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Research Article

The phytochemical investigation from *n*-hexane extract of the lichen *Roccella montagnei*

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ABSTRACT

Introduction: *Roccella montagnei* is widely distributed in subtropical regions. As the continuous study on the hexane extract of *Roccella montagnei* lichen, the isolation and structural determination of five compounds were addressed. **Method:** The crude extract was obtained from the dried lichen powder's extraction at room temperature. The *n*-hexane, *n*-hexane-ethyl acetate, and ethyl acetate extracts were obtained by the liquid-liquid partition method. The organic compounds were isolated from *n*-hexane extract by silica gel and Sephadex LH-20 column chromatography. Their chemical structures were identified by the NMR and HR-ESI-MS data analysis and the comparison of their NMR data with the published data. **Results:** Five compounds were isolated and chemically structural identified, consisting of 3β-hydroxy-7α-methoxystigmast-5-ene **(1)**, sekikaic acid **(2)**, lichenxanthone **(3)**, (+)-6,8-dihydroxy-3-propyl-3,4-dihydroisocoumarin **(4)**, and ar-turmerone **(5)**. **Conclusion:** To the best of our knowledge, except **3** which was reported from this species for the first time, four isolated compounds left did not known to be present in *Roccella* genus before.

Key words: *Roccella montagnei*, lichen, sterol, aromatic compound

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INTRODUCTION

Rocclella genus distributes in the subtropical regions, Mediterranean and mainly in the Northern hemisphere[1]. *Roccella montagnei* species is commonly found along the Coromandel coast and in the mangrove forest in Indian and in the South of Vietnam[2]. The previously chemical investigations on this species showed the presence of depside, depsidone, quinone, sterol, usnic acid derivatives, and phenolic compounds[3–5]. The bioactive assessments on extracts and isolated compounds from this species revealed anti-inflammatory, antimicrobial, anti-arthritic, antioxidant, and anticancer activities[2,4,6,7]. The phytochemical investigation on this species was further studied on *n*-hexane extract led to the isolation and structural elucidation of 5 compounds.

MATERIALS AND METHODS

General experimental procedures

NMR spectra were recorded on Bruker Avance at 500 MHz for ^{1}H-NMR and 125 MHz for ^{13}C-NMR or on Bruker Avance III at 400 MHz for ^{1}H-NMR and 100 MHz for ^{13}C-NMR. In addition, the HR-ESI-MS spectra were acquired on a Bruker MicrOTOF-Q 10187. The NMR and MS spectra were done at the Center Analysis Laboratory of the University of Science, Vietnam National University (VNU)–Ho Chi Minh City and the Institute of Drug Quality Control Ho Chi Minh city.

Plant material

The lichen *Roccella montagnei* was collected at Tuy Phong District, Binh Thuan Province, Vietnam, in June 2018. The scientific name of the lichen was authenticated by Dr. Holger Thüs, Life Science Department, The Natural History Museum, Cromwell Road, SW7 5BD London, England, UK. In addition, a voucher specimen (No US–B024) was deposited in the Herbarium of Department of Organic Chemistry, Faculty of Chemistry, University of Science, VNU HCM.

Extraction and isolation

The fresh lichen *Roccella montagnei* (7.5 kg) was cleaned, air-dried, and ground into powder. Then, 876.8 g of crude extract was prepared using the above lichen powder in ethanol (3x10L) at room temperature. Next, this crude extract was applied to liquid-liquid partition step with *n*-hexane (100%), *n*-hexane:ethyl acetate (1:1, v/v), and ethyl acetate (100%) in turn to afford extracts, including *n*-hexane (H, 200.9 g), *n*-hexane:ethyl acetate (1:1) (H:EA, 225.5 g), and ethyl acetate (EA, 313.6 g).

The *n*-hexane extract was subjected to silica gel column chromatography which was eluted with *n*-

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hexane: ethyl acetate (13:1) to give seven sub-fractions (coded, PH1-PH7). PH2 (43.7 g) was applied to Sephadex-LH20, eluted with methanol to obtain five sub-fractions (coded, 2.1-2.5). Then, two compounds, **1** (10 mg) and **5** (8.7 mg) were isolated from sub-fraction 2.2 (4.5 g) by the silica gel column chromatography method, eluted with the solvent system of *n*-hexane:chloroform: ethyl acetate (15:1:1). Next, PH4 (6.7 g) was separated into four sub-fractions 4.1 to 4.1 by the Sephadex-LH20 column chromatography, eluted with methanol. Afterward, sub-fractions 4.3 (2.4 g) was subjected to the C-18 reversed-phase silica gel column chromatography, eluted with the solvent system of Me: H_2O (15:1) to obtain **3** (11 mg) and **4** (7 mg). The same procedure was applied to sub-fraction PH7 (50.8 g) to afford **2** (9.5 mg).

RESULTS

From the *n*-hexane extract of the lichen *Roccella montagnei*, collected at Binh Thuan Province, five compounds, **1** (10 mg), **2** (9.5 mg), **3** (11 mg), **4** (7 mg), and **5** (8.7 mg), were isolated. Their physical properties and spectroscopic data were performed as follows.

3β-Hydroxy-7α-methoxystigmast-5-ene (1): Colorless powder. The ^{1}H-NMR ($CDCl_3$): δ_H 3.62 (*tt*, 5.0, 11.0 Hz, H-3), 2.36 (*ddd*, 1.8, 5.0, 13.0, H-4a), 2.30 (*ddt*, 1.5, 11.0, 13.0, H-4b), 5.74 (*dd*, 2.0, 5.0, H-6), 3.29 (*brt*, 4.0, H-7), 1.96 (*dt*, 3.5, 12.5, H-12), 0.66 (*s*, H-18), 0.98 (*s*, H-19), 0.92 (*d*, 6,5 Hz, H-21), 0.81 (*d*, 7.0 Hz, H-26), 0.83 (*d*. 6.5 Hz, H-27), 0.86 (*t*, 7.5 Hz, H-29), 3.35 (*s*, -OCH_3). The ^{13}C-NMR ($CDCl_3$): δ_C 36.9 (C-1), 31.6 (C-2), 71.6 (C-3), 42.5 (C-4), 146.3 (C-5), 120.9 (C-6), 74.1 (C-7), 37.4 (C-8), 42.9 (C-9), 37.6 (C-10), 21.0 (C-11), 39.2 (C-12), 42.3 (C-13), 49.2 (C-14), 24.4 (C-15), 28.4 (C-16), 55.9 (C-17), 11.6 (C-18), 18.4 (C-19), 36.3 (C-20), 19.0 (C-21), 34.1 (C-22), 26.2 (C-23), 46.0 (C-24), 29.4 (C-25), 19.2 (C-26), 20.0 (C-27), 23.3 (C-28), 12.2 (C-29), 56.9 (-OCH_3).

Sekikaic acid (2): Colorless solid. The ^{1}H-NMR ($CDCl_3$): δ_H 6.38 (*s*, H-3), 6.38 (*s*, H-5), 2.99 (*m*, H-8), 1.74 (*m*, H-9), 0.94 (*t*, 7.2 Hz, H-10), 3.83 (*s*, 4-OCH_3), 6.43 (*s*, H-5′), 2.97 (*m*, H-8′), 1.64 (*m*, H-9′), 1.00 (*t*, 6.8 Hz, H-10′), 3.89 (*s*, 4′-OCH_3). The ^{13}C-NMR (Acetone-d_6): δ_C 105.5 (C-1), 165.8 (C-2), 99.7 (C-3), 165.4 (C-4), 111.4 (C-5), 149.0 (C-6), 169.3 (C-7), 39.2 (C-8), 26.1 (C-9), 14.6 (C-10), 55.9 (4-OCH_3), 107.0 (C-1′), 157.3 (C-2′), 125.6 (C-3′), 156.2 (C-4′), 106.7 (C-5′), 146.8 (C-6′), 174.2 (C-7′), 39.2 (C-8′), 25.7 (C-9′), 14.6 (C-10′), 56.5 (4′-OCH_3). Selected HMBC correlations: see Figure 2.

Lichenxanthone (3): White crystal. The ^{1}H-NMR ($CDCl_3$): δ_H 6.30 (*d*, 2.0 Hz, H-2), 6.34 (*d*, 2.4 Hz, H-4), 6.69 (*d*, 2.4 Hz, H-5), 6.67 (*d*, 2.0 Hz, H-7), 2.85 (*s*, H-9), 3.87 (*s*, 3-OCH_3), 3.90 (*s*, 6-OCH_3), 13.39 (*s*, 1-OH).

(+)-6,8-Dihydroxy-3-propyl-3,4-dihydroisocoumarin (4): Colorless needle crystal, $[\alpha]_D^{20}$ = + 170 (*c* 0.1, MeOH). HR-ESI-MS: *m/z* 245.0794 $[M+Na]^+$. The ^{1}H-NMR ($CDCl_3$): δ_H 4.53 (*m*, H-3), 2.82 (*dd*, 4.4, 16.4 Hz, H-4a), 2.88 (*dd*, 10.4, 16.0 Hz, H-4b), 6.31 (*brs*, H-5), 6.21 (*brs*, H-7), 1.68 (*m*, H-1′a), 1.88 (*dddd*, 5.2, 7.6, 10.0, 13.6 Hz, H-1′b), 1.49 – 1.58 (*m*, H-2′), 0.97 (*t*, 7.2 Hz, H-3′), 6.00 (*brs*, 6-OH), 11.20 (*s*, 8-OH).

Ar-turmerone (5): Yellow solid, $[\alpha]_D^{20}$ = 0 (*c* 0.2, MeOH). The ^{1}H-NMR ($CDCl_3$): δ_H 2.31 (*s*, H-1), 7.10 (*s*, H-3/H-7; H-4/H-6), 3.29 (*m*, H-8), 2.72 (*dd*, 8.0, 16.4 Hz, H-9a), 2.60 (*dd*, 8.0, 16.4 Hz, H-9b), 6.02 (*s*, H-11), 2.10 (*d*, 1.6 Hz, H-13), 1.85 (*d*, 1.6 Hz, H-14), 1.24 (*d*, 6.8 Hz, H-15). The ^{13}C-NMR ($CDCl_3$): δ_C 21.1 (C-1), 135.9 (C-2), 129.2 (C-3/C-7), 126.8 (C-4/C-6), 143.5 (C-5), 35.4 (C-8), 52.8 (C-9), 200.1 (C-10), 124.2 (C-11), 155.3 (C-12), 20.9 (C-13), 27.9 (C-14), 22.1 (C-15). Selected HMBC correlations: see Figure 2.

DISCUSSION

Compound **1** was isolated as a colorless powder. The ^{1}H-NMR spectrum showed an olefinic methine proton signal at δ_H 5.74 (*dd*, 2.0, 5.0, H-6), two oxygenated methine protons at δ_H 3.62 (*tt*, 5.0, 11.0 Hz, H-3) and 3.29 (*brt*, 4.0, H-7), a methoxy proton signal at δ_H 3.35 (*s*, -OCH_3) and the rest proton signals resonating at high magnetic field including two singlets (δ_H 0.66 and 0.98), three doublets (δ_H 0.92, 0.81, and 0.83) and a triplet (δ_H 0.86) methyl signals which characterized for the stigmastane skeleton. It corresponded to the presence of a methoxy carbon and 29 carbons of the stigmastane. Two olefinic carbon signals resonated at δ_C 146.3 and 120.9 were a quaternary olefinic carbon (=C<, C-5) and a methine carbon (=CH-, C-6), respectively, in stigmast-5-ene as usual. The proton H-3 showed the large coupling constant value of 11.0 Hz with both axial protons H-2 and H-4, which approved the β-configuration of the hydroxy group at C-3. Pettit and co-worker[8] reported that the 7-methoxystigmast-5-ene compounds displayed a large coupling constant of 8.2 Hz of proton H-7α and a small coupling constant of 4.8 Hz of proton H-7β. The compound **1** revealed the signal at δ_H 3.29 (*brt*, 4.0) of H-7, demonstrating the α-configuration of the 7-methoxy group. Based on the above analysis and the good compatibly NMR data with those published

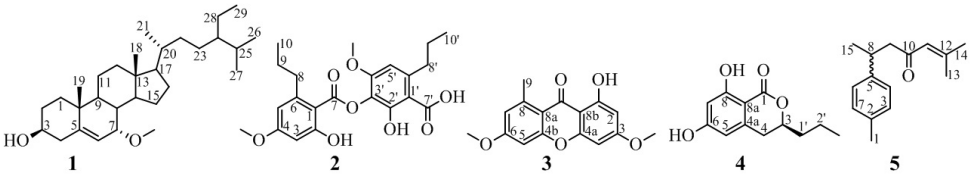

Figure 1: The chemical structures of isolated compounds **1**-**5**

in the literature[8], **1** was suggested to be 3β-hydroxy-7α-methoxystigmast-5-ene.

Compound **2** was isolated as a colorless solid. The ^{1}H-NMR spectrum displayed aromatic proton signals at δ_H 6.38 (2H, *s*, H-3/H-5) of a tetra-substituted benzene ring and 6.43 (*s*, H-5′) of a penta-substituted one. Two methoxy proton signals were observed at δ_H 3.83 (*s*, 4-OCH_3), 3.89 (*s*, 4′-OCH_3). At the higher magnetic field, it showed signals of two *n*-propyl moieties at δ_H [2.99 (*m*, H-8), 1.74 (*m*, H-9), 0.94 (*t*, 7.2 Hz, H-10)] and [2.97 (*m*, H-8′), 1.64 (*m*, H-9′), 1.00 (*t*, 6.8 Hz, H-10′)] which were further identified by the HMBC cross-peaks as shown in Figure 2. The ^{13}C-NMR spectrum showed 22 signals consisting of twelve signals of two benzene rings from 99.7 to 165.8 ppm, two carboxyl carbons at δ_C 169.3 (C-7) and 174.2 (C-7′), two methoxy carbons at δ_C 55.9 (4-OCH_3) and 56.5 (4′-OCH_3), and six final carbon signals from 14.6 to 39.2 ppm belonging to two *n*-propyl chains. The position of two methoxys were C-4 and C-4', which were confirmed by HMBC correlations of the methoxy protons to carbons at δ_C 165.4 (C-4) and 156.2 (C-4′). The HMBC correlations of H-8 to carbon C-1, C-5, and C-6, of H-8' to carbons C-1', C-5', and C-6' determined the positions of two n-propyl groups at C-6 and C-6'. All other HMBC correlations confirmed the chemical structure of **2**. Additionally, the comparison of NMR data of **2** with the published data[9] showed good compatibility; therefore, **2** was assigned as sekikaic acid.

Compound **3** was isolated as a white crystal. The ^{1}H-NMR spectrum showed a signal at δ_H 13.39 (*s*, 1-OH) of the proton of a phenolic hydroxy group which was chelated to an *ortho*-carbonyl group, two *meta*-doublet signals which had the multiplet skewing effect together at δ_H 6.30 (*d*, 2.0 Hz, H-2), 6.34 (*d*, 2.4 Hz, H-4) of a tetra-substituted benzene ring, two other *meta*-doublet signals δ_H 6.69 (*d*, 2.4 Hz, H-5), 6.67 (*d*, 2.0 Hz, H-7) of the second tetra-substituted benzene ring. The moderate magnetic zone revealed signals of two methoxy groups at δ_H 3.87 (*s*, 3-OCH_3) and 3.90 (*s*, 6-OCH_3). The final proton signal at δ_H 2.85 (*s*, H-9) was belonged to a methyl group connected to a benzene ring. Besides, the NMR data of **3** showed highly relevant to the published data[10], **3** was thus determined as lichenxanthone.

Compound **4** was isolated as a colorless needle crystal. The HR-ESI-MS of **4** showed the *sodiated* ion peak at *m/z* 245.0794 $[M+Na]^+$ (calcd. for $C_{12}H_{14}O_4Na$, 245.0790) which deduced its molecular formula to be $C_{12}H_{14}O_4$. The ^{1}H-NMR spectrum displayed a singlet proton signal at δ_H 11.20 (*s*, 8-OH) of a phenolic hydroxy group which was chelated to an *ortho*-carbonyl group. Two broad-singlet proton signals at 6.31 (*brs*, H-5) and 6.21 (*brs*, H-7) suggested the presence of a 1,2,3,5-tetra-substituted benzene ring. A very broad-singlet signal integrated one proton at δ_H 6.00 (*brs*, 6-OH) was deduced to a hydroxy group which did not exist the intramolecular hydrogen bond. There was a multiplet signal at δ_H 4.53 (H-3) of an oxygenated methine group in the magnetic zone of protons on the carbon attached to the single-bonded oxygen. Signals of two non-equivalent protons of a methylene group deshielded *at* δ_H 2.82 (*dd*, 4.4, 16.4 Hz, H-4a) and 2.88 (*dd*, 10.4, 16.0 Hz, H-4b) due to the attachment to sp^2 quaternary carbon and a chiral methine group. At highest magnetic field, the observation of a triplet signal, integrated three protons at 0.97 (*t*, 7.2 Hz, H-3′) belonged a methyl group which was adjacent one methylene group. Four remaining protons at δ_H 1.68 (1H, *m*, H-1′a), 1.88 (1H, *dddd*, 5.2, 7.6, 10.0, 13.6 Hz, H-1′b), 1.49 (1H, *m*, H-2'a), and 1.58 (1H, *m*, H-2′b) were deduced the presence of two methylene groups. Based on the above information and the good compatibility of its NMR data with those published in the literature[11], along with its dextrorotatory activity $[\alpha]_D^{20}$ = + 170 (*c* 0.1, MeOH), **4** was determined as (+)-6,8-dihydroxy-3-propyl-3,4-dihydroisocoumarin.

Compound **5** was isolated as a yellow solid. The ^{1}H-NMR spectrum of **5** displays a singlet proton signal integrated four-protons at δ_H 7.10 (, H-3/H-7; H-4/H-6) para-disubstituted benzene ring, a singlet

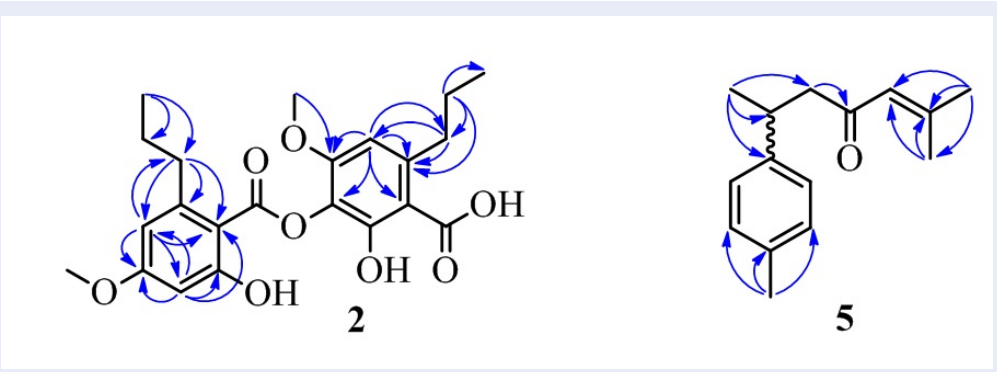

Figure 2: Selected HMBC correlations of **2** and **5**

olefinic proton at δ_H 6.02 (1H, *s*, H-11) of a methine group =CH- attached to two quaternary carbons. At the high magnetic field, the proton spectrum displayed signals at δ_H 2.10 (*d*, 1.6 Hz, H-13) and 1.85 (*d*, 1.6 Hz, H-14), which possessed HMBC correlations to the same olefinic carbons at δ_C 124.2 (C-11), 155.3 (C-12). These signals suggested the presence of -CH=C(CH_3)$_2$ moiety. A methyl proton signal resonated at 2.31 (*s*, H-1) was suggested to attach to the benzene ring (as *para*-$CH_3C_6H_4$-), which was further confirmed by HMBC cross-peaks of this proton signal to aromatic carbons at δ_C 135.9 (C-2) and 129.2 (C-3/C-7). A proton signal appearing as a doublet, integrated three-protons at 1.24 (*d*, 6.8 Hz, H-15) was assigned to the methyl group attached to the other methine group. This methyl proton signal showed HMBC correlations to a quaternary aromatic carbon C-5 at 143.5 (C-5), a methine carbon C-8 (35.4), and a methylene carbon C-9 (52.8), which demonstrated the presence of CH_3-CH($C_6H_4CH_3$)-CH_2- fragment. The ^{13}C-NMR spectrum showed a ketone carbon signal shielded at 200.1 (C-10), deduced to be the ketone group conjugated to the double bond. It corresponded to the sole quaternary olefinic carbon C-12 shifted to the higher frequency at 155.3 ppm. All the rest of HMBC correlations supported the chemical structure as shown. Additionally, the comparison of its NMR data to those reported in the literature[12] gave further evidence to confirm the chemical structure of **5** as ar-turmerone. The optical rotation value of $[\alpha]_D^{20}$ = 0 suggested **5** to be a racemic mixture of ar-turmerone. Ar-turmerone was known as the major bioactive compound of *Curcuma longa* species and possessing anti-inflammatory and neuroprotective property[13].

CONCLUSION

From the *n*-hexane extract of the lichen *Roccella montagnei*, five compounds were isolated consisting of a sterol (3β-hydroxy-7α-methoxy-stigmast-5-ene), a depside (sekikaic acid), a xanthone (lichenxanthone), a coumarin derivative ((+)-6,8-dihydroxy-3-propyl-3,4-dihydroisocoumarin), and an ar-turmerone **(5)**. Their chemical structures were elucidated by NMR, MS spectroscopic data analysis, optical rotations, and the comparison to the published data. Four isolated compounds **1**, **2**, **4**, and **5** were reported to presence in the *Roccella* genus for the first time while **3** had been already isolated from other species of this genus. The ongoing studies on this species are in progress.

ABBREVIATIONS

HR-ESI-MS: High resolution-Electrospray ionization-Mass spectrometry
^{1}H-NMR: Proton nuclear magnetic resonance
^{13}C-NMR: Carbon-13 nuclear magnetic resonance
HSQC: Heteronuclear single quantum coherence
HMBC: Heteronuclear multiple bond correlation
s: singlet
brs: broad singlet
d: doublet
t: triplet
m: multiplet

COMPETING INTEREST

The authors declare no competing financial interest.

AUTHORS' CONTRIBUTION

Duong T.H contributed to conducting experiments, acquisition of data, and interpretation of data. Nguyen T. H. T interpreted NMR and MS data as well as gave final approval of the manuscript to be submitted.

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