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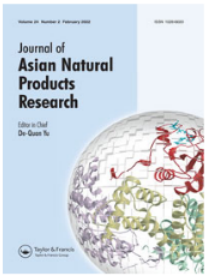

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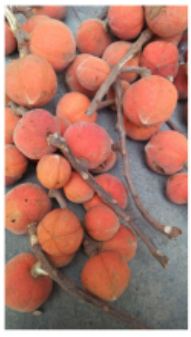
Limonoids from the fruits of *Chisocheton lasiocarpus* (Meliaceae)

Dewa Gede Katja[a], Erina Hilmayanti[b], Nurlelasari[b], Tri Mayanti[b], Desi Harneti[b], Rani Maharani[b,c], Kindi Farabi[b,c], Darwati[b], Ronny Lesmana[c,d], Sofa Fajriah[e], Unang Supratman[b,c], Mohamad Nurul Azmi[f] and Yoshihito Shiono[g]

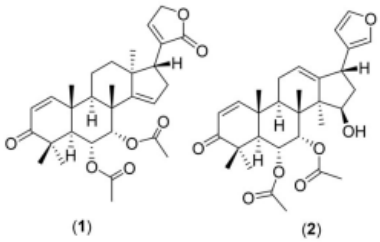
[a]Departement of Chemistry, Faculty of Mathematics and Natural Sciences, Sam Ratulangi University, Manado 95115, Indonesia; [b]Department of Chemistry, Faculty of Mathematics and Natural Sciences, Universitas Padjadjaran, Jatinangor 45363, Sumedang, West Java, Indonesia; [c]Central Laboratory of Universitas Padjadjaran, Jatinangor, Sumedang 45363, Indonesia; [d]Physiology Division, Department of Biomedical Sciences, Faculty of Medicine, Universitas Padjadjaran, Jatinangor 45363, Indonesia; [e]Research Center for Chemistry, Indonesian Science Institute, Serpong 15311, South Tangerang, Indonesia; [f]School of Chemical Sciences, Universiti Sains Malaysia, Minden, Penang 11800, Malaysia; [g]Department of Bioresources Engineering, Faculty of Agriculture Yamagata University, Tsuruoka-shi, Yamagata 997-8555, Japan

ABSTRACT

Two new azadirone-type limonoids, namely lasiocarpine A (**1**) and lasiocarpine B (**2**) were isolated from the fruit of *Chisocheton lasiocarpus* along with three known limonoids (**3**–**5**). UV, IR, one- and two- dimensional NMR, and mass spectrometry were used to determine the chemical structure of the isolated compounds. Furthermore, their cytotoxic activity against breast cancer cell line MCF-7 was evaluated using PrestoBlue reagent. From these compounds, lasiocarpine A (**1**) showed the strongest activity with an IC_{50} value of 43.38 μM.



Chisocheton lasiocarpus Fruits



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CONTACT Dewa Gede Katja dewakatja20@gmail.com Departement of Chemistry, Faculty of Mathematics and Natural Sciences, Sam Ratulangi University, Manado 95115, Indonesia; Unang Supratman unang.supratman@unpad.ac.id Department of Chemistry, Faculty of Mathematics and Natural Sciences, Universitas Padjadjaran, Jatinangor 45363, Sumedang, West Java, Indonesia

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1. Introduction

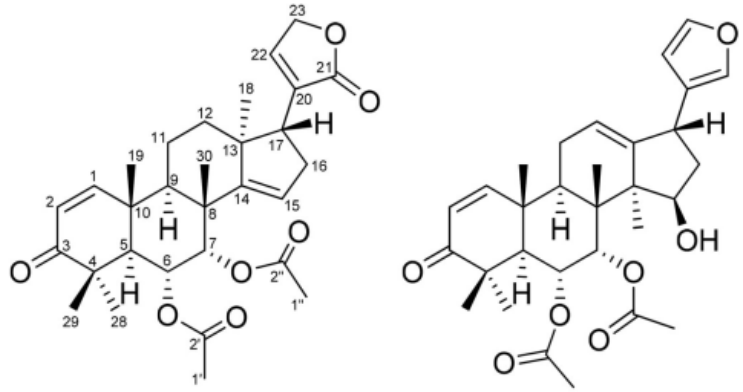
Limonoid is a class of naturally occurring compounds derived from triterpenoids that formed by the loss of four terminal carbons to form a 4,4,8-trimethyl-17-furanilsteroid skeleton. Further modification of the limonoid skeleton allows a wide and complex structural diversity of this compound [1–3]. They are produced abundantly in Meliaceae and Rutaceae plants but less common in Cneoraceae and Simaroubaceae families [4–6]. Limonoids from Meliaceae family have more diverse structures and one of the genera that contributes the most limonoid content is the *Chisocheton* genus. This type of compound has been reported to be found in all tissues including barks, stembarks, leaves, twigs, roots, seeds, and fruits [7, 8].

Chisocheton plants consist of 53 species distributed from eastern India, Nepal, Myanmar, South China, Thailand, Philippines, Malaysia, Papua New Guinea, and Indonesia to northern Australia [8, 9]. In Indonesia, these plants can be found on the islands of Sumatra, Java, Kalimantan, Sulawesi, and Papua [10, 11]. In the study conducted on limonoid compounds from Indonesian *Chisocheton* plants, dysobinol from *C. macrophyllus* seed [12] and pentandricine B-D from *C. pentandrus* stembark were reported [13]. In the further phytochemical investigation of *Chisocheton* plants, *C. lasiocarpus* was reported as an endemic plant in native habitat from Maluku to Solomon Islands [14]. However, there is still limited phytochemicals report of this plant. As continuous search for cytotoxic compound from Indonesian *Chisocheton* plants, five limonoids involving new azadirone-type limonoids (**1**–**2**) were isolated from the fruit of *C. lasiocarpus*. Herein, we report their isolation, structural elucidation and cytotoxic activity against MCF-7 breast cancer cells lines.

2. Results and discussion

The methanol extract of *C. lasiocarpus* fruit was dissolved in water and extracted by liquid-liquid extraction techniques successively using *n*-hexane, ethyl acetate, and *n*-butanol. The phytochemical analysis of the extracts showed that the ethyl acetate extract contained an abundance of limonoid content. The separation of the ethyl acetate extract was conducted using column chromatography on silica gel and octadecyl silane as the stationary phase to give five limonoids, **1**–**5** (Figures 1 and S1).

Lasiocarpine A (**1**) was obtained as a colorless amorphous solid (MeOH) with a molecular formula of $C_{30}H_{38}O_7$ based on analysis of HR-TOFMS spectra with peak ion-molecule $[M+H]^+$ at *m/z* 511.2691 having twelve degrees of unsaturation. Meanwhile, the UV spectrum showed maximum absorption at 230 nm (log ε 2.62), indicating the presence of a conjugated system. The IR spectrum showed the presence of C-H aliphatic (ν_{max} 2917 cm^{-1}), conjugated carbonyl (ν_{max} 1729 cm^{-1}), conjugated carbonyl ester (ν_{max} 1676 cm^{-1}), *gem*-dimethyl (ν_{max} 1447 cm^{-1}), and ether groups (ν_{max} 1084 cm^{-1}). Furthermore, the ^{1}H-NMR spectrum (Table 1) showed five tertiary methyls typical for azadirone-type limonoid skeleton at δ_H 0.86 (3H, *s*, CH_3-18), 1.25 (3H, *s*, CH_3-19), 1.18 (3H, *s*, CH_3-28), 1.34 (3H, *s*, CH_3-30), 1.24 (3H, *s*, CH_3-29), two additional methyl singlets from acetoxy groups at δ_H 2.00 (3H, *s*, CH_3-1′) and 2.04 (3H, *s*, CH_3-1″), four sp^2 methines at δ_H 5.36 (1H, *d*, *J* = 1.5 Hz, H-15), 5.91 (1H, *d*, *J* = 10.0 Hz, H-2), 7.14 (1H, *d*, *J* = 10.0 Hz, H-1), and 7.21 (1H, *d*, *J* = 1.5 Hz,



(1) (2)

Figure 1. Chemical structures of compounds (1) and (2).

Table 1. ^{1}H and ^{13}C NMR spectral data for compounds 1 and 2 (500 MHz for ^{1}H and 125 MHz for ^{13}C).

	Compound 1		Compound 2	
	^{13}C- NMR δ_C (mult.)	^{1}H-NMR δ_H [(ΣH; mult.; J (Hz)]	^{13}C- NMR δ_C (mult.)	^{1}H-NMR δ_H [(ΣH; mult.; J (Hz)]
1	157.3 (d)	7.14 (1H, d, 10.0)	157.3 (d)	7.05 (1H, d, 10.0)
2	126.2 (d)	5.91 (1H, d, 10.0)	125.8 (d)	5.91 (1H, d, 10.0)
3	204.7 (s)	–	204.5 (s)	–
4	40.9 (s)	–	44.6 (s)	–
5	48.0 (d)	2.49 (1H, d, 12.5)	47.4 (d)	2.60 (1H, d, 12.5)
6	69.9 (d)	5.44 (1H, d, 2.5)	70.0 (d)	5.48 (1H, dd, 2.5, 12.5)
7	74.6 (d)	5.42 (1H, d, 2.5)	75.6 (d)	5.73 (1H, d, 2.5)
8	43.2 (s)	–	42.6 (s)	–
9	37.1 (d)	2.26–2.31 (1H, m)	39.7 (d)	2.35–2.37 (1H, m)
10	45.0 (s)	–	41.1 (s)	–
11	16.5 (t)	1.68–1.81 (2H, m)	23.5 (t)	1.96–2.02 (2H, m)
12	32.7 (t)	1.88–1.95 (2H, m)	116.0 (d)	5.30–5.33 (1H, m)
13	47.3 (s)	–	151.5 (s)	–
14	158.1 (s)	–	53.1 (s)	–
15	119.2 (d)	5.36 (1H, d, 3.5)	81.6 (d)	4.16 (1H, br. s)
16	34.1 (t)	2.06–2.08 (1H, m)	42.2 (t)	2.10–2.23 (2H, m)
17	50.9 (d)	2.8 (1H, t, 7.5)	37.7 (d)	3.81 (1H, t, 10.0)
18	20.8 (q)	0.86 (3H, s)	20.2 (q)	1.07 (3H, s)
19	20.5 (q)	1.25 (3H, s)	28.4 (q)	1.29 (3H, s)
20	134.1 (s)	–	127.5 (s)	–
21	174.2 (s)	–	138.9 (s)	7.27 (1H, d, 5.0)
22	146.6 (d)	7.21 (1H, d, 2.5)	109.9 (d)	6.23 (1H, s)
23	70.3 (t)	4.83 (2H, d, 2.5)	143.1 (d)	7.35 (1H, d, 2.0)
28	21.4 (q)	1.18 (3H, s)	20.8 (q)	1.18 (3H, s)
29	31.7 (q)	1.24 (3H, s)	31.4 (q)	1.25 (3H, s)
30	26.9 (q)	1.34 (3H, s)	20.3 (q)	1.33 (3H, s)
2′	170.1 (s)	–	169.9 (s)	–
1′	21.2 (q)	2.00 (3H, s)	21.2 (q)	2.03 (3H, s)
2"	170.3 (s)	–	171.4 (s)	–
1"	21.1 (q)	2.04 (3H, s)	21.6 (q)	2.14 (3H, s)

H-22), three proton signals of oxygenated carbon including one oxygenated methylene at δ_H 4.83 (2H, *d*, J = 2.5 Hz, H-23), two oxygenated methines at δ_H 5.42 (1H, *d*, J = 2.5 Hz, H-7) and 5.44 (1H, *d*, J = 2.5 Hz, H-6), and several aliphatic signals in the shielded region were also observed.

The ^{13}C NMR and DEPT 135° spectra (Table 1) showed 30 carbon signals and inferred the presence of five quaternary methyl groups that are a characteristic of intact azadirone-type limonoid at δ_C 20.8 (C-18), 20.5 (C-19), 21.4 (C-28), 31.7 (C-29), 26.9 (C-30), and two quaternary methyls from two acetoxy groups at δ_C 21.2 (C-1′) and 21.1 (C-1′′). The signals at δ_C 77.3 (C-1), 126.2 (C-2), and 204.7 (C-3) in the ^{13}C-NMR spectrum represented the α,β-unsaturated carbonyl moiety at the ring-A. Furthermore, two sp^2 methine carbons at δ_C 119.2 (C-15) and 146.6 (C-22), together with two sp^2 quaternary carbons at δ_C 158.1 (C-14) and 134.1 (C-20), were also observed as double bonds at those position. One lactone carbonyl at δ_C 174.2 (C-21), two ester carbonyls at δ_C 170.1 (C-2′) and 170.3 (C-2′′), and three oxygenated carbon signals at δ_C 74.6 (C-7), 69.9 (C-6) and 70.3 (C-23) were observed in the ^{13}C-NMR spectrum. The acetoxy groups were bonded to two oxygenated carbons and the carbon at δ_C 70.3 (C-23) was a signal for methylene carbon at the lactone side chain. These functionalities accounted for seven out of the twelve degrees of unsaturation, and five degrees belong to pentacyclic ring of azadirone-type limonoid [15, 16]. The comparison between the NMR spectra of **1** and pentrandicine D isolated from *C. pentandrus* [16] and 23-dehydroxyazadironolide isolated from *Azadirachta indicia* [17] showed that compound **1** has similar rings A, B, C, and D but with two acetoxy groups and α,β-unsaturated-γ-lactone side chain instead. All the assignments from ^{1}H, ^{13}C NMR, and DEPT spectra of **1** were supported by ^{1}H–^{1}H COSY, HMQC, and HMBC spectra. The ^{1}H-^{1}H COSY spectrum of compound **1** showed correlations between H_1-H_2, H_5-H_6-H_7, H_9-H_{11}-H_{12}, and H_{15}-H_{16}-H_{17}, and H_{22}-H_{23}. This confirmed the partial structure of intact limonoid azadirone-type skeleton with two acetoxy groups at ring B and α,β-unsaturated-γ-lactone with the lactone carbonyl at the position of C-21. Furthermore, the HMBC experiment was conducted to confirm the position of each functional groups of the skeleton (Figure 2), the correlations of H-1 to C-3, C-5, and C-9 supporting the presence of 1-en-3-on moiety at ring A, a typical characteristic of azadirone-type limonoid [18, 19]. It also showed a cross peak from H-15 to C-13, C-16, and C-17 and inferred the position of the double bond between C-14 and C-15. Similarly, the cross peaks of H-22 and H-23 to C-20 and C-21 as well as H-17 to C-20 showed the α,β-unsaturated-γ-lactone with the lactone carbonyl at the position of C-21 and that C-20 connected to C-17.

The relative configuration of **1** was determined by the NOESY experiment (Figure 3). Based on biosynthetic approach, CH_3-30 and CH_3-29 was on the β-orientation while the CH_3-18 was on the α-orientation [20]. The spectrum showed the correlations between H-6, H-7, and H-17 to CH_3-30, indicating both oxygenated protons H-6/H-7 and H-17 were β-orientation and the acetoxy groups, as well as the lactone group, were at the opposite sides at α-orientation. That was supported by the correlations of both methyls of the acetoxy groups and H-22 with CH_3-18 at α-orientation. Furthermore, H-5 and H-9 as protons at asymmetry carbons were determined as α-orientation based on its correlations with CH_3-18. Therefore, compound **1** was elucidated as a new azadirone-type limonoid, named lasiocarpine A.

Lasiocarpine B (**2**) was isolated as a white amorphous solid (MeOH), with a molecular formula of $C_{30}H_{38}O_7$ following the analysis of HR-TOFMS at *m/z* 511.2685 $[M+H]^+$ with twelve degrees of unsaturation. In addition, the UV spectrum showed

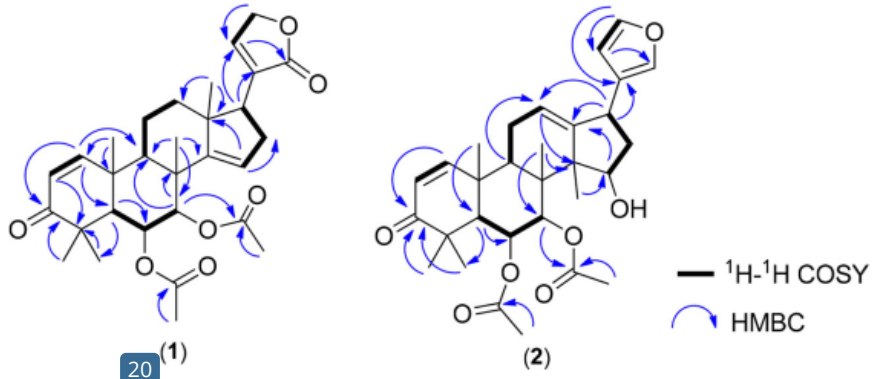


Figure 2. Selected HMBC and ^{1}H-^{1}H COSY correlations.

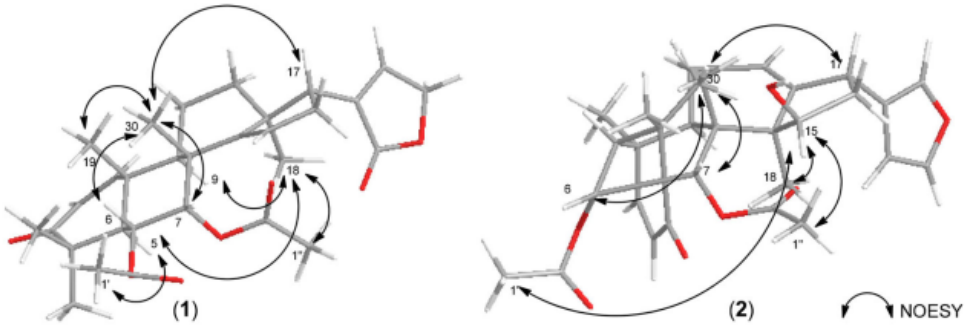


Figure 3. Selected NOESY correlations of compounds **1** and **2**.

maximum absorption at 230 nm (log ε 2.61), indicating the presence of a conjugated system. The IR spectrum were similar with compound **1** besides the presence of hydroxyl group at ν_{max} 3315 cm^{-1}. In addition, the 1D NMR spectra of **2** (Table 1) were superimposed with compound **4** [21], and showed similar signals except for the presence of sp^3 methine carbon typical of C-17 in compound **2**. Additionally, one sp^2 quaternary carbon of the double bond between C-14 and C-17 at **4** was replaced by a sp^2 methine carbon at C-12 of compound **2**, and inferred the double bond was between C-12 and C-13. This was supported by the ^{1}H–^{1}H COSY spectrum that showed the correlations between H_9-H_{11}-H_{12} and H_{15}-H_{16}-H as well as by HMBC spectrum from the cross peaks between H-9 to C-12, H-12 to C-14 and C-17, H-18 and H-15 to C-13, which confirmed the double bond at positions C-12 and C-13. In addition, the relative configuration was determined by NOESY spectrum, in which both H-7 and H-6 showed correlations with H-30, indicating a similar orientation of these protons. Meanwhile, the hydroxyl group of C-15 at β-orientation was determined based on the correlation of H-15 to both methyls at the acetyl groups and CH_3-18, and the structure of **2** was inferred as a new azadirone-type limonoid named lasiocarpine B.

The remaining compounds were identified as nimonolactone (**3**) [17, 22], toonaciliatone C (**4**), and toonaciliatone F (**5**) [21] by comparison of the observed spectroscopy data and previous report.

Table 2. Cytotoxicity of compounds 1–5 against MCF-7 breast cancer cells.

Compounds	IC_{50} (μM)
Lasiocarpine A (**1**)	43.38
Lasiocarpine B (**2**)	168.04
Nimonolactone (**3**)	149.15
Toonaciliatone C (**4**)	827.31
Toonaciliatone F (**5**)	256.79
Cisplatin*	15.9

Note. *Positive control.

Table 2 showed the cytotoxic activity of compounds **1**–**5** evaluated against the MCF-7 breast cancer cell line (Table 2) [23]. Based on the IC_{50} value, compound **1** that contains the γ-lactone and two acetyl groups showed the strongest cytotoxic activity, while compound **3** with one acetyl and γ-lactone group exhibited a significant decrease of the cytotoxic activity. Therefore, the presence of γ-lactone and diacetyl groups have role of cytotoxic activity for these types of limonoids.

3. Experimental

3.1. General experimental procedures

IR spectra were measured on Thermo Scientific™ Nicolet™ Summit FTIR Spectrometer with DTGS KBr detector and generate with Thermo Scientific™ OMNIC™ Paradigm Software (Thermo Fisher Scientific, Madison, WI, USA), and UV spectra were recorded on TECAN Infinite M200 pro (Männedorf Switzerland) with methanol p.a as solvent. NMR spectra were measured by JEOL JNM-ECZ500R/S1 spectrometer (Tokyo, Japan) at 500 MHz for ^{1}H, 125 MHz for ^{13}C and TMS as an internal standard, and mass spectra were measured by Waters QTOF-HRTOFMS-XEVotm mass spectrometer (Waters, Milford, MA, USA). Optical rotations were measured with an ATAGO AP-300 automatic polarimeter (ATAGO, Saitama, Japan), while melting points were measured using the M-565 apparatus (Buchi, Flabil, Switzerland). Furthermore, column chromatography was conducted on silica gel 60 (70–230 and 230–400 mesh, Merck, Darmstadt, Germany). Thin-layer chromatography was carried out on silica gel 60 F_{254} (Merck, 0.25 mm) and spots were detected under ultraviolet-visible light (λ 254 nm) and followed by spraying with Ehrlich's reagent (*p*-dimethylaminobenzaldehyde in 1:1 hydrochloric acid and ethanol).

3.2. Plant material

Chisocheton lasiocarpus fruits (Miq.) were collected from Bogor Botanical Garden, Bogor, West Java, Indonesia in August 2019. The identification of the plant was conducted by Mr. Harto, the staff of the Bogoriense Herbarium, Bogor, and the voucher specimen (VII. G. 168) was deposited at the herbarium.

3.3. Extraction and isolation

The dried fruit (1.2 kg) was extracted using methanol for 6 days and the solvent was evaporated to produce concentrated methanol extract (270 g). Furthermore, the extract was fractionated successively with *n*-hexane, ethyl acetate, and *n*-butanol followed by solvent removal to obtain concentrated *n*-hexane (36.5 g), ethyl acetate (28.1 g), and *n*-butanol (23.6 g) extracts.

The ethyl acetate extract was separated by vacuum liquid chromatography on silica gel 60 using a gradient of *n*-hexane and ethyl acetate to yield seven fractions (E.A–E.G). Meanwhile, fraction E.B (0.4 g) was chromatographed on silica gel using dichloromethane and ethyl acetate (8:2) solvent to obtain four subfractions (E.B1-E.B4). Subfraction E.B1 (45 mg) was chromatographed on ODS eluted with methanol: water (8:2) to produce compound **1** (5 mg). Subfraction E.B2 (50 mg) was chromatographed on ODS with methanol: acetonitrile: water (4:3:3) to yield compound **2** (3.5 mg). Similarly, subfraction E.B3 (55 mg) was chromatographed on ODS using an isocratic solvent of methanol: acetonitrile: water (4:4:2) to yield compound **3** (4 mg). Fraction E.C (2.4 g) was chromatographed on silica gel using gradient solvent of *n*-hexane and ethyl acetate to yield five subfractions (E.C1-E.C5). Subfraction E.C3 (0.9 g) was chromatographed on silica gel using *n*-hexane: dichloromethane: ethyl acetate (5:3:2) to yield three fractions (E.C3A- E.C3C). Also, subfraction E.C3B (0.2 mg) was chromatographed on ODS using an isocratic solvent of methanol: water (7:3) to yield compounds **4** (27 mg) and **5** (31 mg).

3.3.1. Lasiocarpine A (1)

Colorless amorphous solid; m.p. degraded under its melting point; $[\alpha]_D^{28.2}$+12.1 (c 0.51, $CHCl_3$); UV (MeOH) λ_{max} (log ε): 230 nm (2.62); IR (KBr) ν_{max} 2917, 2848, 1729, 1676, 1447, and 1084 cm^{-1}; ^{1}H-NMR spectral data ($CDCl_3$, 500 MHz) see Table 1; ^{13}C-NMR spectral data ($CDCl_3$, 125 MHz), see Table 1; HR-TOFMS (positive ion mode): *m/z* 511.2691 $[M+H]^+$ (calcd for $C_{30}H_{39}O_7$, 511.2696).

3.3.2. Lasiocarpine B (2)

White amorphous solid; m.p. degraded under its melting point; $[\alpha]_D^{28.3}$+17.6 (c 0.23, $CHCl_3$); UV (MeOH) λ_{max} (log ε): 230 nm (2.61); IR (KBr) ν_{max} 3315, 2955, 1731, 1668, and 1042 cm^{-1}; ^{1}H-NMR spectral data ($CDCl_3$, 500 MHz) see Table 1; ^{13}C-NMR spectral data ($CDCl_3$, 125 MHz), see Table 1; HR-TOFMS (positive ion mode): *m/z* 511.2685 $[M+H]^+$ (calcd for $C_{30}H_{39}O_7$, 511.2696).

3.4. Determination of cytotoxic activity

The cytotoxic activity was determined by the same PrestoBlue® assay as previously reported by Nurlelasari et al., 2021 [23].

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Disclosure statement

No potential conflict of interest was reported by the authors.

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References

[1] S.L. Chong, K. Awang, M.T. Martin, M.R. Mokhtar, G. Chan, M. Litaudon, F. Gueritte, and K. Mohamad, *Tetrahedron Lett.* **53**, 5355 (2012).
[2] J.D. Connolly, and R.A. Hill, *Dictionary of Terpenoids* (Chapman & Hall, London, 1991), pp. 1120–1410.
[3] J.D. Connolly, C. Labbé, D.S. Rycroft, and D.A.H. Taylor, *J. Chem. Soc. Perkin Trans. 1*, 2959 (1979).
[4] X. Fang, Y. Di, Z. Geng, C. Tan, J. Guo, J. Ning, and X. Hao, *Eur. J. Org. Chem.* **2010**, 1381 (2010).
[5] G. Yan, J. Li, S. Chen, Y. Liu, J.L. Wu, X.M. Zhu, and N. Li, *Phytochem. Lett.* **35**, 15 (2020).
[6] R. Tundis, M.R. Loizzo, and F. Menichini, *Crit. Rev. Food. Sci. Nutr. Rev. Food Nutr.* **54**, 225 (2014).
[7] A. Roy, and S. Saraf, *Biol. Pharm. Bull.* **29**, 191 (2006).
[8] J.A. Shilpi, S. Saha, S. Chong, L. Nahar, S.D. Sarker, and K. Awang, *Chem. Biodivers.* **13**, 483 (2016).
[9] S.L. Chong, A. Hematpoor, H. Hazni, M. Sofian-Azirun, M. Litaudon, U. Supratman, M. Murata, and K. Awang, *Phytochem. Lett.* **30**, 69 (2019).
[10] B.E. Umali, and H.A.M. Vossen, Plant Resources of South East Asia. No. 14. Vegetable Oils and Fats (Prosea Foundation, Bogor, 2002). pp. 250–255.
[11] K. Heyne, The Useful Indonesian Plants Research and Development (Agency, Ministry of Forestry, Jakarta, 1982). pp. 1029–1031.
[12] Nurlelasari, D.G. Katja, D. Harneti, M.M. Wardayo, U. Supratman, and K. Awang, *Chem. Nat. Compd.* **53**, 83 (2017).
[13] U. Supratman, S. Salam, W. Naibaho, M. Fajar, D.G. Nurlelasari, D. Katja, R. Harneti, A.T. Maharani, R. Hidayat, R. Lesmana, M.A. Nafiah, and Y. Shiono, *Phytochem. Lett.* **35**, 63 (2020).
[14] I.R. Hancock, and C.P. Henderson, *Res. Bull.* 7 (1988).
[15] I.A. Najmuldeen, A.H.A. Hadi, K. Mohamad, K. Awang, K.A. Ketuly, M.R. Mukhtar, H. Taha, M. Nordin, M. Litaudon, F. Gueritte, A.E. Nugroho, and H. Morita, *Heterocycles* **84**, 1265 (2012).
[16] N. Supriatno, T. Herlina, D. Harneti, R. Maharani, A.T. Hidayat, T. Mayanti, U. Supratman, M.N. Azmi, and Y. Shiono, *Nat. Prod. Res.* **32**, 2610 (2018).
[17] M. Takagi, Y. Tachi, J. Zhang, T. Shinozaki, K. Ishii, T. Kikuchi, M. Ukiya, N. Banno, H. Tokuda, and T. Akihisa, *Chem. Biodivers.* **11**, 451 (2014).
[18] D. Lavie, E.C. Levy, and M.K. Jain, *Tetrahedron* **27**, 3927 (1971).
[19] Q.G. Tan, and X.D. Luo, *Chem. Rev.* **111**, 7437 (2011).
[20] P.M. Dewick, *Medicinal Natural Products: A Biosynthetic Approach*, 3rd ed. (A John Wiley & Sons Ltd, UK, 2009). pp. 234–306.
[21] S.Y. Jiang, J.Q. Liu, J.J. Xia, Y.X. Yan, and M.H. Qiu, *Helv. Chim. Acta* **95**, 301 (2012).
[22] G. Gopalakrishnan, S.N.D. Pradeep, V. Kasinath, R.K.M. Siva, R. Malathi, and S.S. Rajan, *Tetrahedron Lett.* **42**, 6577 (2001).
[23] Nurlelasari, I. Rahmayanti, S. Salam, A. Safari, D. Harneti, R. Maharani, A.T. Hidayat, M. Tanjung, R. Retnowati, Y. Shiono, and U. Supratman, *Appl. Biol. Chem.* **64**, 35 (2021).

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