

Occurrence of terpenes, polyketides, and tannins in some Japanese lichens and green mosses

Waill A. Elkhateeb, Ghoson M. Daba

Department of Chemistry of Natural and Microbial Products, Pharmaceutical Industries Researches Division, National Research Centre, El Buhouth Street, Dokki, Giza, Egypt

Correspondence to Waill A. Elkhateeb, PhD, Department of Chemistry of Natural and Microbial Products, Pharmaceutical Industries Researches Division, National Research Centre, El Buhouth Street, Dokki 12311, Giza, Egypt. Tel: (+20)1013241936; fax: (+20) 233 387 758; E-mail: waillahmed@yahoo.com

Received: 27 March 2020

Revised: 19 April 2020

Accepted: 2 June 2020

Published: 24 August 2020

Egyptian Pharmaceutical Journal 2020, 19:216–223

Terpenes, polyketides, and tannins are valuable chemical classes that are famous for their varied biological activities such as being antioxidant, anticancer, antibiotic, and immunosuppressant agents. On the other hand, lichens and mosses are rich sources of biologically active compounds. However, rare studies have described neither the chemical analyses nor the biological activities of such samples. In this review, the chemical constitutions of five Japanese originated lichens and moss samples belonging to the species *Candelariella vitellina*, *Lepraria incana*, *Dirinaria applanata*, *Brachythecium velutinum*, and *Brachythecium rutabulum* were described with focus on three chemical classes which are terpenes such as Dechloromycorrhizin A, Hericenone A, demethoxyviridin, Scytalidic acid, Ovellin B, Ceriporic acid B, Ganoderatriol, Fomefficinic acid A, Ganoderol A, Ganoderol F; polyketides such as Chaetoquadrin A, Comazaphilone C, Hormothamnione, Arnottianamide, Avermutin, 4'-Hydroxyphlebiarubrone, 4'-Hydroxyphlebiarubrone, Citropone A, Atrovenetin; and finally secondary metabolites (tannins) such as 5'-methoxydehydrodiconiferyl alcohol, ellagic acid 3,3'-di-O-methyl ether, 5,5'-dehydrodiferulic acid, 3,3',4-tri-O-methylellagic acid, and 5'-methoxydehydrodiconiferyl alcohol.

Keywords:

Brachythecium velutinum, *Candelariella vitellina*, *Dirinaria applanata*, *Lepraria incana*, *Brachythecium rutabulum*, terpenes, polyketides, tannins, biological activities

Egypt Pharmaceut J 19:216–223

© 2020 Egyptian Pharmaceutical Journal
1687-4315

Introduction

Lichens are symbiotic associations of fungi with microalgae and/or cyanobacteria, which are considered among the slowest growing organisms, with strong tolerance to adverse environmental conditions [1]. Lichens are a valuable source of many natural classes with varying biological potentials including antiviral, antifungal, analgesic, antipyretic, antioxidant, and anticancer effects [2,3]. The potential of lichens for the monitoring of radionuclides has been well documented [4,5]. Lichens can grow on rocks and exist as epiphytes on trees and leaves [6]. Most of the lichens are terrestrial and few are marine with the ability to adapt water and saline stress, extreme temperature, and air pollutants [7] Lichens produce a wide array of biologically active primary (intracellular) and secondary (extracellular) metabolites (Fig. 1). More than 1000 metabolites were extracted from lichens, some of these compounds are exclusively produced by lichens, while others were commonly observed in fungal extracts and those of higher plants [3,5]. In recent times, lichens and their secondary metabolites have been getting increased attention due to their nutritional value and pharmaceutical potential; lichens are used in medicine for many purposes such as for treating bronchitis, spleen enlargement, asthma, heart and

stomach disorders, vomiting, treating wounds, and skin disorders [1,8,9]. Lichens metabolites (also known as lichen substances) are either primary or secondary metabolites [8,9]. Primary metabolites are required for the growth and maintenance of cells, and those metabolites include amino acids, proteins, polyols, polysaccharides, vitamins, and carotenoids. On the other hand, lichen secondary metabolites do not contribute in growth, development, or reproduction but they are usually derived from primary metabolism [2,5,8].

Candelariella

Candelariella (known as crustose lichen) is a well-known and commonly occurring genus, growing on many types of substrates, particularly in exposed and nitrogen-enriched regions. The most prominent components of the lichen flora are from species belonging to the genus *Candelariella* on road-side trees, limestone rocks, and in alpine, terricolous habitats. However, the knowledge of the distribution and ecology of individual species is still poor for many

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

Figure 1



Candelariella vitellina (Photographs taken by Waill A. Elkhateeb, Locality: Hakozaki Higashi-ku Fukuoka-shi Japan).

Figure 2



Lepraria incana (Photographs taken by Waill A. Elkhateeb, Locality: Hakozaki Higashi-ku Fukuoka-shi Japan).

species. Few lichenologists collect and study *Candelariella*, possibly because of the presumed difficulties in correctly identifying the species [10]. *Candelariella vitellina* (also known as egg yolk

lichen) is a common and widespread crustose lichen. It is characterized by its green-yellow to orange-yellow colors, and it grows on the bark, rock, and wood all over the world (Fig. 2). *C. vitellina* belongs to the kingdom Fungi, class lecanoromycetes, order *Candelariales*, and family *Candelariaceae*. This promising lichen is a rich source of antioxidants and anticancer compounds. *C. vitellina* is a common green-yellow lichen found on the barks, woods, and rocks in Japanese forests. High-performance liquid chromatography and -high-resolution electrospray ionization mass spectrometry analyses revealed seven new compounds and 11 natural compounds of terpenes and polyketides [11,12].

Lepraria

The genus *Lepraria* Ach., with a worldwide distribution, comprises morphologically simple lichen-forming fungi that never develop fruiting bodies. Thallus crustose to sub-foliose or squamulose, with a powdery, granular, cottony, membranous or sub-squamulose to sub-foliose appearance; variously colored, but not very bright, grayish, greenish and creamy hues prevalent; thin to thick, soft or hard [13]. The lichen *Lepraria incana* (also known as dust lichen) belongs to the kingdom Fungi, class lecanoromycetes, order: Lecanorales, Family: Stereocaulaceae (Fig. 3). It is a common lichen that grows on many substrates in the pattern of granulated patches or dust-like form. Rare studies have been conducted describing the chemical analysis and biological activities of this lichen. Previous chemical investigation showed that *L. incana* contained

Figure 3



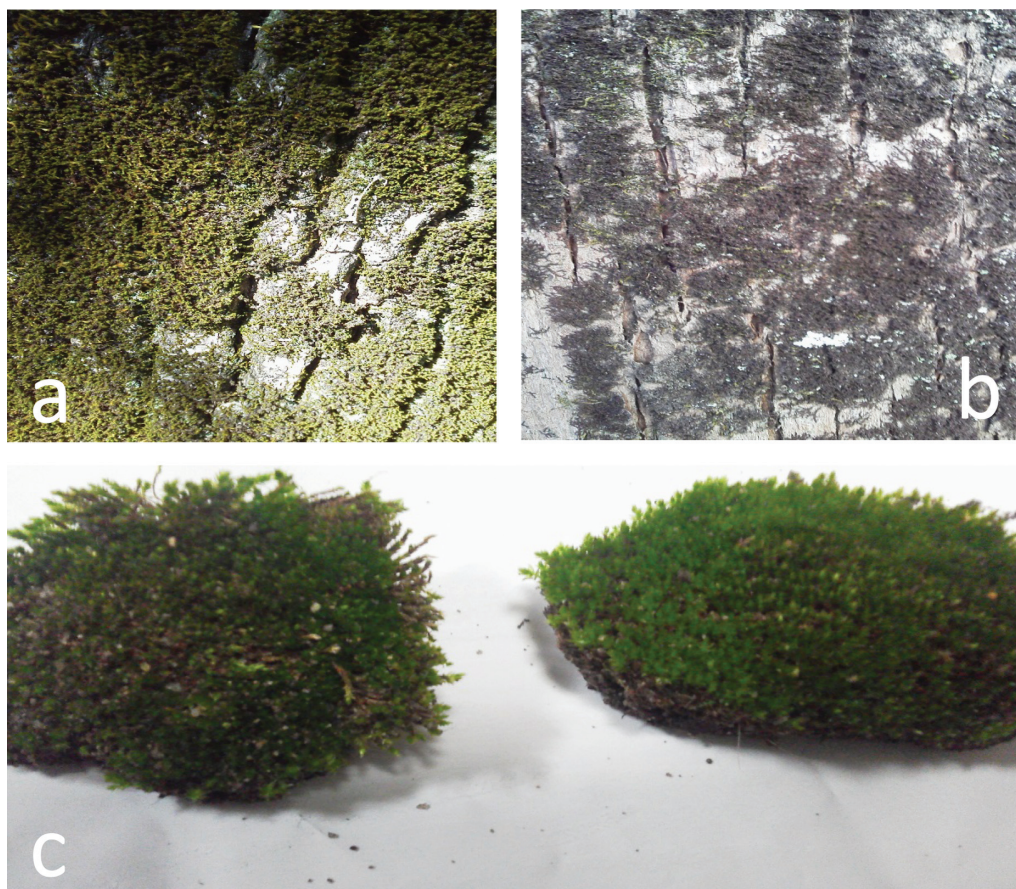
Dirinaria applanata (Photographs taken by Waill A. Elkhateeb, Locality: Hakozaki Higashi-ku Fukuoka-shi Japan).

Divaricatic acid, nordivaricatic acid, zeorin [13], and atranorin; anthraquinones in addition to parietin, fallacinal, parietinic acid and citreorosein [14], gyrophoric acid, lecanoric acid, thamnolic acid, and an unknown terpenoid [15].

Dirinaria

Dirinaria genus is widely distributed in the tropical and subtropical areas that comprised approximately 36 species worldwide [16]. *Dirinaria applanata* is a worldwide spreading lichen that belongs to the kingdom Fungi, class Lecanoromycetes, order: Teloschistales, Family: Caliciaceae. Chemical analyses conducted on this lichen are described in few studies [17,18]. *D. applanata* is a foliose lichen, which is widely distributed in tropical areas (Fig. 4). Previous chemical investigations showed that *D. applanata* contained atranorin, carotenoids divaricatinic acid and its ester derivatives, methyl hematommate, methyl β - orcinolcarboxylate, ramalinic acid, lichenxanthones, tannins, and terpenes such as the novel hopane 1β -acetoxy- 21α -hopane- $3\beta,22$ -diol [17–21].

Figure 4



Green moss: (a) *Brachythecium velutinum* (green), (b) *Brachythecium velutinum* (brown), and (c) *Brachythecium rutabulum* (photographs taken by Waill A. Elkhateeb, locality: Hakozaki Higashi-ku Fukuoka-shi, Japan).

Green moss

Brachytheciaceae is a family of mosses, class Hypnales from the order Hypnales. The family includes more than 40 genera and 250 species. The most common genus is *Brachythecium* and the most common species are *Brachythecium rutabulum* and *Brachythecium velutinum*. *B. rutabulum* and *B. velutinum* (also known as Velvet Feather-moss) is a common moss which was previously classified as lichen. It occurs on the wood, including the branches, base and roots of trees, and on dead wood, as well as stones and compacted soil. *B. rutabulum* and *B. velutinum* were a large moss, growing in lax, glossy, bright green, or yellowish green tufts or patches. It is common in Europe and Asia and occurs in many habitats, such as soil (both in woodland and non-forest vegetation), tree boles, logs, stones, and walls [22]. These species are frequently found in man-made habitats such as lawns in gardens, where it is regarded as an unwanted plant. Antibacterial properties of *B. rutabulum* extracts have been recently reported by Singh *et al.* [23], and their use has been reported in the Himalayas [24]. Some mosses have recently been confirmed as sources of antibacterial substances. *B. rutabulum* extract shows antibacterial activity against, for example, *Bacillus subtilis*, *Escherichia coli*, and *Staphylococcus aureus*, and antifungal activity against, for example, *Aspergillus flavus*, *Candida albicans*, and *Trichophyton rubrum* [23], and acts as an antioxidant [25]. Rare studies were conducted describing the chemical analysis and biological activities of this moss. It should be noted that all lichens mentioned in this review are Japanese originated (Fig. 4) [17], .

Chemical constitution of some Japanese lichens and green mosses

Terpenes are a chemical class of compounds that represent a major section of secondary metabolites [26]. *Terpenes* basically consist of five-carbon isoprene units, which are assembled to each other as many isoprene units in numerous ways. Terpenoids are modified terpenes with different functional groups with oxidized methyl group removed or located at different positions [27]. According to the number of these isoprene units, terpenes are generally classified into monoterpenes (having two isoprene units, 10 carbon atoms), sesquiterpenes (having three isoprene units, 15 carbon atoms), diterpenes (having four isoprene units, 20 carbon atoms), triterpenes (having six isoprene units, 30 carbon atoms), and tetraterpenes (carrying eight isoprene units, 40 carbon atoms). Among various biological activities, many members of terpenes are specifically potent anticancer agents, exhibit antimalarial activity [27].

As shown in Table 1, *C. vitellina* is rich in various bioactive organic compounds belonging to terpenes such as dechloromycorrhizin A, hericenone A, demethoxyviridin, scytalidic acid, ovellin B, ceriporic acid B, ganoderatriol, fomefficinic acid A, ganoderol A, and ganoderol F. Majority of these compounds exhibit well-known biological activities. *B. velutinum* chemical analysis revealed the presence of many terpenes compounds such as bufotalin, dantaxusin A, moreollic acid, dihydroisomorellin, suberixanthin, taxuspine B, and taxuspine C, while only the terpenes tetrahydroxyoleanenoic-acid 28-O- β -D-glucopyranosyl ester, taxuspine B, and taxuspine C were detected in the extract of the lichen *B. rutabulum*. The lichen *L. incana* showed variety of terpenes including pavoninin-2, terpecurcumin Q, ergosterol acetate, taxuspine C, and lantadene A methyl ester (Table 1). Finally, Gaigrandin, terpecurcumin Q, ergosterol acetate, taxuspine C, and dichrostachine F are the only terpenes detected in the extract of the lichen *D. applanata*.

On the other hand, polyketides represent a huge group of secondary metabolites [26]. Many polyketides have antimicrobial, immunomodulatory, and immunosuppressive properties. Moreover, polyketides include the main chemical structure of different parasiticides, anticancer, and hypocholesterolemic compounds. Polyketide pharmaceutical market has recorded annual sales of as high as 20 billion dollars in the first decade of the 21st century [53]. *C. vitellina* sample from Japan was also a rich source of polyketides such as chaetoquadrin A, comazaphilone C, hormothamnione, arnottianamide, avermutin, 4'-hydroxyphlebiarubrone, 4'-hydroxyphlebiarubrone, citropone A, and atrovetin (Table 1). Among the remaining listed lichens, polyketides were represented by schisantherin I which was detected in the *B. rutabulum* extract.

Tannins are a class of water-soluble polyphenolic biomolecules that bind to and precipitate proteins and various other organic compounds including amino acids and alkaloids. Some members of tannins are among the famous plant growth regulators and pesticides. They have many biological activities as antioxidants, metal chelators, anti-inflammatory, and anticancer agents [54]. Among the described lichens and mosses tannins detected include 5'-methoxydehydrodiconiferyl alcohol in the extract of *B. velutinum*. *L. incana* extract was rich in tannins such as ellagic acid 3,3'-di-O-methyl ether, 5,5'-dehydrodiferulic acid, 3,3',4'-tri-O-methylellagic acid, and 5'-methoxydehydrodiconiferyl alcohol.

Table 1 LC-HRESIMS analysis of the methanolic extract of some Japanese lichens and green mosses

No.	<i>m/z</i> experimental	Formula	Suggested compound	Chemical class	Activity	References
<i>Candelariella vitellina</i>						
1	331.15442	C ₁₉ H ₂₂ O ₅	Hericenone A	Terpenes	Cytotoxic	Rama Rao and Reddy [28]
2	361.16473	C ₂₀ H ₂₄ O ₆	Chaetoquadrin A	Polyketide	Inhibit mouse liver monoamine oxidase	Kim <i>et al.</i> [29]
3	417.15454	C ₂₂ H ₂₄ O ₈	Comazaphilone C	Polyketide	Antibacterial, cytotoxic	Gao <i>et al.</i> [30]
4	401.12302	C ₂₁ H ₂₀ O ₈	Hormothamnione	Polyketide	Cytotoxic	Gerwick <i>et al.</i> [31]
5	382.12869	C ₂₁ H ₁₉ NO ₆	Arnottianamide	Polyketide	Cytotoxic	Yang <i>et al.</i> [32]
6	371.11279	C ₂₀ H ₁₈ O ₇	Avermutin	Polyketide	Cytotoxic	Engström <i>et al.</i> [33]
7	323.09152	C ₁₉ H ₁₄ O ₅	Demethoxyviridin	Terpenes	Antioxidant	Wang <i>et al.</i> [34]
8	405.19070	C ₂₂ H ₂₈ O ₇	Scytalidic acid	Terpenes	No reported activity	
9	416.17020	C ₂₂ H ₂₅ NO ₇	Ovellin B	Terpenes	Cytotoxic	Belofsky <i>et al.</i> [35]
10	321.07587	C ₁₉ H ₁₂ O ₅	4'-Ydroxyphlebiarubrone	Polyketide	No reported activity	
11	311.09174	C ₁₈ H ₁₄ O ₅	Ligustrone B	Polyketide	No reported activity	
12	343.11789	C ₁₉ H ₁₈ O ₆	Atrovenetin	Polyketide	Antioxidant	Ishikawa <i>et al.</i> [36]
13	355.28442	C ₂₁ H ₃₈ O ₄	Ceriporic acid B	Terpenes	Antioxidant	Rahmawati <i>et al.</i> [37]
14	439.35672	C ₃₀ H ₄₆ O ₂	Ganoderol A	Terpenes	Cytotoxic	Chen <i>et al.</i> [38]
15	455.35144	C ₃₀ H ₄₆ O ₃	Ganoderol F	Terpenes	Cytotoxic	Chen <i>et al.</i> [38]
16	457.36728	C ₃₀ H ₄₈ O ₃	Ganodermatriol	Terpenes	Cytotoxic	Liu <i>et al.</i> [39]
17	469.36700	C ₃₁ H ₄₈ O ₃	Fomefficinic acid A	Terpenes	Cytotoxic	Shen <i>et al.</i> [40]
18	394.12833	C ₂₂ H ₁₉ NO ₆	Citropone A	Polyketide	No reported activity	
19	502.32721	C ₂₈ H ₄₃ N ₃ O ₅	Beauverolide D	Cyclic peptide	No reported activity	
20	516.34253	C ₂₉ H ₄₅ N ₃ O ₅	Beauverolide E	Cyclic peptide	No reported activity	
21	564.34235	C ₃₃ H ₄₅ N ₃ O ₅	Beauverolide F	Cyclic peptide	No reported activity	
<i>Brachythecium velutinum</i> (Brown)						
1	465.1016	C ₂₁ H ₂₀ O ₁₂	Hyperoside	Flavonoid glycoside	Antidepressant, antioxidant	Park <i>et al.</i> [41]
2	303.0488	C ₁₅ H ₁₀ O ₇	Robinetin	Flavonoid aglycone	multidrug resistance proteins inhibitor	van Zanden <i>et al.</i> [42]
3	287.0542	C ₁₅ H ₁₀ O ₆	Scutellarein	Flavonoid aglycone	Anticancer	Shi <i>et al.</i> [43]
4	445.2548	C ₂₆ H ₃₆ O ₆	Bufootalin	Terpenes	Anticancer	Zhang <i>et al.</i> [44]
5	621.2695	C ₃₅ H ₄₀ O ₁₀	Dantaxusin A	Terpenes	No reported activity	
6	593.2745	C ₃₄ H ₄₀ O ₉	Moreollic acid	Terpenes	Cytotoxic	Asano <i>et al.</i> [45]
7	623.2853	C ₃₅ H ₄₂ O ₁₀	Taxuspine B	Terpenes	Inhibit drug transport activity of P-glycoprotein in multidrug-resistant cells	Kobayashi <i>et al.</i> [46]
8	607.2901	C ₃₅ H ₄₂ O ₉	Taxuspine C	Terpenes	Inhibit drug transport activity of P-glycoprotein in multidrug-resistant cells	Kobayashi <i>et al.</i> [46]
9	547.2692	C ₃₃ H ₃₈ O ₇	Dihydroisomorellin	Terpenes	Anticancer	Kobayashi <i>et al.</i> [46]
<i>Brachythecium velutinum</i> (Green)						

(Continued)

Table 1 (Continued)

No.	<i>m/z</i> experimental	Formula	Suggested compound	Chemical class	Activity	References
1	365.2061	C ₂₄ H ₂₈ O ₃	Ugonstilbene A	Phenols	Anti-inflammatory	Asano <i>et al.</i> [45]
2	366.1903	C ₁₉ H ₂₇ NO ₆	Harzianic acid	Alkaloid	Antibiotic, Plant growth promoting	Asano <i>et al.</i> [45]
3	389.1587	C ₂₁ H ₂₄ O ₇	5'-Methoxydehydrodiconiferyl alcohol	Tannin	No reported activity	
4	593.2745	C ₃₄ H ₄₀ O ₉	Moreollic acid	Terpenes	Cytotoxic	Asano <i>et al.</i> [45]
5	623.2853	C ₃₅ H ₄₂ O ₁₀	Taxuspine B	Terpenes	Inhibit drug transport activity of <i>P-glycoprotein</i> in multidrug-resistant cells	Kobayashi <i>et al.</i> [46]
6	607.2903	C ₃₅ H ₄₂ O ₉	Taxuspine C	Terpenes	Inhibit drug transport activity of <i>P-glycoprotein</i> in multidrug-resistant cells	Kobayashi <i>et al.</i> [46]
7	593.4369	C ₄₂ H ₅₆ O ₂	Suberixanthin	Terpenes	No reported activity	
<i>Brachythecium rutabulum</i>						
1	325.0698	C ₁₈ H ₁₂ O ₆	Sterigmatocystine	Xanthene	Cytotoxic	Kobayashi <i>et al.</i> [46]
2	639.2798	C ₃₅ H ₄₂ O ₁₁	Propinquanin B	Polyketide	Cytotoxic	Kobayashi <i>et al.</i> [46]
3	623.2853	C ₃₅ H ₄₂ O ₁₀	Taxuspine B	Terpenes	Inhibit drug transport activity of <i>P-glycoprotein</i> in multidrug-resistant cells	Kobayashi <i>et al.</i> [46]
4	607.2901	C ₃₅ H ₄₂ O ₉	Taxuspine C	Terpenes	Inhibit drug transport activity of <i>P-glycoprotein</i> in multidrug-resistant cells	Kobayashi <i>et al.</i> [46]
5	653.2955	C ₃₆ H ₄₄ O ₁₁	Schisantherin I	Polyketide	Anti-inflammatory	Ci <i>et al.</i> [47]
6	661.4631	C ₃₉ H ₆₄ O ₈	Tetrahydroxyoleanoic-acid 28-O-β-D-glucopyranosyl ester	Terpenes	No reported activity	
<i>Lepraria incana</i>						
1	331.0438	C ₁₆ H ₁₀ O ₈	Ellagic acid 3,3'-di-O-methyl ether	Tannin	Antitumor	Zhang <i>et al.</i> [48]
2	387.1065	C ₂₀ H ₁₈ O ₈	5,5'-Dehydrodiferulic acid	Tannin	No reported activity	
3	345.0596	C ₁₇ H ₁₂ O ₈	3,3',4-Tri-O-methylellagic acid	Tannin	Antitumor	Alam and Tsuboi [49]
4	389.1587	C ₂₁ H ₂₄ O ₇	5'-Methoxydehydrodiconiferyl alcohol	Tannin	No reported activity	
5	620.4150	C ₃₅ H ₅₇ NO ₈	Pavoninin-2	Terpenes	No reported activity	
6	571.3073	C ₃₆ H ₄₂ O ₆	Terpecurcumin Q	Terpenes	Anticancer	Lim. [50]
7	439.3565	C ₃₀ H ₄₆ O ₂	Ergosteryl acetate	Terpenes	No reported activity	
8	607.2903	C ₃₅ H ₄₂ O ₉	Taxuspine C	Terpenes	Inhibit drug transport activity of <i>P-glycoprotein</i> in multidrug-resistant cells	Kobayashi <i>et al.</i> [46]
9	567.4009	C ₃₆ H ₅₄ O ₅	Lantadene A methyl ester	Terpenes	Antitumor	Sharma <i>et al.</i> [51]
<i>Dirinaria applanata</i>						
1	331.0438	C ₁₆ H ₁₀ O ₈	Ellagic acid 3,3'-di-O-methyl ether	Tannin	Antitumor	Zhang <i>et al.</i> [48]
2	387.1065	C ₂₀ H ₁₈ O ₈	5,5'-Dehydrodiferulic acid	Tannin	No reported activity	
3	345.0596	C ₁₇ H ₁₂ O ₈	3,3',4-Tri-O-methylellagic acid	Tannin	Antitumor	Alam and Tsuboi [49]
4	389.1587	C ₂₁ H ₂₄ O ₇	5'-Methoxydehydrodiconiferyl alcohol	Tannin	No reported activity	
5	425.2134	C ₂₂ H ₃₂ O ₈	Gaigrandin	Terpenes	No reported activity	
6	571.3073	C ₃₆ H ₄₂ O ₆	Terpecurcumin Q	Terpenes	Anticancer	Lim. [50]
7	439.3565	C ₃₀ H ₄₆ O ₂	Ergosteryl acetate	Terpenes	No reported activity	
8	607.2903	C ₃₅ H ₄₂ O ₉	Taxuspine C	Terpenes	Inhibit drug transport activity of <i>P-glycoprotein</i> in multidrug-resistant cells	Kobayashi <i>et al.</i> [46]
9	621.3057	C ₃₆ H ₄₄ O ₉	Dichrostachine F	Terpenes	Anticancer	Long <i>et al.</i> [52]

Also, same tannins (ellagic acid 3,3'-di-O-methyl ether, 5,5'-dehydrodiferulic acid, 3,3',4-tri-O-methylellagic acid, 5'-methoxydehydrodiconiferyl alcohol) were detected in the extract of *D. applanata*.

Conclusion

Screening for novel compounds are extremely important nowadays due to the emergence of new fatal diseases especially cancers, infections caused by drug-resistant microbes, or the currently spreading Corona virus disease caused by COVID-19 virus. Lichens are generous source of novel compounds that can be investigated for their potential biological activities. In this review, the chemical composition of some lichens originated in Japan and green mosses is described showing their richness in bioactive compounds especially from the chemical classes of terpenes, polyketides, and tannins. Majority of members of such chemical classes are known as promising antiviral, anticancer, antioxidant, antimicrobial, immunomodulatory, and immunosuppressive agents. Further studies on those marvelous group can contribute in discovering potent and/or novel compounds capable of competing with currently used drugs or even replace such drugs.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

- Salgado F, Albornoz L, Cortez C, Stashenko E, Urrea-Vallejo K, Nagles E, et al. Secondary metabolite profiling of species of the Genus *Usnea* by UHPLC-ESI-OT-MS-MS. *Molecules* 2017;23:54.
- Molnar K, Farkas E. Current results on biological activities of lichen secondary metabolites: a review. *Z Naturforsch C* 2010; 65:157–173.
- Shrestha G, St Clair LL. Lichens: a promising source of antibiotic and anticancer drugs. *Phytochem Rev* 2013; 12:229–244.
- Dalvand A, Jahangiri A, Iranmanesh J. Introduce lichen *Lepraria incana* as biomonitor of Cesium-137 from Ramsar, northern Iran. *J Environ Radioact* 2016; 160:36–41.
- Elkhateeb WA, Daba GM. Lichens, an alternative drugs for modern diseases. *Int J Res Pharm Biosci* 2019; 6:5–9.
- Petrzik K, Vondrák J, Barták M, Peksa O, Kubešová O. Lichens – a new source or yet unknown host of herbaceous plant viruses?. *Eur J Plant Pathol* 2014; 138:549–559.
- Nash TH III (editor). *Lichen Biology*. 2nd ed. Cambridge: Cambridge University Press; 2008.
- Calcott MJ, Ackerley DF, Knight A, Keyzers RA, Owen JG. Secondary metabolism in the lichen symbiosis. *Chem Soc Rev* 2018; 47:1730–1760.
- Crawford SD. Lichens used in traditional medicine. In: Branislav Ranković, editor. *Lichen Secondary Metabolites*. Cham: Springer; 2019. 31–97.
- Westberg M, Clerc P. Five species of *Candelaria* and *Candelariella* (Ascomycota, Candelariales) new to Switzerland. *MycKeys* 2012; 3:1.
- El-Garawani IM, Elkhateeb WA, Zaghlol GM, Almeer RS, Ahmed EF, Rateb ME, Moneim A. Candelariella vitellina extract triggers in vitro and in vivo cell death through induction of apoptosis: a novel anticancer agent. *Food Chem Toxicol* 2019; 127:110–119.
- Elkhateeb WA, Daba GM, El-Dein AN, Sheir DH, Fayad W, Shaheen MN, et al. Insights into the in-vitro hypocholesterolemic, antioxidant, antitumor, and anticancer activities of the methanolic extracts of a Japanese lichen, *Candelariella vitellina*, and a Japanese mushroom, *Ganoderma applanatum*. *Egypt Pharm J* 2020; 19:77–83.
- Lauri SAAG, Andres SAAG, Randlane T. World survey of the genus *Lepraria* (Stereocaulaceae, lichenized Ascomycota). *Lichenologist* 2009; 41:25–60.
- Laundon JR. *Lepraria* in the British Isles. *Lichenologist* 1992; 24:315–350.
- Makarova II, Himelbrant DE, Shapiro IA. Key to the species of *Lepraria* Ach. In Russia. In *Novitates Systematicae Plantarum Non Vascularum*, Tomus XL:258–273
- Elix JA. *Dirinaria*. *Flora Aust* 2009; 57:509–517.
- Ahmed EF, Elkhateeb WA, Taie HA, Rateb ME, Fayad W. Biological capacity and chemical composition of secondary metabolites from representatives Japanese lichens. *J Appl Pharm Sci* 2017; 7:098–103. ?
- Nguyen TT, Nguyen QC, Mai VH, Phan QT, Do PQ, Nguyen TD, et al. A new hopane derivative from the lichen *Dirinaria applanata*. *Nat Prod Res* 2019; 24:1–5.
- Czeczuga B, Czeczuga-Semeniuk E, Aptroot A. The individual variation in carotenoid content of the lichen species *Dirinaria applanata* (Fee) Awasthi. *Feddes Rept* 2008; 112:81–85.
- Jayalal U, Oh SS, Joshi S, Oh SO, Hur JS. The lichen *Dirinaria picta* new to South Korea. *Mycobiology* 2013; 41:155–158.
- Tuan NT, Van Hieu M, Thanh NQ, Van Loi H, Nghia LH, Hoa TT, Kenji K. Novel hopanoic acid and depside from the Lichen *Dirinaria applanata*. *Rec Nat Prod*. 2020; 14:248–255.
- Frey W, Frahm J-P, Fischer E, Lobin W. *The Liverworts, Mosses and Ferns of Europe*. Colchester: Harley Books; 2006.
- Singh M, Rawat AKS, Govindarajan R. Antimicrobial activity of some Indian mosses. *Fitoterapia* 2007; 78:156–158.
- Pant G, Tewari SD, Pargaien MC, Bisht LS. Bryological activities in north-west Himalaya-II. A bryophyte foray in the ascot region of district Pithoragarh (Kumaun Himalayas). *Bryol Times* 1986; 39:2–3.
- Stebel A, Smolarz HD, Jankowska-Biaszczyk M, Trylowski M, Bogucka-Kocka M. Seasonal variation in antioxidant activity of selected mosses from Poland. *Fragment Nat* 2016; 49:65–73.
- Goga M, Elečko J, Marcincinová M, Ručová D, Bačkorová M, Bačkor M. Lichen metabolites: an overview of some secondary metabolites and their biological potential. *Coevol Secondary Metabol* 2020; 16:175–209.
- Perveen S, Al-Taweel A. editors. *Terpenes and Terpenoids*. BoD-Books on Demand 2018.
- Rama Rao AV, Reddy RG. First unambiguous total synthesis of hericenone A: proposed structure revised. *Tetrahedron Lett* 1992; 33:4061–4064.
- Kim UB, Furkert DP, Brimble MA. Total synthesis of chaetoquadrins A-C. *Org Lett* 2013; 15:658–661.
- Gao SS, Li XM, Zhang Y, Li CS, Cui CM, Wang BG. Comazaphilones A-F, azaphilone derivatives from the marine sediment-derived fungus *Penicillium commune* QSD-17. *J Nat Prod* 2011; 74:256–261.
- Gerwick WH, Lopez A, Van Duyn GD, Clardy J, Ortiz W, Baez A. Hormothamnione, a novel cytotoxic styrylchromone from the marine cyanophyte hormothamnion enteromorphoides grunow. *Tetrahedron Lett* 1986; 27:1979–1982.
- Yang CH, Cheng MJ, Lee SJ, Yang CW, Chang HS, Chen IS. Secondary metabolites and cytotoxic activities from the stem bark of *Zanthoxylum nitidum*. *Chem Biodivers* 2009; 6:846–857.
- Engström K, Brishammar S, Svensson C, Bengtsson M, Andersson R. Anthraquinones from some *Drechslera* species and *Bipolaris sorokiniana*. *Mycol Res* 1993; 97:381–384.
- Wang GQ, Chen GD, Qin SY, Hu D, Awakawa T, Li SY, et al. Biosynthetic pathway for furanosteroid demethoxyviridin and identification of an unusual pregnane side-chain cleavage. *Nat Commun* 2018; 9:1–13.
- Belofsky GN, Jensen PR, Renner MK, Fenical W. New cytotoxic sesquiterpenoid nitrobenzoyl esters from a marine isolate of the fungus *Aspergillus versicolor*. *Tetrahedron* 1998; 54:1715–1724.
- Ishikawa Y, Morimoto K, Iseki S. Atrovenetin as a potent antioxidant compound from *Penicillium* species. *J Am Oil Chem Soc* 1991; 68:666–668.
- Rahmawati N, Ohashi Y, Watanabe T, Honda Y. Ceriporic acid B, an extracellular metabolite of *Ceriporiopsis subvermispora*, suppresses the depolymerization of cellulose by the Fenton reaction. *Biomacromolecules* 2005; 6:2851–2856.

- 38 Chen S, Li X, Yong T, Wang Z, Su J, Jiao C, *et al.* Cytotoxic lanostane-type triterpenoids from the fruiting bodies of *Ganoderma lucidum* and their structure-activity relationships. *Oncotarget* 2017; 8:10071–10084.
- 39 Liu JQ, Wang CF, Li Y, Luo HR, Qiu MH. Isolation and bioactivity evaluation of terpenoids from the medicinal fungus *Ganoderma sinense*. *Planta Med* 2012; 78:368–376.
- 40 Shen CC, Lin CF, Huang YL, Wan ST, Chen CC, Sheu SJ, *et al.* Bioactive components from the mycelium of *Antrodia salmonea*. *J Chin Chem Soc* 2013; 55:854–857.
- 41 Park JY, Han X, Piao MJ, Oh MC, Fernando PM, Kang KA, *et al.* Hyperoside induces endogenous antioxidant system to alleviate oxidative stress. *J Cancer Prev* 2016; 21:41.
- 42 van Zanden JJ, Wortelboer HM, Bijlsma S, Punt A, Usta M, van Bladeren PJ, *et al.* Quantitative structure activity relationship studies on the flavonoid mediated inhibition of multidrug resistance proteins 1 and 2. *Biochem Pharmacol* 2005; 69:699–708.
- 43 Shi X, Chen G, Liu X, Qiu Y, Yang S, Zhang Y, *et al.* Scutellarein inhibits cancer cell metastasis in vitro and attenuates the development of fibrosarcoma in vivo. *Int J Mol Med* 2015; 35:31–38.
- 44 Zhang DM, Liu JS, Tang MK, Yiu A, Cao HH, Jiang L, *et al.* Bufotalin from *Venenum Bufonis* inhibits growth of multidrug resistant HepG2 cells through G2/M cell cycle arrest and apoptosis. *Eur J Pharmacol* 2012; 692:19–28.
- 45 Asano J, Chiba K, Tada M, Yoshii T. Cytotoxic xanthenes from *Garcinia hanburyi*. *Phytochemistry* 1996; 41:815–820.
- 46 Kobayashi J, Ogiwara A, Hosoyama H, Shigemori H, Yoshida N, Sasaki T, *et al.* Taxuspines A–C, new taxoids from Japanese yew *Taxus cuspidata* inhibiting drug transport activity of p-glycoprotein in multidrug-resistant cells. *Tetrahedron* 1994; 50:7401–7416.
- 47 Ci X, Ren R, Xu K, Li H, Yu Q, Song Y, *et al.* Schisantherin A exhibits anti-inflammatory properties by down-regulating NF- κ B and MAPK signaling pathways in lipopolysaccharide-treated RAW 264.7 cells. *Inflammation* 2010; 33:126–136.
- 48 Zhang H, Guo ZJ, Xu WM, You XJ, Han L, Han YX, Dai LJ. Antitumor effect and mechanism of an ellagic acid derivative on the HepG2 human hepatocellular carcinoma cell line. *Oncol Lett* 2014; 7:525–530.
- 49 Alam A, Tsuboi S. Total synthesis of 3, 3',4-tri-O-methylellagic acid from gallic acid. *Tetrahedron* 2007; 63:10454–10465.
- 50 Lim TK. *Edible Medicinal and Non-Medicinal Plants*. Vol 9, Netherlands: Springer; 2015.
- 51 Sharma M, Sharma PD, Bansal MP. Lantadenes and their esters as potential antitumor agents. *J Nat Prod* 2008; 71:1222–1227.
- 52 Long C, Marcourt L, Raux R, David B, Gau C, Menendez C, *et al.* Meroterpenes from *Dichrostachys cinerea* inhibit protein farnesyl transferase activity. *J Nat Prod* 2009; 72:1804–1815.
- 53 Weissman KJ. Introduction to polyketide biosynthesis. In: Hopwood DA, editor. *Complex Enzymes in Microbial Natural Product Biosynthesis*, Part B: Polyketides, Aminocoumarins and Carbohydrates Methods in Enzymology. California, USA: Academic Press; 2009. 3–16.
- 54 Singh AP, Kumar S. Applications of tannins in industry. In: *Tannins-Structural Properties, Biological Properties and Current Knowledge*. Alfredo Aires, IntechOpen. 2019. 1–19. DOI: 10.5772/intechopen.85984.