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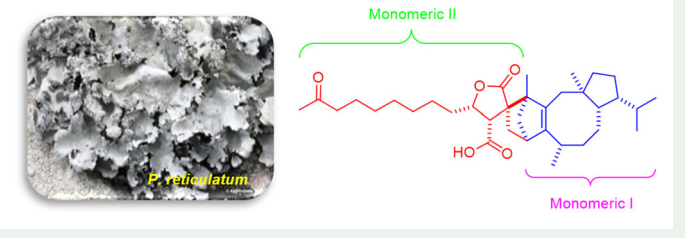
Reticulatin, a novel C_{43}-spiroterpenoid from the lichen *Parmotrema reticulatum* growing in Vietnam

Thuc-Huy Duong[a], Van-Kieu Nguyen[b,c], Jirapast Sichaem[d], Thanh-Nha Tran[a], Thanh-Hung Do[e], Nguyen-Kim-Tuyen Pham[f], Thi-Anh-Tuyet Nguyen[a], Thi-Hoai-Thu Nguyen[g], Dinh-Tri Mai[h,i], Ngoc-Hong Nguyen[j] and Bui-Linh-Chi Huynh[k]

[a]Department of Chemistry, Ho Chi Minh City University of Education, Ho Chi Minh City, Vietnam; [b]Institute of Fundamental and Applied Sciences, Duy Tan University, Ho Chi Minh City, Vietnam; [c]Faculty of Natural Sciences, Duy Tan University, Da Nang, Vietnam; [d]Research Unit in Natural Products Chemistry and Bioactivities, Faculty of Science and Technology, Thammasat University Lampang Campus, Lampang, Thailand; [e]NTT Hi-Tech Institute, Nguyen Tat Thanh University, Ho Chi Minh City, Vietnam; [f]Faculty of Environmental Science, Sai Gon University, Ho Chi Minh City, Vietnam; [g]Faculty of Basic Sciences, University of Medicine and Pharmacy at Ho Chi Minh City, Ho Chi Minh City, Vietnam; [h]Graduate University of Science and Technology, Vietnam Academy of Science and Technology, Ho Chi Minh City, Vietnam; [i]Institute of Chemical Technology, Vietnam Academy of Science and Technology, Ho Chi Minh City, Vietnam; [j]CirTech Institute, Ho Chi Minh City University of Technology (HUTECH), Ho Chi Minh City, Vietnam; [k]Department of Nature, Dong Nai University, Biên Hòa, Vietnam

ABSTRACT

A novel C_{43}-spiroterpenoid, reticulatin (**1**), was isolated from the lichen *Parmotrema reticulatum* (Taylor) M. Choisy (Parmeliaceae). Five previously-reported compounds were also isolated: zeorin (**2**), leucotylin (**3**), lupeol (**4**), betulinic acid (**5**), and dihydroreynosin (**6**). The structures were elucidated by 1D, 2D NMR, and HRESIMS spectroscopy and comparison with the literature. We propose that reticulatin is a biosynthetic product of fusicoccadiene and vinapraesorediosic acid A *via* Diels-Alder addition. Reticulatin is the first C_{43}-spiroterpenoid identified from lichen metabolites. All compounds were evaluated for inhibition of α-glucosidase. Compound **1** showed the most potent inhibition, with an IC_{50} value of 3.90 μM, much lower than that of the acarbose positive control (IC_{50} 165 μM).



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CONTACT Ngoc-Hong Nguyen nn.hong@hutech.edu.vn; Bui-Linh-Chi Huynh hainhanchi@yahoo.com.vn
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1. Introduction

Lichens are symbiotic organisms in which fungi (mycobionta) cooperate with algae or cyanobacteria (photobionts) to produce unique metabolites (Müller 2001; Boustie and Grube 2005). *Parmotrema reticulatum* (Taylor) M. Choisy is one of the lichens of the *Parmotrema* genus, which are widespread in the high-altitude forests of Vietnam. Lichen metabolites have medical applications as an anticancer (Ghate et al. 2013; Poornima et al. 2016), antioxidative (Ghate et al. 2013), antifungal (Shivanna and Garampalli 2014), antimicrobial (Poornima et al. 2017), and antibacterial (Sinha and Biswas 2011; Rajan et al. 2016), and are cardioprotective (Pol et al. 2017). Chemical analysis reveals the presence of depsides and depsidones such as gyrophoric acid, atranorin, chloroatranorin, consalazinic acid, and salazinic acid (Din et al. 2010). However, their isolation has not been reported. This study analyzed *P. reticulatum* as part of a wider investigation of Vietnamese lichens (Duong et al. 2015, 2017; Duong, Beniddir et al. 2018; Duong, Ha et al. 2018; Nguyen et al. 2018, 2020). We report the isolation and structural elucidation of reticulatin (**1**), a novel terpenoid, from the *n*-hexane extract of lichen *P. reticulatum,* as well as five previously-reported compounds: zeorin (**2**) (König and Wright 1999), leucotylin (**3**) (Brahmachari and Chatterjee 2002), lupeol (**4**) (Abdullahi et al. 2013), betulinic acid (**5**) (Cichewicz and Kouzi 2004), and dihydroreynosin (**6**) (Ogura et al. 1978). Their structures were elucidated from spectroscopic analysis and comparison with the existing literature. The six compounds were assayed for α-glucosidase inhibition, using *p*-nitrophenyl-α-D-glucopyranoside (*p*NPG) as substrate.

2. Results and discussion

Compound **1**, a white amorphous powder, had a deprotonated ion peak at *m/z* 665.5139 on the HRESI mass spectrum, suggesting a molecular formula of $C_{43}H_{70}O_5$ (calcd. for $C_{43}H_{69}O_5$-H, 665.5145). HSQC and ^{1}H NMR analysis identified one oxymethine proton (δ_H 4.44, 1H, td, $J = 8.0$, 4.5 Hz), six methyl groups (δ_H 0.74, 0.87, and 0.98, each doublet and δ_H 0.75, 1.23, and 2.13, each singlet), six methines (δ_H 2.87 (brd, $J = 3.0$ Hz), 2.67 (d, $J = 8.5$ Hz), 2.56, 2.08, 1.79, and 1.70), three methylenes (δ_H 2.41 (t, $J = 7.5$ Hz), 2.09 (s) and 2.16 (dd, $J = 12.5$, 4.0 Hz)/1.96 (dd, $J = 12.5$, 3.0 Hz)), and other upfield signals in the range of 1.20–1.80 ppm. A high-magnitude ^{1}H-NMR peak between 1.20 and 1.30 ppm indicated the presence of an aliphatic chain. This was further supported by the ^{13}C signals in the range of 29.5–29.8 ppm. As in the HSQC spectrum, ^{13}C NMR identified one carbonyl carbon (δ_C 209.9), one carboxyl carbon (δ_C 180.4), one lactone carbonyl carbon (δ_C 174.2), two olefinic carbons (δ_C 150.4, 141.1), seven methine carbons (δ_C 79.3, 52.9, 48.2, 47.6, 40.8, 30.4, and 28.6), twenty one methylene carbons (δ_C 51.2, 44.0, 41.9, 40.3, 39.2, 37.0, 35.3, 29.5 $\times$ 11, 25.5, 24.2, 24.1, and 21.0), six methyl carbons (δ_C 29.7, 23.6, 21.8, 19.1, 18.2, and 13.4), and three quaternary carbons (δ_C 61.5, 58.6, and 46.4). These spectroscopic data suggested that compound **1** had a binary structure: Part I a diterpene core and Part II γ-butyrolactone aliphatic acid (Figure 1).

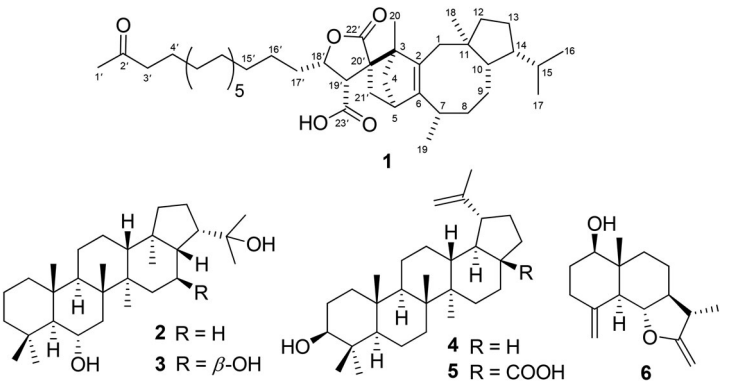

Figure 1. Chemical structures of **1–6.**

In the Part I spin system, the COSY and HMBC correlations provided structural elucidation. The COSY spectrum characterized the spin system through H-10/H-14, H-14/H_2-12, H_2-12/H_2-13, H_2-13/H-15, H-15/H_3-16, and H_3-17 in the A-ring (Supplementary material Figure S1). The HMBC showed correlations from H_3-18 (δ_H 0.75) to C-10 (δ_C 48.2), C-11 (δ_C 46.4), and C-12 (δ_C 41.9); H-15 (δ_H 1.70), H_3-16 (δ_H 0.87), and H_3-17 (δ_H 0.74) to C-14 (δ_C 47.6); and H-10 (δ_H 1.79) to C-13 (δ_C 21.0) and C-14 (δ_C 47.6). This comprised the A-ring structure (Supplementary material Figure S1). HMBC correlations were found from H_3-18 (δ_H 0.75, s) to C-1 (δ_C 40.3); H_3-19 (δ_H 0.98) to C-6 (δ_C 150.4), C-7 (δ_C 30.4), and C-8 (δ_C 37.0); and H-10 (δ_H 1.79) to C-8 (δ_C 37.0). This structure for the B-ring was supported by COSY correlations through H-10/H-9, H-9/H_2-8, H_2-8/H-7, and H-7/H_3-19. HMBC cross-peaks from H_3-20 (δ_H 1.23)to C-2 (δ_C 141.1), C-3 (δ_C 61.5), and C-4 (δ_C 51.2); and H-5 (δ_H 2.87) to C-2 (δ_C 141.1) and C-6 (δ_C 150.4). This completed the elucidation of the Part I structure. Spectroscopic data closely matched those from fusicoccadiene (Kato et al. 1998). The connection between Parts I and II was defined at C-20′ (Part II) from HMBC correlations of H_3-20 (δ_H 1.23, s) with C-20′ (δ_C 58.6) and H-5 (δ_H 2.87) with C-20′ and C-21′ (δ_C 39.2).

In Part II, HMBC correlations of H_3-1′ (δ_H 2.13) with C-2′ (δ_C 209.9) and C-3′ (δ_C 44.0), of H_2-3′ (δ_H 2.41) with C-1′ (δ_C 29.7), and C-2′ (δ_C 209.9) and C-4′ (δ_C 24.1) suggested a terminal methylketone group in the long chain. The presence of the carboxylic acid group at C-19′ was inferred from HMBC correlations of H-19′ (δ_H 2.67, 1H, d, $J = 8.5$ Hz) with C-20′ (δ_C 58.6), and C-21′ (δ_C 39.2) with C-22′ (δ_C 174.2). ^{1}H-^{1}H COSY correlations of H-18′ with H-19′ indicated that they were adjacent. The downfield chemical shift of H-18′ (δ_H 4.44) and HMBC cross-peaks of H-18′ and H-21′ with C-22′ (δ_C 174.2) indicated the presence of a lactone-ring D. HMBC correlations of H-19′ (δ_H 2.67) with C-17′ (δ_C 35.3) and of H-17′ (δ_H 1.70/1.61) with C-18′ (δ_C 79.3) and C-19′ (δ_C 52.9) suggested that the long chain was anchored at C-18′ (δ_C 79.3). This was given support by the ^{1}H-^{1}H COSY spectrum (Supplementary material Figure S1), and suggested a chemistry resembling that of aliphatic acids with a γ-butyrolactone moiety, as are common in lichens of the *Parmotrema* genera (Huynh et al. 2016). Compound **1** was therefore identified as reticulatin.

The structural similarities between Part I and fusicoccadiene, and between Part II and vinaprasorediosic acid A, suggested that the latter may be the biosynthetic

precursors of reticulatin (Supplementary material Figure S3). In particular, vinaprasorediosic acid A (i) was isomerized to its analogue (ii) (Supplementary material Figure S3). Conversion of lichesterinic acid to protolichesterinic acid was reported in Bloomer et al. (1970). The activated double bond of the intermediate at C-20′ and C-21′ initiates Diels-Alder addition with fusicoccadiene (iii) to form reticulatin. Kato et al. (1994) reported the derivation from fusicoccadiene of the natural adducts plagiospirolides A-E.

The relative stereochemistry of compound **1** was determined from NOESY correlations. In Part I, the synfacial orientation of the isopropyl group at C-14, H_3-18 (δ_H 0.75), and H_3-19 (δ_H 0.98) was established. Correlation of H-14/H-10/H-7 suggested the same β-face. In Part I, detailed comparison of NMR data from **1** with those from plagiospirolides showed strong similarity, supporting the relative configuration of **1** (Kato et al. 1994). Kato and co-workers also identified an exo-favoured adduct from the steric orientation of H_3-19, supported by single crystal X-ray crystallography. We propose that compound **1** has the same relative configuration at C-3, C-5, and C-20′. NOESY correlations of H-19′/H_3-20 with H-5/H_3-19 supported this. The syn orientations of H-19′ and H-18′ were determined from the NOESY correlation between them. Interestingly, H-19′ and H-18′ had a coupling constant of 8.5 Hz, similar to that of *syn*-protons in the γ-lactone 2-ethyl-4-methyl-5-oxotetrahydrofuran-3-carboxylic acid series (Stortz and Maier 2000).

Compounds **1–6** were evaluated for α-glucosidase inhibition. Compound **1** showed the most potent α-glucosidase inhibitory activity, with an IC_{50} value of 3.90 μM, exceeding that of the acarbose positive control (IC_{50} 165 μM). The α-glucosidase inhibition of **2-5** were reported in our previous investigations (Sichaem et al. 2017; Phan et al. 2020). The other compound showed no inhibition of α-glucosidase, with IC_{50} > 300 μM.

3. Experimental

3.1. General experimental procedures

NMR spectra were recorded on a Bruker Avance III spectrometer (500 MHz for ^{1}H NMR and 125 MHz for ^{13}C NMR) using residual solvent signals of chloroform-*d* at δ_H 7.26, δ_C 77.8 as internal reference. HR–ESI–MS was recorded using a MicrOTOF–Q mass spectrometer on an LC-Agilent 1100 LC-MSD Trap spectrometer. Thin layer chromatography (TLC) was carried out using precoated silica gel 60 F_{254} or 60 RP–18 F_{254S} (Merck). Spots were visualized by spraying with 10% H_2SO_4 solution followed by heating. Gravity column chromatography was performed on silica gel 60 (0.040–0.063 mm, Himedia). The IR spectra was measured on IS50 ATR Thermo Scienctific, Switzerland and FTIR/NIR Spectrometer-Frontier/Perkin Elmer, USA instruments. Optical rotations were measured on a Kruss digital polarimeter.

3.2. Lichen material

Thallus of lichen *P. reticulatum* was collected in Dong Nai province, Vietnam in March 2020. The formal classification of the lichen was done by Dr. Thi-Phi-Giao Vo, Faculty

of Biology, Ho Chi Minh University of Science, National University – Ho Chi Minh City. A voucher specimen (UEL-003) was deposited in the herbarium of the Department of Organic Chemistry, Ho Chi Minh University of Education.

3.3. Extraction and isolation

The material (1.8 kg) was cleaned, air-dried, and ground, then macerated with acetone (10 L x 3) at room temperature. The filtrated solution was concentrated under reduced pressure. In the course of evaporation, a precipitate was filtered out (115 g). The remaining solution was concentrated to afford the crude acetone extract (480 g). This crude extract was subjected to silica gel column chromatography, using solvents of *n*-hexane, *n*-hexane:EtOAc (1:1, v/v) and EtOAc as eluents. This afforded extracts of *n*-hexane (H, 70 g), *n*-hexane:EtOAc (HEA, 51 g), and EtOAc (EA, 180 g). Extract H was washed with acetone (200 mL × 3), leaving 20 g of TH solid. The remaining acetone solution was evaporated, yielding extract SH (45 g). This was dissolved in methanol then subjected to Sephadex LH-20 gel chromatography. Repeated elution with methanol yielded four fractions (SH1-4). Fraction SH2 (12 g) was subjected to silica gel column chromatography, then eluted with a gradient of *n*-hexane:chloroform (from 4:1 to 1:1 v/v) to afford fractions SH2.1-SH2.3. Fraction SH2.1 (2.7 g) was rechromatographed, using the same procedure, yielding subfractions SH2.1.1-SH2.1.3. Fraction SH2.1.1 (401 mg) was subjected to reverse-phase C18 column chromatography and eluted with methanol:water (95:5, v/v), providing **1** (11 mg) and **6** (21 mg). Subfraction SH2.1.2 (1.8 g) was subjected to silica gel chromatography then eluted with *n*-hexane:EtOAc (9:1, v/v), yielding **2** (201 mg), **3** (15 mg), **4** (129 mg), and **5** (85 mg).

3.3.1. Reticulatin (1)

White amorphous powder; $[\alpha]_D^{25}$ +137 (*c* 0.1, $CHCl_3$); IR cm^{-1} (neat): 2918, 2850, 1737, 1725, 1687, 1625, 1462, 1385, 1222, 1194, 1166; ^1H NMR ($CDCl_3$, 500 MHz) δ_H 4.44 (1H, td, $J = 8.0$, 4.5 Hz, H-18′), 2.87 (1H, d, $J = 3.0$ Hz, H-5), 2.67 (1H, d, $J = 8.5$ Hz, H-19′), 2.56 (1H, m, H-7), 2.41 (2H, t, $J = 7.5$ Hz, H-3′), 2.27 (1H, d, $J = 7.0$ Hz, H-4a), 2.16 (1H, dd, $J = 12.5$, 4.0 Hz, H-21′a), 2.13 (3H, s, H-1′), 2.09 (2H, s, H-1), 2.08 (1H, m, H-14), 1.96 (1H, dd, $J = 12.5$, 3.0 Hz, H-21′b), 1.79 (1H, m, H-10), 1.70 (2H, m, H-15, H-17′a), 1.61 (1H, m, H-17′b), 1.51 (2H, m, H-4′), 1.48 (1H, m, H-9a), 1.45 (1H, m, H-8a), 1.43 (3H, m, H-13), 1.38 (2H, m, H-12), 1.35 (1H, m, H-4b), 1.34 (2H, m, H-8b, H-9b), 1.29-1.24 (24H, m, H-5′ to H-16′), 1.23 (3H, s, H-20), 0.98 (3H, d, $J = 6.5$ Hz, H-19), 0.87 (3H, d, $J = 6.5$ Hz, H-16), 0.75 (3H, s, H-18), 0.74 (3H, d, $J = 8.0$ Hz, H-17). ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 209.9 (C-2′), 180.4 (C-23′), 174.2 (C-22′), 150.4 (C-6), 141.1 (C-2), 79.3 (C-18′), 61.5 (C-3), 58.6 (C-20′), 52.9 (C-19′), 51.2 (C-4), 48.2 (C-10), 47.6 (C-14), 46.4 (C-11), 44.0 (C-3′), 41.9 (C-12), 40.8 (C-5), 40.3 (C-1), 39.2 (C-21′), 37.0 (C-8), 35.3 (C-17′), 30.4 (C-7), 29.7 (C-1′), 29.5 (C-5′ to C-15′), 28.6 (C-15), 25.5 (C-16′), 24.2 (C-9), 24.1 (C-4′), 23.6 (C-16), 21.8 (C-18), 21.0 (C-13), 19.1 (C-17), 18.2 (C-19), 13.4 (C-20); HRESIMS *m/z*: $[M-H]^-$ 665.5139 for $C_{43}H_{69}O_5$-H (calcd. 665.5145).

3.4. α-glucosidase inhibition assay

The α-glucosidase inhibitory activity of the compounds was determined using a method adapted from Devi et al. (2020). All samples were analyzed in triplicate at five different concentrations around the IC_{50} values, and the mean values were retained. The inhibition percentage (%) was calculated as follows: Inhibition (%) = $[1 - (A_{sample}/A_{control})] \times 100$.

4. Conclusions

Six compounds (**1–6**) were isolated from the lichen *P. reticulatum*. Their structures were elucidated as reticulatin (**1**), zeorin (**2**), leucotylin (**3**), lupeol (**4**), betulinic acid (**5**), and dihydroreynosin (**6**). Compound **1** is a novel lichen metabolite C_{43}-spiroterpenoid. We propose that this is derived from the precusors fusicoccadiene and vinapraesorediosic acid A *via* Diels-Alder cycloaddition. Compound **1** showed potent inhibition of α-glucosidase, with an IC_{50} of 3.90 μM.

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Disclosure statement

No potential conflict of interest was reported by the authors.

References

Abdullahi SM, Musa AM, Abdullahi MI, Sule MI, Sani YM. 2013. Isolation of lupeol from the stem-bark of *Lonchocarpus sericeus* (Papilionaceae). Scholars Acad J Biosci. 1(1):18–19.

Bloomer JL, Eder WR, Hoffman WF. 1970. Biosynthesis of (+)-protolichesterinic acid in *Cetraria islandica*. J Chem Soc Perkin 1. 13:1848–1850.

Boustie J, Grube M. 2005. Lichens-a promising source of bioactive secondary metabolites. Plant Genet Resour. 3(2):273–287.

Brahmachari G, Chatterjee D. 2002. Triterpenes from *Adiantum lunulactum*. Fitoterapia. 73(5): 363–368.

Cichewicz RH, Kouzi SA. 2004. Chemistry, biological activity, and chemotherapeutic potential of betulinic acid for the prevention and treatment of cancer and HIV infection. Med Res Rev. 24(1):90–114.

Devi AP, Duong TH, Ferron S, Beniddir MA, Dinh MH, Nguyen VK, Pham NKT, Mac DH, Boustie J, Chavasiri W, et al. 2020. Salazinic acid-derived depsidones and diphenylethers with α-glucosidase inhibitory activity from the lichen *Parmotrema dilatatum*. Planta Med. 86(16):1216–1224.

Din LB, Zakaria Z, Samsudin MW, Elix JA. 2010. Chemical profile of compounds from lichens of Bukit Larut, Peninsular Malaysia. Sains Malaysiana. 39(6):901–908.

Duong T-H, Beniddir MA, Genta-Jouve G, Aree T, Chollet-Krugler M, Boustie J, Ferron S, Sauvager A, Nguyen H-H, Nguyen K-P-P, et al. 2018. Tsavoenones A–C: unprecedented polyketides with a 1, 7-dioxadispiro [4.0. 4.4] tetradecane core from the lichen *Parmotrema tsavoense*. Org Biomol Chem. 16(32):5913–5919.,

Duong TH, Chavasiri W, Boustie J, Nguyen KPP. 2015. New meta-depsidones and diphenyl ethers from the lichen *Parmotrema tsavoense* (Krog & Swinscow) Krog & Swinscow, Parmeliaceae. Tetrahedron. 71(52):9684–9691.

Duong TH, Ha XP, Chavasiri W, Beniddir MA, Genta-Jouve G, Boustie J, Chollet-Krugler M, Ferron S, Nguyen HH, Yamin BM, et al. 2018. Sanctis A–C: three racemic procyanidin analogues from the Lichen *Parmotrema sancti-angelii*. Eur J Org Chem. 2018(19):2247–2253.

Duong TH, Huynh BLC, Chavasiri W, Chollet-Krugler M, Nguyen VK, Nguyen THT, Hansen PE, Le Pogam P, Thüs H, Boustie J, et al. 2017. New erythritol derivatives from the fertile form of *Roccella montagnei*. Phytochemistry. 137:156–164.

Ghate NB, Chaudhuri D, Sarkar R, Sajem AL, Panja S, Rout J, Mandal N. 2013. An antioxidant extract of tropical lichen, *Parmotrema reticulatum*, induces cell cycle arrest and apoptosis in breast carcinoma cell line MCF-7. PLoS One. 8(12):e82293.

Huynh BL, Le DH, Takenaka Y, Tanahashi T, Nguyen KP. 2016. New phenolic compounds from the lichen Parmotrema praesorediosum (Nyl.) Hale (Parmeliaceae). Magn Reson Chem. 54(1): 81–87.

Kato N, Wu X, Nishikawa H, Nakanishi K, Takeshita H. 1993. Stereocontrolled synthesis of optically active Plaglospirolides A and B. Synlett. 1993(04):293–295.

Kato N, Wu X, Nishikawa H, Nakanishi K, Takeshita H. 1994. Total synthesis of optically active plagiospirolides A and B: highly stereoselective biomimetic Diels-Alder reaction. J Chem Soc Perkin Trans 1. 8(8):1047–1053.

Kato N, Zhang C-S, Matsui T, Iwabuchi H, Mori A, Ballio A, Sassa T. 1998. Isolation of (+)-fusicocca-2,10(14)-diene, a 5-8-5 tricyclic diterpene hydrocarbon biosynthetically related to the fusicoccin aglycon from *Fusicoccum amygdali* and confirmation of its structure by total synthesis. J Chem Soc, Perkin Trans 1. 16(16):2473–2474.

König GM, Wright AD. 1999. ^{1}H and ^{13}C-NMR and biological activity investigations of four lichen-derived compounds. Phytochem Anal. 10(5):279–284.

Kumar K, Siva B, Sarma VUM, Mohabe S, Reddy AM, Boustie J, Tiwari AK, Rao NR, Babu KS. 2018. UPLC-MS/MS quantitative analysis and structural fragmentation study of five *Parmotrema* lichens from the Eastern Ghats. J Pharm Biomed Anal. 156:45–57.

Müller K. 2001. Pharmaceutically relevant metabolites from lichens. Appl Microbiol Biotechnol. 56(1-2):9–16.

Nguyen VK, Duong TH, Nguyen KPP, Sangvichien E, Wonganan P, Chavasiri W. 2018. Chemical constituents of the lichen *Usnea baileyi* (Stirt.) Zahlbr. Tetrahedron Lett. 59(14):1348–1351.

Nguyen V-K, Genta-Jouve G, Duong T-H, Beniddir MA, Gallard J-F, Ferron S, Boustie J, Mouray E, Grellier P, Chavasiri W, et al. 2020. Eumitrins C-E: structurally diverse xanthone dimers from the Vietnamese lichen Usnea baileyi. Fitoterapia. 141:104449.

Ogura M, Cordell GA, Farnsworth NR. 1978. Anticancer sesquiterpene lactones of *Michelia compressa* (magnoliaceae). Phytochemistry. 17(5):957–961.

Pol CS, Savale SA, Khare R, Verma N, Behera BC. 2017. Antioxidative, cardioprotective, and anticancer potential of two lichenized fungi, *Everniastrum cirrhatum* and *Parmotrema reticulatum*, from Western Ghats of India. J Herbs Spices Med Plants. 23(2):142–156.

Poornima S, Ponmurugan P, Ahmed KSZ, Ayyappadasan G, Aldhafiri FK, Santhanaraj B. 2016. Evaluation of anti-cancer properties of lichens using albino wistar rats as an animal model. CRJ. 4(6):84–89.

Poornima S, Ponmurugan P, Mythili Gnanamangai B, Nagarjun N, Ayyappadasan G. 2017. Evaluation of antimicrobial, antioxidant and anticancer activities of few macrolichens collected from *Eastern Ghats* of Tamil Nadu, India. Int Res J Pharm. 8(3):39–43.

Phan HVT, Duong TH, Pham DD, Pham HA, Nguyen VK, Nguyen TP, Nguyen HH, Nguyen NH, Ang PS, Phontree K, Sichaem J. 2020. Design and synthesis of new lupeol derivatives and their α-glucosidase inhibitory and cytotoxic activities. Nat Prod Res.DOI:10.1080/14786419.2020.1758095.

Rajan VP, Gunasekaran S, Ramanathan S, Murugaiyah V, Samsudin MW, Din LB. 2016. Biological activities of four *Parmotrema* species of Malaysian origin and their chemical constituents. J App Pharm Sci. 6(8):036–043.

Reddy SD, Siva B, Kumar K, Babu VSP, Sravanthi V, Boustie J, Nayak VL, Tiwari AK, Rao CHV, Sridhar B, et al. 2019. Comprehensive analysis of secondary metabolites in *Usnea longissima* (Lichenized Ascomycetes, Parmeliaceae) using UPLC-ESI-QTOF-MS/MS and pro-apoptotic activity of barbatic acid. Molecules. 24(12):2270–2288.

Shivanna R, Garampalli RH. 2014. Efficacy of lichen extracts as biocontrol agents against *Fusarium oxysporum* F. sp. capsici. Arch Appl Sci Res. 6(4):273–277.

Sichaem J, Aree T, Lugsanangarm K, Tip-Pyang S. 2017. Identification of highly potent α-glucosidase inhibitory and antioxidant constituents from Zizyphus rugosa bark: enzyme kinetic and molecular docking studies with active metabolites. Pharm Biol. 55(1):1436–1441.

Sinha S, Biswas M. 2011. Evaluation of antibacterial activity of some lichen from Ravangla, Sikkim, India. Int J Pharm Bio Sci. 2(4):23–28.

Sporle J, Becker H, Allen NS, Gupta MP. 1991. Spiroterpenoids from *Plagiochila moritziana*. Phytochemistry. 30(9):3043–3047.

Sporle J, Becker H, Gupta MP, Veith M, Huch V. 1989. Novel C-35 terpenoids from the Panamanian Livewort *Plagiochila moritziana*. Tetrahedron. 45(16):5003–5014.