Phytochemistry Letters 26 (2018) 88–92

Contents lists available at ScienceDirect

Phytochemistry Letters

journal homepage: www.elsevier.com/locate/phytol

Four new sesquiterpenes from *Atractylodes lancea*

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ARTICLE INFO

Keywords:
Sesquiterpenes
Chemical constituents
Atractylodes lancea
Calculated electronic circular dichroism

ABSTRACT

Four new sesquiterpene compounds, (5*R*,7*R*,10*S*)-3-*O*-*β*-D-glucopyranosylisopterocarpolone-11-*O*-*β*-D-apiofuranosyl-(1 → 6)-*β*-D-glucopyranoside (**1**), (5*R*,7*R*,10*S*)-14-carboxylisopterocarpolone-11-*O*-*β*-D-glucopyranoside (**2**), (1*R*,7*R*,10*R*)-1-hydroxylcarissone-11-*O*-*β*-D-glucopyranoside (**3**), and (1*R*,7*R*,10*S*)-10,11-dihydroxy-4-guaien-3-one 11-*O*-*β*-D- glucopyranoside (**4**), were isolated from the *Atractylodes lancea* by high-performance liquid chromatography. The compounds' structures were elucidated through detailed spectroscopic methods.

1. Introduction

The rhizomes of *Areactylodes lanceae* (Compositae) are used as Chinese folk medicines. It is reported that these rhizomes can remove dampness, invigorate the spleen, and dispel pathogenic wind and cold effects (Chinese Pharmacopoeia Commission, 2005). The root of *A. lanceae* has shown therapeutic potential for treating such maladies as rheumatic diseases, digestive disorders, night blindness, and influenza (Koonrungsesomboon et al., 2014). The plant is mainly distributed in the provinces of Jiangsu, Hubei and Henan, China. The Maoshan area in the Jiangsu is the area of the genuine medicinal herb. To date, many compounds, such as sesquiterpenes and polyacetylenes, have been isolated from this plant (Meng et al., 2010; Xu et al., 2016a,b; Xu et al., 2017). In our continuing research, four new sesquiterpenes were obtained from *A. lancea*. These compounds' structures were identified as eudesmane sesquiterpenes (1–3) and guaiane sesquiterpene (4) by detailed spectroscopic means (Fig. 1). In the bioactive assays, compounds 1–4 were evaluated against the inhibitory effect on PTP1 B and α-glycosidase enzyme. All of the compounds exhibited weak α-glycosidase enzyme inhibition activities and weak PTP1 B inhibition activities.

2. Results and discussion

Compound **1** was obtained as a white powder, $[\alpha]_D^{20}$ −5.5° (*c* 0.09, MeOH). The IR spectrum of **1** showed the presence of hydroxyl groups (3401 cm^{-1}), carbonyl groups (1658 cm^{-1}), and an olefinic bond (1617 cm^{-1}). The UV spectrum showed the maximum absorption at 256 nm, suggesting the existence of the conjugated system. **1** possessed a molecular formula of $C_{32}H_{52}O_{17}$ (Ω = 7) on the basis of HR-ESI–MS at *m/z* 709.3283 $[M+H]^+$. The ^1H NMR spectrum (Table 1) showed four methyl protons at δ_H 0.83, 1.14, 1.18, and 1.88, three anomeric proton signals at δ_H 4.79 (d, *J* = 3.0 Hz), 4.51 (d, *J* = 7.5 Hz) and 4.31 (d, *J* = 7.5 Hz), which suggested the presence of four methyl and three sugars in compound **1**. Additionally, a series of aliphatic hydrogen signals at δ_H 1.00–2.50 were also observed. The ^{13}C NMR spectrum showed 32 carbon signals (Table 1). According to HSQC, the ^{13}C NMR spectra displayed 3 sets of sugar carbon signals at δ_C 109.2, 75.9, 78.6, 73.2, 63.3, δ_C 103.0, 74.2, 77.0, 69.9, 76.4, 61.0, and δ_C 96.9, 73.6, 76.9, 70.3, 75.1, 67.9. The three saccharide moieties were assigned to be *β*-form (apiose and glucose) by the ^{13}C NMR data and the coupling constants of the anomeric proton signals. Furthermore, acid hydrolysis of **1** yielded D-glucose and D-apiose based on the GC analysis, which suggested that there were two *β*-D-glucopyrancoses and one *β*-D-apiose in compound **1**. Except for 17 saccharide moiety carbons, the rest of the 15 carbon signals suggested the existence of sesquiterpene group with α,*β*-unsaturated ketone coupling with olefinic carbon signals at δ_C 144.9 and 150.0 and a carbonyl carbon signal at δ_C 193.8. Apart from two unsaturations of α,*β*-unsaturated ketone fragments and three unsaturations of the sugar groups, the remaining two unsaturations determined that aglycone was a bicyclic sesquiterpene. Furthermore, the NMR data of bicyclic sesquiterpene were closely similar to those of eudesmane aglycone of 3-hydroxylisopterocarpolone-3-*O*-*β*-D-glucopyranoside (Xu et al., 2016b), which confirmed that bicyclic sesquiterpene of **1** was α,*β*-unsaturated ketone eudesmane. Thus, compound **1** included a eudesmane aglycone, two *β*-D-glucopyrancoses, and a *β*-D-apiose. In the HMBC spectrum, it was found that the relations of H-1‴/C-6″, H-1″/C-11, and H-1′/C-3 indicated that the apiose group and two glucose groups were located at the C-6″ of glucose, C-11, and C-3 of

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https://doi.org/10.1016/j.phytol.2018.05.023
Received 13 March 2018; Received in revised form 4 May 2018; Accepted 11 May 2018

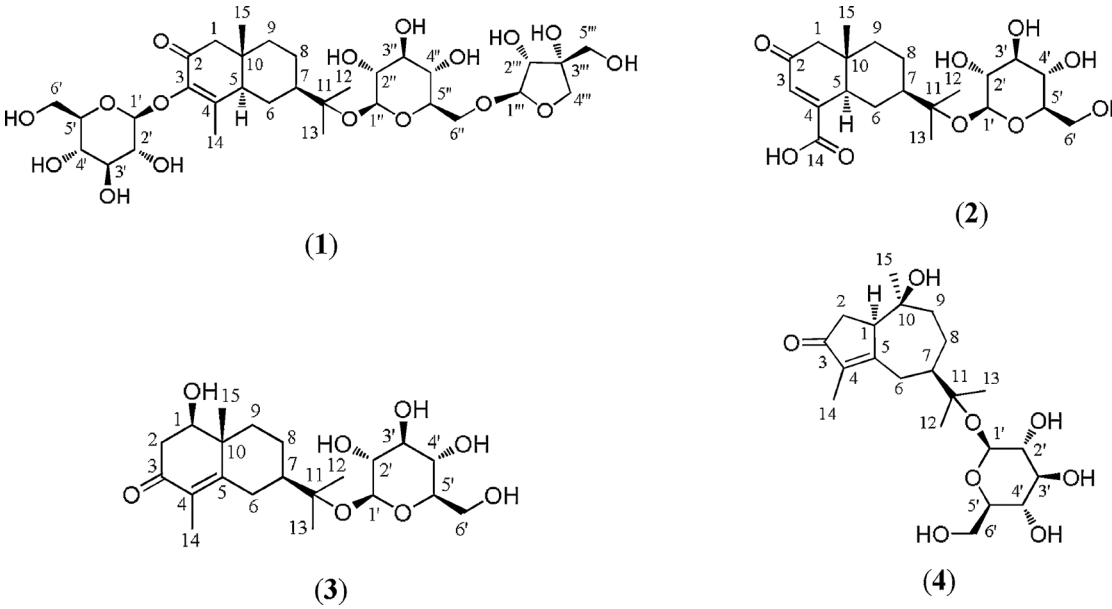

Fig. 1. Structures of compounds **1–4**.

Table 1
NMR Data (500 MHz) Spectroscopic Data for Compounds **1 − 4** in DMSO-d_6.

NO.	1		2		3		4	
	δ_H	δ_C	δ_H	δ_C	δ_H	δ_C	δ_H	δ_C
1a	2.35, d (16.0)	53.6	2.47, d (18.5)	53.1	3.55, dd (5.0, 13.0)	72.7	2.61, dd (2.0, 6.5)	53.1
1b	2.14, m		2.38, overlap					
2a		193.8		201.2	2.45, dd (13.0, 16.0)	42.5	2.33, dd (2.0, 18.0)	36.5
2b					2.33, dd (5.0, 13.0)		2.19, dd (6.5, 18.0)	
3		144.9	6.46, d (3.0)	130.7		196.9		208.0
4		150.0		147.2		127.9		135.1
5	2.46, d (12.0)	46.2	2.35, dt (3.0,12.5)	41.1		163.0		174.9
6a	2.16, m	23.7	1.99, d (12.5)	21.3	2.91, overlap	28.2	3.01, overlap	28.4
6b	1.02, m		0.97, d (12.5)		1.89, overlap		2.01, t (11.5)	
7	1.52, m	47.4	1.44, overlap	46.4	1.45, m	47.5	1.74, overlap	44.4
8a	1.55, m	21.3	1.68, brd (13.0)	20.9	1.70, m	21.6	1.76, overlap	22.4
8b	1.25, m		1.20, m		1.39, m		1.38, m	
9a	1.45, m	39.0	1.59, brd (12.5)	39.4	2.02, d (13.5)	37.6	1.93, dt (4.5, 14.0)	37.0
9b	1.33, m		1.44, overlap		1.15, m		1.64, dt (4.5, 14.0)	
10		36.5		36.5		41.1		70.5
11		78.6		78.2		78.0		79.1
12	1.14, s	22.5	1.13, s	23.4	1.18, s	22.2	1.14, s	21.3
13	1.18, s	24.8	1.13, s	24.1	1.20, s	24.7	1.16, s	24.3
14	1.88, s	14.5		167.9	1.67, s	10.6	1.59, s	7.5
15	0.83, s	16.4	0.74, s	16.6	1.05, s	16.2	1.15, s	31.4
Glc-1′	4.51, d (7.5)	103.0	4.28, d (7.5)	96.9	4.31, d (7.5)	97.1	4.32, d (7.5)	97.0
2′	3.12, overlap	74.2	2.89, t (8.5)	73.6	2.91, m	73.7	2.93, t (8.5)	73.8
3′	3.16, overlap	77.0	3.14, t (8.5)	77.1	3.15, t (8.5)	77.1	3.15, t (8.5)	77.2
4′	3.10, overlap	69.9	3.00, m	70.4	3.02, t (8.5)	70.4	3.02, overlap	70.4
5′	3.02, overlap	76.4	3.05, m	76.4	3.05, m	76.4	3.05, m	76.4
6′a	3.61,brd (11.5)	61.0	3.62, brd (11.0)	61.3	3.61, brd (11.0)	61.3	3.62, brd (11.5)	61.3
6′b	3.43, m		3.35, overlap		3.39, m		3.35, dd (5.5, 11.5)	
Glc-1″	4.31, d (7.5)	96.9						
2″	2.91, overlap	73.6						
3″	3.16, overlap	76.9						
4″	2.95, overlap	70.3						
5″	3.24, m	75.1						
6″a	3.80, brd (10.5)	67.9						
6″b	3.36, overlap							
Api-1‴	4.79, d (3.0)	109.2						
2‴	3.70, d (3.0)	75.9						
3‴		78.6						
4‴a	3.83, d (9.5)	73.2						
4‴b	3.57, d (9.5)							
5‴	3.32, overlap	63.3						

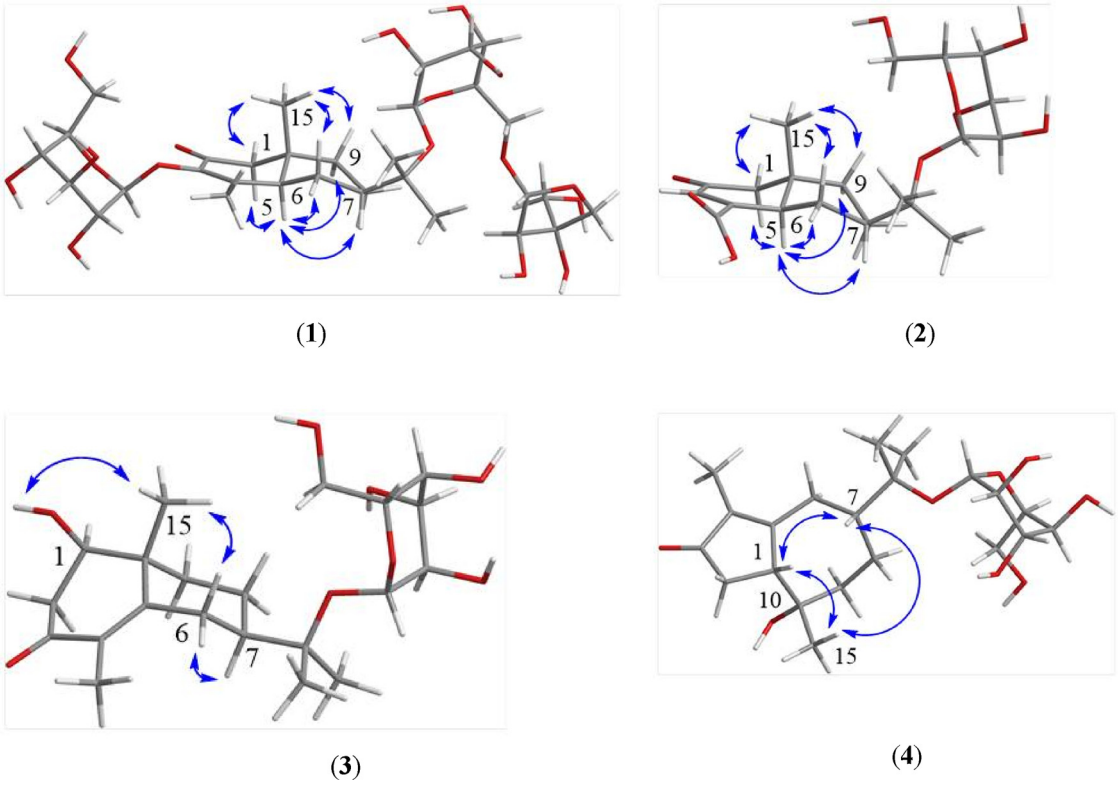

Fig. 2. ROESY correlations of compounds **1**–**4**.

aglycone positions, respectively. Thus, compound **1** was preliminarily identified as 3-*O*-*β*-D-glucopyranosylisopterocarpolone-11-*O*-*β*-D-apiofuranosyl-(1 → 6)-*β*-D-glucopyranoside.

The stereochemistry of **1** was determined on the basis of its ROESY and ECD spectra (Figs. 2 and 3). In the ROESY spectrum, the relations of H-5/H-1a, H-6a, H-7, and H-9b (δ_H 1.33, m), H_3-15/H-1b, H-6b, and H-9a suggested that the relative configuration of C-5, C-7 and C-10 was consistent with that of (5*R*,7*R*,10*S*)-3-hydroxylisopterocarpolone-3-*O*-*β*-D-glucopyranoside (Xu et al., 2016b). In the ECD spectrum, **1** exhibited an identical negative Cotton effect at 322 nm ($\Delta e = -1.74$) with (5*R*,7*R*,10*S*)-3-hydroxylisopterocarpolone-3-*O*-*β*-D-glucopyranoside, explaining the same absolute configurations (Snatzke, 1965; Gawronski, 1982). Thus, the absolute stereochemistry at the C-5,7,10 positions in **1** were shown to be 5*R*,7*R*,10*S*. Finally, compound **1** was identified and named (5*R*,7*R*,10*S*)-3-*O*-*β*-D-glucopyranosylisopterocarpolone-11-*O*-*β*-D-apiofuranosyl-(1 → 6)-*β*-D-glucopyranoside.

Compound **2** was isolated as a white powder, $[\alpha]_D^{20}$ −4.6° (*c* 0.1, MeOH). The IR spectrum of **2** showed the absorptions attributable to hydroxyl (3386 cm^{-1}), carbonyl (1716, 1650 cm^{-1}), and an olefinic bond (1610 cm^{-1}). The molecular formula $C_{21}H_{32}O_9$ ($\Omega = 6$) of

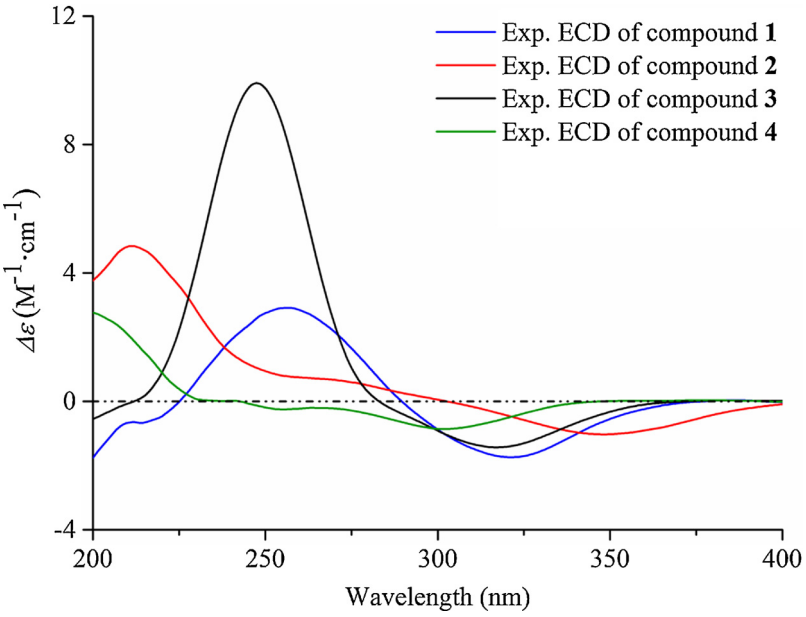

Fig. 3. Experimental and calculated ECD spectra of compounds **1**–**4**.

compound **2** was determined by HR-ESI–MS at *m/z* 429.2058 $[M+H]^+$ (calcd 429.2125).

The ^1H NMR spectrum (Table 1) showed a single olefinic hydrogen signal at δ_H 6.46, an anomeric proton signal at δ_H 4.28, three methyl protons at δ_H 1.13 (6H), and 0.74 (3H), and a series of aliphatic hydrogen signals at δ_H 1.00–2.50. The ^{13}C NMR spectrum showed 21 carbon signals (Table 1). Except for β-D-pyranoglucose carbon signals at δ_C 96.9, 73.6, 77.1, 70.4, 76.4, and 61.3, the remaining 15 carbon signals were confirmed as a sesquiterpene skeleton. Additionally, two olefinic carbon signals at δ_H 130.7 and 147.2, two conjugated carbonyl carbon signals at δ_C 167.9 and 201.2 in the ^{13}C NMR and a series of aliphatic hydrogen signals at δ_H 1.00–2.50 in the ^1H NMR, were observed. Combining with unsaturation, sesquiterpene groups were concluded to be an α,β-unsaturated ketone fragment sesquiterpene with a bicyclic structure. Furthermore, the NMR data of bicyclic sesquiterpene were similar to aglycone of 3-hydroxylisopterocarpolone-3-*O*-β-D- glucopyranoside (Xu et al., 2016b), except for the olefinic hydrogen signals (H-3). The relations of H-3/COOH (δ_C 167.9) in HMBC confirmed that the C-4 position linked with a carboxy group instead of methyl group. Therefore, bicyclic sesquiterpene was concluded to be eudesmane with a carboxy group. Additionally, β-D-pyranoglucose was confirmed to be located at C-11 by the relation of H-1′/C-11 in HMBC. Thus, the planar structure of **2** was identified as 14-carboxylisopterocarpolone-11-*O*-β-D-glucopyranoside.

The stereochemistry of **2** was determined by the same method as compound **1**. Furthermore, **2** displayed a similar negative Cotton effect at 348 nm ($\Delta\varepsilon = -1.03$) with (5*R*,7*R*,10*S*)-3-hydroxylisopterocarpolone-3-*O*-β-D-glucopyranoside (Xu et al., 2016b), explaining the same absolute configurations of C-5, C-7 and C-10 in the ECD spectrum. Consequently, the absolute stereochemistry of **2** was shown to be 5*R*,7*R*,10*S*. Thus, compound **2** was defined as (5*R*,7*R*,10*S*)-14-carboxylisopterocarpolone-11-*O*-β-D-glucopyranoside.

Compound **3** was obtained as a white powder, $[\alpha]_D^{20}$ +42.1° (*c* 0.15, MeOH). The IR spectrum of **3** showed the presence of hydroxyl groups (3380 cm^{-1}), carbonyl groups (1651 cm^{-1}), and an olefinic bond (1604 cm^{-1}). The molecular formula was determined to be $C_{21}H_{34}O_8$ (Ω = 6) based on the *m/z* 415.2311 $[M+H]^+$ in HR-ESI–MS.

Analysis of the ^1H and ^{13}C NMR data (Table 1) indicated the presence of four methyl groups, a carbonyl group, an olefinic bond, and β-D-pyranoglucose. These groups were similar to those of compounds **1** and **2**. The aglycone of **3** was concluded preliminarily to be eudesmane sesquiterpene and showed an oxymethine (H-1) at δ_C 72.7 in ^{13}C NMR. The oxymethine confirmed that the hydroxyl was linked with C-1 by the correlations of H-15/C-1, and H-2/C-1 in the HMBC spectrum. In addition, the correlations of H-15/C=C (C-5, δ_C 163.0) and H-2/C=C (C-4, δ_C 127.9) confirmed that the double bond was located at the C-4 and C-5 positions, and the carbonyl group was assigned to C-3 position by the correlations of H-2 and H-14/C-3 in the HMBC spectrum. According to the above conclusions, eudesmane sesquiterpene of **3** was 1-hydroxy-3-carbonyl-Δ-4,5-eudesmane. Additionally, β-D-pyranoglucose was confirmed to be located at C-11 by the relation of H-1′/C-11 in HMBC. Thus, the planar structure of **3** was identified as 1-hydroxylcarissone-11-*O*-β-D-glucopyranoside.

Furthermore, the stereochemistry of **3** was also confirmed by its ROESY and ECD spectra data (Figs. 2 and 3). In the ROESY spectrum, the relations of H-7/H-6a, H-15/OH-1 and H-15/H-6b suggested that H-1 and H-7 were on the same side of the eudesmane ring plane. In the ECD spectrum, compound **3** exhibited an identical negative Cotton effect at 317 nm ($\Delta\varepsilon = -1.43$) (Snatzke, 1965; Gawronski, 1982). Thus, the absolute stereochemistry of **3** was determined to be 1*R*,7*R*,10*R*. Finally, compound **3** was identified as depicted and named (1*R*,7*R*,10*R*)-1-hydroxylcarissone-11- *O*-β-D-glucopyranoside.

Compound **4** was also obtained as a white powder, $[\alpha]_D^{20}$ −61.2° (*c* 0.08, MeOH). The IR of **4** showed the presence of hydroxyl groups (3394 cm^{-1}), carbonyl groups (1680 cm^{-1}), and an olefinic bond (1630 cm^{-1}). Compound **4** possessed a molecular formula of $C_{21}H_{34}O_8$, which was determined by HR-ESI–MS at *m/z* 415.2312 $[M+H]^+$ (calcd 415.2332).

The ^1H and ^{13}C NMR data showed that compound **4** (Table 1) possessed four methyl protons at δ_H 1.14, 1.15, 1.16, and 1.59, an anomeric proton signal at δ_H 4.32, β-D-pyranoglucose carbon signals at δ_C 97.0, 73.8, 77.2, 70.4, 76.4, and 61.3, and a carbonyl group at δ_C 208.0. Compound **4** also has an α,β-unsaturated ketone sesquiterpene aglycone according to the above data. Compared with eudesmane sesquiterpene of compound **3**, the chemical shifts of α,β-unsaturated ketone in **4** moved to the low field. Thus, the α,β-unsaturated ketone was preliminarily deduced to be located in the structure of cyclopentane, rather than cyclohexane. According to the reported results, the data of the sesquiterpene moiety of compound **4** were in agree with those of 11-*O*-β-D-glucopyranosyl-4-guaien-3-one (Yu et al., 2011), so the sesquiterpene structure of compound **4** was confirmed to be a guaiane sesquiterpene. In addition, OH and glucose were located at C-7 and C-11 by the correlation signals OH/C-1 and C-9, H-1′/C-11 in the HMBC spectrum, respectively. Thus, the planar structure of **4** was identified as 10,11-dihydroxy-4-guaien-3-one 11-*O*-β-D-glucopyranoside.

Similarly, the stereochemistry of **4** was elucidated on its ROESY and ECD spectra data (Figs. 2 and 3). In the ROESY spectrum, the relations of H-1/H-7 and H-15, H-7/H-15 suggested that the relative configurations of C-1, C-7 and C-10 were consistent with that of (1*S*,7*R*,10*R*)-11,15-dihydroxy-4-guaien-3-one 11-*O*-β-D-glucopyranoside (Xu et al., 2017). At the same time, compound **4** exhibited similar Cotton effects in the range of 200 ~ 400 nm in the ECD spectra, indicating that their absolute configurations were consistent. Thus, the absolute stereochemistry at the C-1, 7, 10 positions in **4** were shown to be 1*R*,7*R*,10*S*. Finally, compound **4** was identified and named (1*R*,7*R*,10*S*)-10,11-dihydroxy-4-guaien-3-one 11-*O*-β-D-glucopyranoside.

Sesquiterpenes were the main ingredients isolated from *A. lanceae*, which primarily existed as types of eudesmane, guaiane and spirovetivane. Compounds **1–3** were eudesmane-type, and **4** was guaiane-type, as determined by detailed spectroscopic means (NMR, and MS et al.). The compounds' absolute configurations were determined by using experimental ROESY and ECD spectra, as well as chemical methods. The findings of these compounds add to the diversity of these ingredients. The bioactive assays showed that compounds **1–4** exhibited weak α-glycosidase enzyme inhibition activities and weak PTP1 B inhibition activities.

3. Materials and methods

3.1. Generals

The specific rotations, UV, and ECD data were individually measured on JASCO P-2000, JASCO V-650, and JASCO J-815 spectrometers (JASCO, Easton, MD, U.S.A.). IR spectra were collected by a Nicolet 5700 instrument (Thermo Scientific, Waltham, MA, U.S.A.). NMR spectra were run on a Bruker 500 Hz spectrometer (Bruker-Biospin, Billerica, MA, U.S.A.), and chemical shifts were given in δ (ppm) with DMSO-d_6 peaks as the reference. HRESIMS data were collected using an Agilent 1100 series LC/MSD ESI/TOF instrument (Agilent Technologies, Waldbronn, Germany). GC analyses were performed on an Agilent 7890A system. Reversed-phase preparative HPLC (P-HPLC) was run on a Shimadzu LC-10AT system quipped with an SPD-10A detector (Shimadzu, Japan). An Agilent 1260 series system equipped with an Apollo C18 column (250 × 4.6 mm, 5 μm, Grace Davison) was used for HPLC analyses.

3.2. Plant material

The rhizomes of *A. lancea* were collected at Huanggang City (Hubei Province, China) in June 2014 and were identified by Prof. Lin Ma. A voucher specimen (ID-s-2596) was deposited in the herbarium at the Department of Medicinal Plants, Institute of Materia Medica, Chinese

Academy of Medical Sciences (Beijing 100050, China).

3.3. Extraction and isolation

The root of *Areactylodis Lanceae* (100.0 kg) was exhaustively extracted with 80% ethanol under reflux conditions. The extracts were later concentrated under reduced pressure to give a residue (25.6 kg). The residue was suspended in H_2O (50 L) again, and the suspension was then extracted with petroleum ether, EtOAc and nBuOH. The nBuOH extracts were evaporated and freeze-dried in vacuum to give a residue (1.2 kg). The residue was dissolved in H_2O (1.5 L) again, then chromatographed over a macroporous adsorbent resin (HP-20) column (120 cm × 15 cm). After eluting with H_2O (40 L), the adsorbed constituents were eluted with 15% ethanol, 30% ethanol, 50% ethanol, and 95% ethanol, respectively. The eluting parts were then concentrated under reduced pressure to give H_2O part 824.0 g (A), 15% ethanol part 88.6 g (B), 30% ethanol part 106.4 g (C), 50% ethanol part 53.3 g (D), 95% ethanol part 19.5 g (E) (25.6 kg). The 30% ethanol part (96.4 g) was chromatographed over reversed-phase preparative medium pressure, eluting with H_2O–MeOH (from 100:0 to 0:100) to give 10 fractions. Fr5 part (50 g) was chromatographed over Sephadex LH-20 eluting with H_2O to give 20 fractions. Fr5 was further purified by reversed-phase preparative HPLC using H_2O–CH_3OH (65:35, 5 mL/min) as the mobile phase to yield compound 1 (18.1), 2 (39.0 mg), and 4 (15.7 mg). Fr9 was further purified by reversed-phase preparative HPLC using H_2O–CH_3OH (65:5,5 mL/min) as the mobile phase to yield compound 3 (20.7 mg).

(5*R*,7*R*,10*S*)-3-*O*-*β*-D-glucopyranosylisopterocarpolone-11-*O*-*β*-D-apiofuranosyl-(1 → 6)-*β*-D-glucopyranoside (1): white powder powder; $[\alpha]_D^{20}$ −5.5 (*c* 0.09, MeOH);UV (MeOH) λ_{max} (log ε): 256 (3.90) nm; ECD (MeOH) λ_{max} (Δε): 257 (+2.91), 322 (−1.74) nm; IR(KBr) νmax: 3401, 2927, 2881, 1658, 1617, 1440, 1380, and 1077 cm^{-1}; HR-ESI–MS *m/z*: 709.3245 $[M+H]^+$ (Calcd. for $C_{32}H_{53}O_{17}$, 709.3283); ^1H NMR (DMSO-d_6, 500 MHz) and ^{13}C NMR (DMSO-d_6, 125 MHz) data see Table 1.

(5*R*,7*R*,10*S*)-14-carboxylisopterocarpolone-11-*O*-*β*-D-glucopyranoside (2): white powder powder; $[\alpha]_D^{20}$ −4.6 (*c* 0.10, MeOH);UV (MeOH) λ_{max} (log ε): 239 (3.73) nm; ECD (MeOH) λ_{max} (Δε): 212 (+4.84), 348 (−1.03) nm; IR (KBr) νmax: 3386, 2926, 2874, 1716, 1650, 1610, 1453, 1372, 1078, 1039 cm^{-1}; HR-ESI–MS *m/z*: 429.2058 $[M+H]^+$ (Calcd. for $C_{21}H_{33}O_9$, 429.2125); ^1H NMR (DMSO-d_6, 500 MHz) and ^{13}C NMR (DMSO-d_6, 125 MHz) data see Table 1.

(1*R*,7*R*,10*R*)-1-hydroxylcarissone-11-*O*-*β*-D-glucopyranoside (3): white powder powder; $[\alpha]_D^{20}$ +42.1 (*c* 0.15, MeOH);UV (MeOH) λ_{max} (log ε): 249 (4.03) nm; ECD (MeOH) λ_{max} (Δε): 248 (+9.91), 317 (−1.43) nm; IR (KBr) νmax: 3380, 2973, 2936, 2879, 1651, 1604, 1430, 1370, 1079, 1031 cm^{-1}; HR-ESI–MS *m/z*: 415.2311 $[M+H]^+$ (Calcd. for $C_{21}H_{33}O_9$, 415.2332); ^1H NMR (DMSO-d_6, 500 MHz) and ^{13}C NMR (DMSO-d_6, 125 MHz) data see Table 1.

(1*R*,7*R*,10*S*)-10,11-dihydroxy-4-guaien-3-one 11-*O*-*β*-D-glucopyranoside (4): white powder powder; $[\alpha]_D^{20}$ −61.2 (*c* 0.08, MeOH); UV (MeOH) λ_{max} (log ε): 242 (3.99) nm; ECD (MeOH) λ_{max} (Δε): 255 (−0.25), 302 (−0.86) nm; IR (KBr) νmax: 3394, 2972, 2924, 1680, 1630, 1453, 1387, 1080, 1034 cm^{-1}; HR-ESI–MS *m/z*: 415.2312 $[M+H]^+$ (Calcd. for $C_{21}H_{33}O_9$, 415.2332); ^1H NMR (DMSO-d_6, 500 MHz) and ^{13}C NMR (DMSO-d_6, 125 MHz) data see Table 1.

3.4. Biological assay

3.4.1. PTP1B activity assay

The recombinant human PTP1B protein was amplified by hGSTPTP1B-BL21 Escherichia coli pellets and purified by a GST beads column. The dephosphorylation of para-nitrophenyl phosphate (pNPP) was catalyzed to para-nitrophenol (pNP) by PTP1B. The amount of p-nitrophenol produced was measured at 405 nm wavelength using Microplate spectrophotometer (uQuant, Bio-tek, USA).

3.4.2. α-glycosidase enzyme activity assay

A total of 3 mM PNPG (p-Nitrophenyl-alpha-D-glucopyranoside) (20 μL) and α-glucosidase (20 μL, 1 U/mL in PBS, pH 6.8), PBS (50 μL) and the sample solution (10 μL) were placed in a 96-well microplate and pre-cultured for 15 min at 37 °C. 0.4 M Na_2CO_3 (50 μL) was added and the mixture was incubated for an additional 35 min. The absorbance of each well was measured at 400 nm with a microplate spectrophotometer.

3.5. Acid hydrolysis of compounds

Compound 1 (5 mg) was dissolved in 1 mol/L HCl–dioxane (1:1, 5 mL) and maintained at 60 °C for 6 h. After drying in a vacuum, the residue was partitioned in H_2O (5 mL) and extracted thrice with EtOAc (5 mL). The aqueous solution was evaporated in vacuum to obtain the monosaccharide residue. These monosaccharide residues were processed using a reported method (Hara et al., 1987; Feng et al., 2013; Shen et al., 2013). The configurational assignments of apiose and glucose were established by comparing the retention times of their chiral derivatives with those of standard substances, which were prepared using the identical procedure (D-apiose 14.56 min, D-glucose 20.56 min). The same procedure was operated on compounds 2, 3 and 4, respectively.

Acknowledgments

The authors thank Professor Lin Ma for the plant identification. The authors thank Yinghong Wang for processing NMR data. This project was funded by CAMS Innovation Fund for Medicial Sciences (2016-I2M-1-010).

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.phytol.2018.05.023.

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