review reported the key beneficial characteristics of lichens, such as antimicrobial, anti-

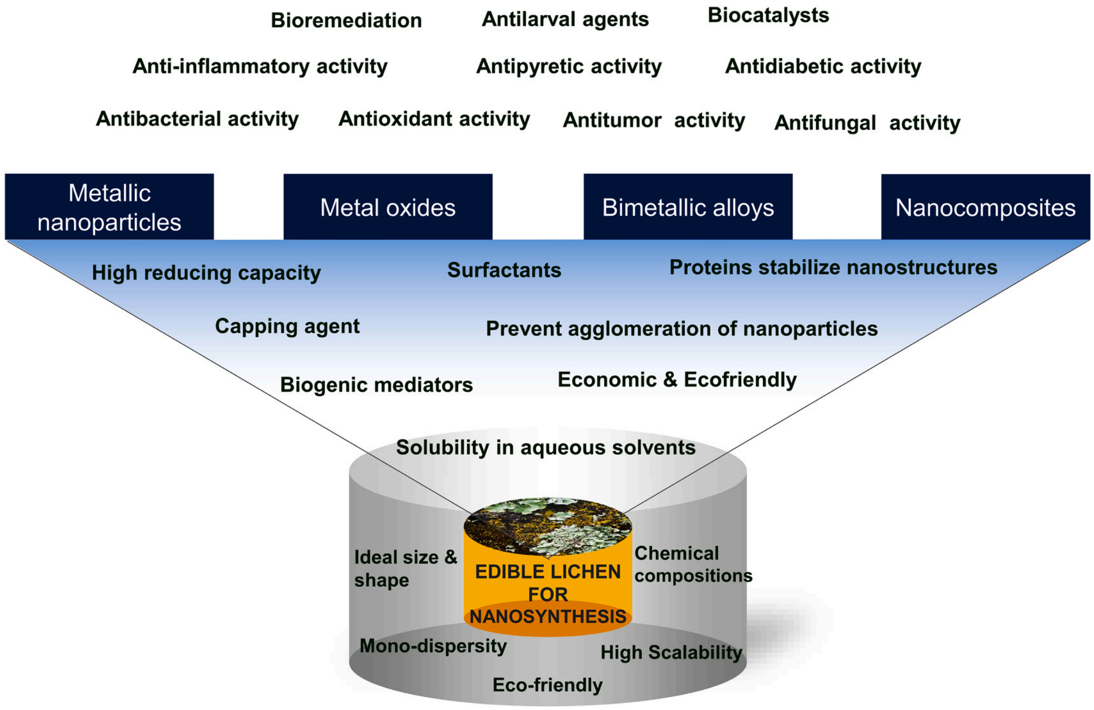

Figure 2. Lichen as a ideal nanoparticle synthesis matrix.

oxidation, and anti-inflammatory activities. However, the major problems in consuming edible liches, such as toxic secondary compounds and undigestible polysaccharides, need careful interventions. Therefore, a clear understanding of edible lichens and their clinical applications is essential to include them in our regular diet and pharmaceutical preparations.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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