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Lichens are the next promising candidates for medicinally active compounds

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Abstract

Biochemical research of lichens went through "exponential" development in recent past only. Lichenized fungi occur in a wide range of habitats from arctic to tropical regions, from the plains to the highest mountains and from aquatic to xeric conditions. Lichens can be found on or within rocks, on soil, on tree trunks and shrubs, on the surface of living leaves, on animal carapaces, and on any stationary, undisturbed man-made surface such as wood, leather, bone, glass, metal, concrete, mortar, brick, rubber, and plastic. Lichens are able to survive in extreme environmental conditions; they can adapt to extreme temperatures, drought, inundation, salinity, high concentrations of air pollutants, and nutrient-poor, highly nitrified environments, and they are the first colonizers of terrestrial habitats (pioneers). In addition, both fungal and algal cells in the lichen thallus are known for their ability to survive in space too. Lichens produce a great variety of secondary metabolites, and most of them are unique to lichen-forming fungi. These chemically diverse (aliphatic and aromatic) lichen substances have relatively low molecular weight. Approximately 1050 secondary compounds have been identified to date. Traditionally many of the lichen have been used to treat a number of ailments. Hence these are the promising candidates for futuristic pharmacological research.

Keywords: Lichen, Secondary Metabolites, Xeric Condition, Pioneers.

1. Introduction

Lichens are symbiotic plant-like organisms, usually composed of a fungal partner, mycobiont, and one or more photosynthetic partners, phytobiont, most often either a green alga or cyanobacterium. Although the dual nature of these lichens is now widely recognized and lichen products have been used in traditional medicine for centuries, they are less studied and understood than the single microorganisms. Lichen species comprise more than 20% of the global fungal biodiversity and as unique symbiotic organisms that occur in some of the most extreme environments on Earth-arctic tundra, hot deserts, rocky coasts, toxic slag heaps, etc. The substances that lichens produce to survive in these extreme environments are also unique but little understood. As our understanding of the bio-regulatory role of different endogenous biomolecules and their mechanism of action develops, more attention is drawn to lichens as a promising source for drug discovery [1]. Although bioactive phenolic compounds with new chemical structures of pharmaceutical interest have been recently reported, most research effort has been focused on the discovery of new lichen species and lichen taxonomy, and despite recent progress, only usnic acid has been used for pharmaceutical and cosmetic product development to date [2].

This review is intended to summarize the past and current research and development trends in the characterization and use of lichens and their bioactive compounds in traditional medicine and other biopharmaceutical applications of commercial interest.

2. Lichen Compounds and Traditional Biomedical Uses

Many lichens are known to produce unique secondary metabolites and have considerable biological activities. Many lichens are edible; however, some lichens contain toxic substances. The lichen compounds may be classified into the following groups: (i) aliphatic lichen substances (including acids, zeorin compounds, polyhydric alcohols); (ii) aromatic lichen substances (including pulvic acid derivatives, depsides, depsidones, quinones, xanthone derivatives, diphenyleneoxide derivatives, nitrogen containing compounds, triterpenes, tetronic acids); and (iii) carbohydrates (polysaccharides). To date, the chemistry of about a third of all lichen species has been studied and about 350 secondary metabolites have been identified. The chemical structures of approximately 200 of them have been established.

Lichen's secondary metabolites are usually insoluble in water and can be extracted into organic solvents. They amount to between 0.1 and 10% of the dry weight of the thallus, sometimes up to 30% [3]. These substances have been mostly identified as lactones (e.g., protolichessterinic acid), phenolic compounds (e.g., atranol and resorcinol), depsides (e.g., diffractic acid), pulvinic acid derivative (e.g., vulpinic acid), dibenzofurans and usnic acids (e.g., usnic acid). In addition, other lichen substances like atranorin, stictic acid, lecanoric acids and pannarin have been frequently studied [4].

Although lichens have been used for medical purposes since ancient times, information on the edible and medicinal uses of lichens is scattered. The medicinal use of lichens can be traced back to the 18th dynasty (1700–1800 BC) when *Evernia furfuracea* (L.) Mann or (Parmeliaceae) was first used as a drug. Some lichens were claimed to be good for coughs, jaundice, rabies and restoring lost hair. Herbal medicine texts made account of several species of lichens including *Cladonia, Evernia, Lobaria, Parmelia, Peltigera, Pertusaria, Physica, Rocella, Usnea* and *Xanthoria*. During the middle age, lichens figured prominently in the herbals used by practitioners. However, lichens have been essentially overlooked to a great extent by the modern pharmaceutical industry, despite all the evidence of biological activity in lichen extracts provided in literature. Decoction of *Pseudoevernia furfuracea* (L.) Zopf. (Parmeliaceae) is used in Alfacar and Viznar in respiratory ailments. *Ramalina bourgeana* Mont. ex Nyl. (Ramalinaceae) is consumed for diuretic and stone dissolving (lithontriptic) properties [5].

The lichen *Xanthoparmelia scabrosa* (Taylor) Hale (Parmeliaceae) is an ingredient in various aphrodisiac formulations sold on the international market. Traditionally, *Cetraria islandica* (L.) was used to treat mild inflammation of the oral and pharyngeal mucosa, dyspepsia, and loss of appetite. In the European folk medicine, *Cetraria islandica* (L.) was used in cancer treatment [6].

Reindeer lichens such as *Cladonia rangiferina* (L.) F. H. Wigg. syn. *Cladina rangiferina* (L.) Nyl. (Cladoniaceae) were commonly used to treat colds, arthritis, fever as well as jaundice constipation, convulsions, coughs, and tuberculosis. Three *Parmelia* sp. are contained in the Indian drug chharila used as aphrodisiac. In India, *Parmelia chinense* finds applications as diuretic and as liniment for headache and powder to heal wounds, whereas the Tinea (ringworm) like disease is treated with *Parmelia sanctiangeli*. *Parmelia peforatum* is medically recognized in Afghanistan. *Parmelia nepalense* (Talyor) Hale ex Sipman is used in Nepal for treatment of toothache and sore throat. In the Western Himalayas, *Thamnolia vermicularis* (Schwartz) Ach. (Icmadophilaceae) is used as antiseptic. In Sikkim (India), *Heterodermia diademata* (Talyor) D.D. Awas., (Physciaceae) was used for cuts and wounds. Several reviews have discussed the pharmaceutical potential and biological activities of lichen substances [7]. Many countries have developed commercial pharmacological products based on lichen substances. For instance, usnic acid was used in anticeptic products in Germany (Camillen 60 Fudes spray and nail oil) and Italy (Gessato™ shaving). However, at high doses, usnic acid has been shown to exhibit toxic effects (acute oral toxicity, LD_{50} of 0.84 g/kg) and fatal hepatotoxicity (500 mg/day of usnic acid) in mice. Icelandic lichens were marketed in cold remedies formulation by the trade names of Isla-MoosR (Engelhard Arzneimittel GmbH & Co. KG, Germany) and Broncholind.

3. Biological activities of lichens

Lichens produce a wide array of biologically active primary (intracellular) and secondary (extracellular) metabolites. Primary metabolites include amino acids, polyols, carotenoids, polysacharids and vitamins. Some, like the polysaccharide cell wall compounds lichenan and isolichenan, have taxonomic significance. Carotenoid compounds have also been intensely studied for dues to evolutionary relationships. Lichen's secondary metabolites, often called lichen acids, are produced primarily by the mycobiont, secreted onto the surface of lichen's hyphae either in amorphous forms or as crystals.

Past and current studies show that lichen's secondary metabolites exert a wide variety of biological activities that include antibiotic, antimycobacterial, antiviral, anti-inflammatory, analgesic, antipyretic, plant growth inhibitory, antiherbivore, enzyme inhibitory, antiproliferative and cytotoxic effects.

3.1 Antibacterial activity

Historically, Burkholder [25] has first pioneered research on lichens as antibacterial agents. One of the most frequently reported lichen-derived products with a strong antimicrobial activity is usnic acid. Usnic acid, evernic acid and vulpinic acid inhibited the growth of the Gram-positive bacteria *Staphylococcus aureus, Bacillus subtilis* and *Bacillus megaterium*, but had no affect on the gram negative bacteria *Escherichia coli* or *Pseudomonas aeruginosa*. Acetone, chloroform, diethyl ether, methanol and petroleum ether extracts of *Parmelia sulcata* containing salazinic acid demonstrated antibacterial activity against *Aeromonas hydrophila, Bacillus cereus, Bacillus subtilis, Listeria monocytogenes, Proteus vulgaris, Yersinia enterocolitica, Staphylococcus aureus, Streptococcus faecalis, Candida albicans* and *Candida glabrata* [8]. Diethyl ether, acetone and ethanol extracts of *Cetraria aculeate* contained protolichesterinic acid with promising antibacterial activity against nine bacteria belonging to Gram-positive and Gram-negative groups. Most of the antibacterial activities were tested on *Bacillus, Pseudomonas, E. coli, Staphylococcus aureus, Kleibsiella, Candida, Salmonella, Yersinia* and *Proteus* sp. [9].

Table 1: Antibacterial activity of lichen species against Gram-positive bacteria

Lichen Test	Active Compound Values	Microbes
Everniastrum cirrhatum	Atranorin, Protolichesterinic acid, Salazinic acid	*Bacillus cereus*
Cladonia foliacea	Usnic acid, Atranorin, Fumarprotocetraric acid	*B. licheniformis*
Everniastrum cirrhatum	Atranorin, Protolichesterinic acid, Salazinic acid	*B. subtilis*
Cladonia crispatula	Depsides, Usnic acid	*Mybobacterium smegmatis*

3.2 Antifungal activities of lichens

The acetone and methanol extracts of *Lasallia pustulata* (L.) Meret. (Umbilicariaceae), *Parmelia sulcata* Taylor and *Umbilicaria crustulosa* (Ach.) Frey (Umbilicariaceae) manifested a very selective antifungal activity. Usnic acid together with isodivaricatic acid, 5-propylresorcinol, and divaricatinic acid were identified as antifungal agents. Petroleum ether extracts of *Parmelia sulcata* containing salazinic acid demonstrated antifungal activity against *Aspergillus niger, Aspergillus fumigatus*, and *Penicillium notatum* [10].

Table 2: Antifungal activity of lichen species

Lichen Test	Active Compound Values	Microbes
Lecanora frustulosa,	Divaricatic acid, Zeorin	*Penicillium verrucosum*
Cladonia furcata	Fumarprotocetraric acid	*Aspergillus flavus*
Everniastrum cirrhatum	Atranorin, Protolichesterinic acid, Salazinic acid	*Botryosphaeria dothidea*
Evernia prunastri, Hypogymnia physodes, Cladonia portentosa	Lichenic acid	*Stagonospora nodorum*

3.3 Antiviral activities of lichens

Antiviral properties have been attributed to various lichen substances. Anthraquinones, especially the polyphenolic and/or polysulphonate substituted types, have been shown to exhibit potent antiviral properties [11]. Cohen *et al*, isolated anthraquinones, bianthrones and hyperacin derivatives from lichens whose antiviral activities were positively correlated with an increasing substitution of chlorine in the anthraquinone structure. It is plausible to suggest that that inhibited symptom development and virus accumulation in four greenhouse-grown *Nicotiana* spp. infected by a tobacco mosaic virus [11,12]

3.4 Anticancer activities of lichens

Some lichen substances like usnic acid, cristazarin, protolichesterinic acid, polyporic acid, depsidone and lichenin have been investigated for antitumor effects on tumor cells-melanoma B-16, P388 leukaemia, K-562 leukaemia, Ehrlich solid tumor and lymphocyte [13] cells. *In vitro* anticancer activities of lichen extracts have been evaluated according to the cell proliferation assay in three cancer cell lines: human pancreatic (PANC-1), prostate (DU-145) and breast (MCF7) cancer cell lines. Usnic acid exhibited an antiproliferative effect on human leukemia cells (K562) and endometrial carcinoma (Ishikawa, HEC-50) cells. A lichen-derived polysaccharide CFP-2 reduced the viability of HL-60 and K562 cells due to apoptotic pathway and telomerase activity, suggesting its possible therapeutic potential against cancer. Protolichesterinic acid isolated from *Cetraria islandica* L. (Ach.) inhibited growth of malignant cell lines. Antiproliferative effects of several lichen compounds in human platelets were ascribed to their inhibitory activities on 12(S)-HETE which plays role in carcinogenesis and metastasation.

Zeytinoglu *et al* [2] reported genotoxic/ antigenotoxic and cytotoxic activities of extracts from *C. aculeata* in bacterial and mammalian cell systems. Pannarin inhibited cell growth and induced cell death in human prostate carcinoma DU-145 cells. The orcinol derivatives, tenuiorin and methyl orsellinate, present in extracts of

Peltigera leucophlebia (Nyl.) Gyeln (Peltigeraceae), exhibited *in vitro* inhibitory activity against 15-lipoxygenase from soybeans. On this account, tenuiorin and methyl orsellinate were further tested for antiproliferative activity on cultured human breast, pancreatic and colon cancer cell lines. Bianthraquinone glycosides, colleflaccinosides isolated from *Collema flaccidum* (Ach.) Ach. (Collemataceae), collected in Israel and Russia, were reported to have antitumor activity [14].

3.5 Anti-insecticidal activities of lichens

Killing larvae of mosquitoes is a successful way of minimizing mosquito population in breeding grounds before they reach adult stage. The most commonly used insecticidal agents are currently based on synthetic chemicals; however, their repeated use has been reported for widespread development of chemical resistance and public concern over possible health problems associated with food and environment. Phytochemicals contain many bioactive ingredients which offer an alternative source of insect control agents and that have little or no harmful effect on non-target organisms and the environment. It is observed that the methanol extract of *R. conduplicans* was active against mosquito larvae [15]. Extracts from lichen *Letharia vulpine* showed potent insecticidal activities against *Spodoptera ornithogalli* and *S. littoralis*. Bioassays with (−)- and (+)-usnic acids against larvae of *Culex pipiens* revealed that the LC50 values were 0.8 and 0.9 ppm, respectively [16].

3.6 Enzyme inhibition activities of lichens

Lichen substances like usnic acids, resorcinol derivatives and atranorin were found to be potent enzyme inhibitors of ornithine decarboxylase and arginine decarboxylase that affect the polyamine metabolism. Atranoin (from *Psedevernia furfuracea*) and resorcinol (from *Protousnea* spp.) were reported for trypsin and tyrosinase inhibition, respectively. Inhibition of tyrosinase (for melanin biosynthesis) and xanthine oxidase (for hyperuricaemia) with lichen extracts were reported by various researchers. Tyrosinase or polyphenol oxidase (monophenol, odiphenol: oxygen oxidoreductase; EC 1.14.18.1) is a copper enzyme that catalyzes two different reactions using molecular oxygen: the hydroxylation of mono-phenols to *o*-diphenols (monophenolase activity) and the oxidation of the *o*-diphenols to *o*-quinones (diphenolase activity). This enzyme is widely distributed in plants, microorganisms and animals where tyrosinase is responsible for melanization. In humans, the melanization is influenced by several mechanisms such as anti-oxidation, direct tyrosinase inhibition, melanin inhibition of migrated cells and hormonal activities. Tyrosinase inhibitors have been frequently used in cosmetics as depigmenting agents for hyper pigmentation.

A concerted effort has been made to search for naturally occurring tyrosinase inhibitors from various organisms, many of them being largely free from harmful adverse effects [17].

3.7 Antioxidant activities of lichens

Many lichen extracts have been reported for antioxidant properties due to their phenolic content. Antioxidant agents inhibit and prevent reactive oxygen species, which can cause degenerative diseases. Natural antioxidants are preferred over many synthetic antioxidants, which can be toxic, for therapeutic applications. Jayaprakasha and Rao [20] examined the antioxidant properties of methyl orsellinate, atranorin, osellinic acid and lecanoric acid. Bhattarai *et al* reported stronger antioxidant activities in extracts from Antarctic lichens than from lichens native to temperate or tropical regions. Phenolic constituents from the lichen *Parmotrema stuppeum* (Nyl.) Hale (Parmeliaceae) including methyl orsenillate, orsenillic acid, atranorin and lecanoric acid showed moderate antioxidant activity. An animal study reported antioxidant activities of lichen *Cetraria islandica* [18, 19].

4. Other uses of lichens

4.1 Industrial Uses of Lichens Brewing and Distilling

Use of lichens instead of hops for the brewing of beer has been mentioned as having occurred in one or more monasteries of Russia and Siberia which had a reputation of serving bitter but highly intoxicating beer to the traveller. Tuckerman further describes a by-product of Lobaria pulmonaria Hoff. When it was used as yellow, nearly insipid mucilage which may be eaten with salt". Alcohol production from lichens is an old art, now replaced by increased cultivation of potatoes, importation of sugar and distillation of wood. Preparation of spirits from lichens was recommended in 1870 as a means of saving grain otherwise diverted into alcohol production. It was claimed that 20 pounds of lichen would yield five liters of 50% alcohol. Stenberg [20] published a report in Stockholm in 1868 on the production of lichen brandy, and included detailed plans for setting up a distillery with figures of possible production levels. By 1893 the manufacture of brandy from alcohol derived from lichens had become a large industry in Sweden, but by 1894, as a result of the local exhaustion of the plants, the industry languished.

Arendt [13] in 1872 reported that this originally Swedish discovery was being applied in the Russian Provinces of Archangel, Pskow Novgorod, etc., and that various distillers exhibited samples of lichen spirits at the Russian Industrial Exhibition in Moscow, which were highly approved by the French and English visitors. The industry was a lucrative one in the northern provinces of Russia, yielding revenue of from 40 to 100%. Others [6] have reported on the carbohydrate composition of lichens on the Kola Peninsula, considered in connection with the problem of glucose production in northern localities. This includes a tabulation of carbohydrates present in eight lichen species, which shows them to be rich in polyhexoses, but poor in cellulose and in pentosan. Two small factories in Kirovsk have demonstrated the possibility of subjecting lichens to preliminary treatment with weak alkali solution in order to convert the bitter tasting lichen acids into soluble form. This is then hydrolyzed with dilute H2SO4, neutralized with chalk and purified with activated charcoal to produce a molasses containing 65 to 70% glucose. From this, crystallized (lump) glucose was obtained.

The yield of molasses was 100%, based on dry lichen weight. However, molasses produced by this process from lichens of the Cladonia group, especially alpestris, has a. bitter taste, "the cause of which the authors are investigating". Lichens vary in the amount of carbohydrates (lichenin) present. *Cetraria islandica* and *Cladonia rangiferina* have been found to yield up to 66% of polysaccharides which are readily hydrolized to glucose and then almost completely fermented to alcohol. Besides sugars capable of fermentation, lichen acids up to 11% of air-dried substance may be present. These acids as well as sodium chloride have been found to retard the process. Experiments with Cladonia rangiferina have shown a total yield of 54.5% sugar which on fermentation produced 176-282 cc. of alcohol per kilo. Maximum returns of alcohol were obtained by steaming the lichens one hour under three atmospheres pressure, adding 2.5% of 25% HC1, resteaming for the same period of time and pressure, and finally neutralizing the product. Subsequent growth of yeast was normal, though fermentation could be accelerated by addition of H_3PO. An interesting modification of this procedure through addition of three parts by weight of H_2SO_4 and one part by weight of NC1 at room temperature gave a pentanitrate similar to cellulose nitrate which, on gelatinizing with a solvent, produced a substance resembling horn [13]. Tanning. The tanning quality of lichens is due to an astringent property (depsides) peculiar to some species. Cetraria islandica and Lobaria pulmonaria were most used, and though not occurring in quantities sufficiently large to warrant industrial application, have been locally employed on a small scale.

Dyeing. Synthetic dyes have largely replaced many formerly common vegetable dyes in the textile industry, primarily because of their low production cost and the fact that they generally surpass the natural products in fastness, particularly light fastness. Of the vegetable dyes, those obtained from lichens were renowned among the peasant dyers of old for their high quality and color, but today are the least known. Some of them are still popular in rural districts of Great Britain and the Western Islands, Iceland, Scandinavia, France and Germany. Interest in lichen dyes is being revived today somewhat in Scandinavia because of their use by the HemslSjd (Home Industries Association), while there is some indication that the Irish Government is trying to reestablish this art in the poorer farming and fishing districts where these skills have been lost. That there is a good economic reason for such revival may be noted by the fact that the production of Harris Tweed cloth, dependent upon lichen dyes, is a carefully organized industry in Great Britain producing a luxury cloth of standard quality and great demand. The most attractive feature of home dyed and woven cloth is not only the dye utilized in its manufacture but also the individuality of the patterns evolved by a particular household or community. When these are standardized, as they may be through government and association intervention, they lose much of their appeal to the retail trade. Under such controls prices tend to rise in excess of the true value, even for handicraft. It has been observed that wool dyed with lichen dyes is not attacked by cloth moths.

4.2 Cosmetics and Perfumes History

Since the 16th Century, or earlier, members of the families Cladoniaeeae, Stictaeeae, Parmetiaeeae and Usneaceae have been utilized as raw materials in the perfume and cosmetic industries. At first this use consisted of drying and grinding the plants to a powder and combining them crudely with other substances, but as the manufacturers became more expert in their trade, these materials were skillfully combined into toilet powders, scented sachets and perfumes of real value. Three lichens commonly used were Evernia prunastri, E. furfuracea and Lobaria pulmonaria which have similar aromatic substances. The trades recognized these lichens under a variety of names, as "Lichen quereinus viridis", "Muscus arboreus, acaciae etodorante", "Eichenmoos" and more commonly as "Mousse de Chine" or Oak-moss and Scented-moss. Ramalina calcaris Fr. was used in place of starch to whiten hair of wigs and perukes. Cyprus Powder, a combination of E. prunastri, Anaptychia ciliaris and Usnea species, was scented with ambergris or musk, and oil of roses, jasmine or orange blossoms for use as a toilet powder in the 17th Century that would whiten, scent and cleanse the hair [19]. After a somewhat lengthy eclipse, these plants reappeared as raw stuffs for perfumery, owing to the creation of scnts with a deep tone and to the demands for the very stable perfumes of modern extraction, to which purposes they are almost universally applied to this day. The principal species used in modern perfumes and cosmetics include *Evernia prnastri*, *E. furfuracea*, *E.*

mesomorpha, Ramalina fraxinea Ach., R. farinacea, R. pollinaria Ach. and perhaps other species of the Ramalinae, though the last-named genus is not rated as so valuable as the former.

Lobaria pulmonaria (Mousse de la base du Chine) is used to some extent and is considered a more costly substance, perhaps because of its relative scarcity. Oak-moss (*E. prunastri*) of Europe is collected in shaded, damp habitats occurring in the central mountain ranges of Europe, the Piedmont of Italy and the forests of Czecho-Slovakia and Herzegovina. Not only the locality but the substratum is given a great deal of attention by the perfumer who differentiates between those plants that grow on oak (greenish) and those found on conifers (greyish); in the latter case rightly so, since resins may be included with the lichen, rendering it less desirable for the trade. In all instances the crop is gathered by peasants or shepherds, as in Jugoslavia, and pressed into large bales for export. The American supply before the war was derived from Jugoslavia, amounting to a few tons" yearly at a cost of from five to seven and one-half cents per pound f.o.b., New York City.

4.3 Chemical Properties of Essential Oil of Lichens

The use of dried, pulverized Oak-moss in the perfume industry is restricted, the principal sale being of extracts, essences and resinoids. Gildermeister and Hoffmann [13] state that the method of treatment involves exhausting the lichen by means of volatile substances and then removing the resins, waxes and chlorophyl with acetone. Addition of alcohol gives an "extract of Oak-moss" which may be used in this form or may be further concentrated in order to obtain a semi-fluid substance. French and German industrial research during the last 30 years has revealed much of the chemical nature of the extracts, gums and mucilages produced when processing lichens.

Gattefoss5 [13] made a study of the essential oils and alcoholic extracts of all those lichens which were utilized as Oak-moss, obtaining data that caused him to conclude that oil of Oak-moss was almost exclusively a compound of phenol called" lichenol", an isomeric compound of carvacrol. These results were verified by St. Pfau [13] who further expressed Ore opinion that sparrassol, a metabolic product of the fungus *Sparassis ramosa*, is identical with methyl everninate resulting from the alcoholysis of everninic acid, present in proportions of about 2.8%, with a characteristic anise seed odor.

Walbaum and Rosenthal [13] repeated the experiments of Gattefoss and arrived at different results. They distilled the oil of *Evernia prunastri* and found that at ordinary temperature it formed an oily crystalline mass of dark color with a very powerful and agreeable odor. Further analysis revealed Gattefoss's error, and orcinol monomethylether, not lichenol (Cl_oH_{140}), is the principal constituent of Oak-moss. This phenol, though not the main odoriferous part of the lichen oil, has a pleasant, creosol like smell, and an ester, fl-orcinol methyl carboxylate (Cl_oH_{204}) which does not enter into the odor of the Oak-moss oil. In the resinous precipitate Walbaum and Rosenthal found ethyl everninate generated only during the extraction through esterification of the everninic acid ($C_7H_{16}0_7$) which was found to occur in a free state in the lichen; when boiled with baryta water it split into orcinol and everninic acid with the liberation of carbon dioxide [14,15]. This acid is closely related to fl-orcinol monomethylether and would be converted into it by the liberation of carbon dioxide. For these reasons Walbaum and Rosenthal felt that the genesis of the principal constituent of the odoriferous substances of Oak-moss had a close connection with the origin of everninic and evernic acids. Stoll and Schener [16] found in the volatile fraction some compounds which may also have a function in producing this odor, mainly thujone, naphthalene, borneol, camphor, civeole, citronellol; guaniol, vanillin, methylnonyl ketone and stearic aldehyde.

4.4 Uses of Essential Oils

The essential oil of Oak-moss or "cincrete" is used in its natural condition in soap as an impalpable powder or in the form of a resinarome. The powder permits production of soap-balls agreeably scented at a reasonable price if the manufacturer can obtain a perfectly impalpable powder; otherwise they give the impression of containing sand. The soap manufacturer maintains the quality of his product by procuring "his raw material from a reliable purveyor. To be sufficiently scented, soap balls should have 1 or 189 by weight of lichen powder. When used for this purpose Oak-moss "concrete" improves, strengthens and cheapens lavender-scented products [17,18]. It is essential in the higher grades of cosmetics in combination with other aromatic oils, e.g., jasmine, tuberose and orange blossom. Iceland Moss, Cetraria islandica, has al-ready been mentioned in connection with foods and medicine; in the field of cosmetics it serves as a source of glycerol in the soap industry and in the manufacture of cold creams because of its lack of odor. Some lichens, e.g., *Sticta fuliginosa* Ach. and *S. sylvatica* Ach., have an objectionable fishy or methylamine smell.

4.5 Gums

The dyeing and paper industries have need for quantities of sizing with which to dress and stiffen silks, to print and stain calico, and to size paper. During the Napoleonic Wars, because of the French monopoly of Senegal Gum, Lord Dundonald attempted to introduce the use of lichen mucilage in place of the French product, but there is no evidence that the English market was interested. At Lyons the French appear to have successfully used lichen mucilage as a substitute for gum arabic in the fabrication of dyed materials [13]. The problem has been investigated by Minford [19] who reports that Iceland Moss and some other lichens may be prepared as lightcolored, transparent and high-grade gelatin, isinglass and similar gelatinous products, corresponding to those obtained from vegetable products for this purpose.

4.6 Lichens for Decorations

The use of lichens for home decorations, funeral wreaths and grave wreaths is commonly exploited in the northern countries of Europe, partly as a result of tradition and the expense of out-of-season flowers. The Cladoniaceae or Reindeer lichens lend themselves best to this purpose and are always used in center-piece table decorations in winter and in connection with Christmas ornaments [20].

In older types of Swedish houses, where the outer or storm window can be separated from the permanent window, the space between at the base is filled with this lichen which may act partly as insulation. Dry lichens are brittle and are usually gathered and worked in the fall of the year when the air is moist; they are woven into wreaths by the poorer farming olass who offer them for sale on market days at low prices. Addition of water, as for cutflowers, does not preserve them but tends to make them moldy. Lichens can maintain themselves on hygroscopic water [21-26]. The Germans had an essential need for this plant also as grave decorations. The gathering of these lichens for decorations is cause for further dispute between Lapp herders and commercial harvesters. Cladonia species are occasionally used in table models and dioramas to represent trees [27].

5. Conclusions

Despite their broad spectrum of biological activities, lichens have for long been overlooked by mycologists and agro-chemists, mainly due to their slow growth in nature and difficulties in their artificial cultivation. Because of that, the stage of large-scale industrial production of lichen metabolites has not been reached yet. More research and development is required to develop, optimize and scale-up promising lichen-based technologies of high industrial and national importance. The biopharmaceutical industry would benefit though the commercialization of biotechnologies aimed at production of natural anti-oxidants, anti-microbial, anti-insecticidal, antipyretic, and anti-cancer agents. Lichens hold great potential that needs to be fully explored and utilized for the benefit of human health and our society.

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