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A NEW HEDERAGENIN GLYCOSIDE FROM *Nephelium lappaceum*

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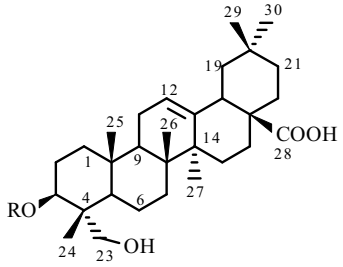
*A new oleane-type triterpene oligoglycoside, hederagenin 3-*O*-(3-*O*-acetyl-*β*-D-xylopyranosyl)-(1→3)-*α*-L-arabinopyranoside (**2**), together with four known compounds, hederagenin (**1**), hederagenin 3-*O*-(4-*O*-acetyl-*α*-L-arabinopyranosyl)-(1→3)-*α*-L-rhamnopyranosyl-(1→2)-*α*-L-arabinopyranoside (**3**), hederagenin 3-*O*-*α*-L-arabinopyranosyl-(1→3)-*α*-L-rhamnopyranosyl-(1→2)-*α*-L-arabinopyranoside (**4**), hederagenin 3-*O*-*β*-D-glucopyranosyl-(1→3)-*α*-L-rhamnopyranosyl-(1→4)-*β*-D-xylopyranoside (**5**), was isolated from the hull of* Nephelium lappaceum*. All the isolates were obtained from the hull of rambutan for the first time.*

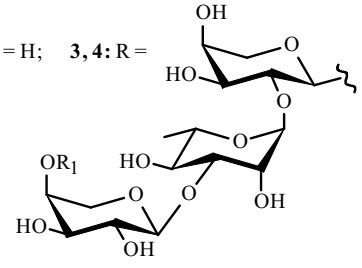
Keywords: *Nephelium lappaceum*, oleane-type triterpene oligoglycosides, hederagenin.

Nephelium lappaceum L., commonly known as "rambutan," is a tropical fruit of the Sapindaceae family [1]. Native to Southeast Asia, rambutan is cultivated for its fruit and sold commercially [1, 2]. It is consumed fresh, canned, or processed, and appreciated for its refreshing flavor and exotic appearance [3]. The seeds are bitter and narcotic, with the roots used for treating fevers, the leaves as poultices, and the bark as an astringent [2]. The rind of rambutan, which is normally discarded, was found to contain extremely high antioxidant and antibacterial activities, and several potential antioxidant activities, including reducing power, *β*-carotene bleaching, linoleic peroxidation, and free radical scavenging activity, were also exhibited [4, 5]. As for the chemical constituents of the hull of *Nephelium lappaceum*, only a few compounds have been reported, mainly phenolic compounds that are responsible for their antioxidant and antibacterial activities [5, 6]. In order to investigate the bioactive constituents of the hull of rambutan, a detailed chemical study of this plant was carried out and a new oleane-type triterpene oligoglycoside (**2**) together with four known compounds (**1**, **3–5**) was isolated from the methanol extract of the hull of rambutan. All these compounds were obtained from the hull of this plant for the first time.



1, 3 - 5

1: R = H; **3, 4:** R =



3: R_1 = Ac; **4:** R_1 = H

5: R =

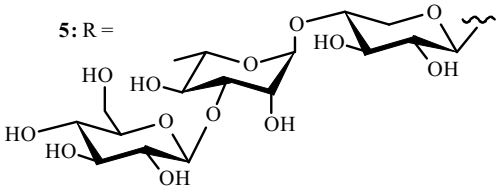


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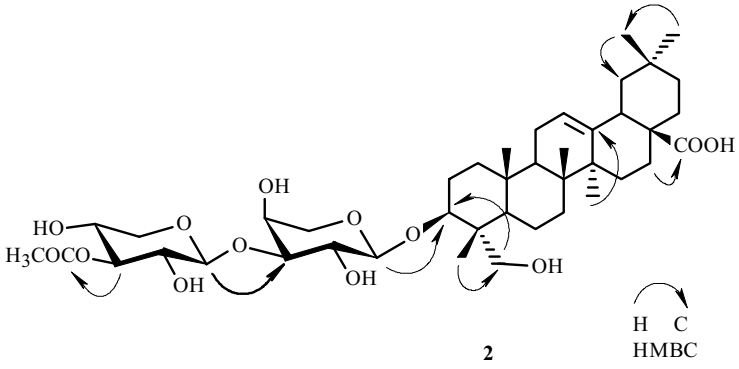
TABLE 1. ^{1}H NMR Spectroscopic Data of **2** (CD_3OD, δ, ppm, J/Hz)

C atom	δ_H	C atom	δ_H
1	1.59 (m), 0.94 (m)	29	0.91 (s)
2	1.58 (m)	30	0.94 (s)
3	3.62 (m)		Ara
5	1.60 (m)	1′	4.59 (d, J = 7.8)
6	1.47 (m)	2′	3.67 (m)
7	1.61 (m), 1.25 (m)	3′	3.62 (m)
9	1.61 (m)	4′	3.94 (m)
11	2.02 (m), 1.59 (m)	5′	3.84 (d, J = 12.8), 3.56 (d, J = 12.1)
12	5.23 (br.s)		Xyl
15	1.77 (m), 1.06 (m)	1″	4.33 (d, J = 7.2)
16	2.02 (m), 1.88 (m)	2″	3.42 (m)
18	2.84 (dd, J = 10.0, 4.4)	3″	4.89 (m)
19	1.74 (m), 1.10 (m)	4″	3.62 (m)
21	1.39 (m), 1.17 (m)	5″	3.89 (m), 3.31 (m)
22	1.74 (m), 1.55 (m)	Acetyl	
23	3.62 (d, J = 11.4), 3.29 (d, J = 11.4)	3″	2.11 (s)
24	0.71 (s)		
25	0.98 (s)		
26	0.81 (s)		
27	1.17 (s)		



2

Fig. 1. Selected HMBC correlations of compound **2**.

Compound **2** was obtained as an amorphous powder. The IR spectrum of **2** showed absorption bands at 1730, 1695, and 1632 cm^{-1} ascribable to ester carbonyl, carboxyl, and olefin functions and broad bands at 3425 cm^{-1} suggestive of hydroxyls (including carboxylic hydroxyl). In the negative-ion ESI-MS of **2**, quasimolecular ion peaks were observed at *m/z* 777 $[M - H]^-$ in accordance with the molecular formula $C_{42}H_{66}O_{13}$, which was further confirmed by analysis of HR-ESI-MS at *m/z* 777.4430 $[M - H]^-$ (calcd 777.4425). The ^{1}H NMR spectrum (Table 1) of **2** exhibited six methyls [δ 0.71, 0.81, 0.91, 0.94, 0.98, 1.17 (3H each, all s, H_3-24, 26, 29, 30, 25, 27)], an olefinic proton [5.23 (1H, br.s, H-12)], and two anomeric protons [4.59 (1H, d, J = 7.8 Hz, inner-Ara-H-1) and 4.33 (1H, d, J = 7.2 Hz, Xyl-H-1) suggesting two sugar units, together with the methyl of acetyl group [2.11 (3H, s)]. Analysis of its ^{13}C NMR and DEPT spectra (Table 2) showed 42 carbon resonances, similar to those of hederagenin 3-*O*-*β*-D-xylopyranosyl-(1→3)-*α*-L-arabinopyranoside [7], except for the additional shifts at δ 172.6 and 21.1 for an acetyl group, suggesting compound **2** was a hederagenin glucoside. The presence of the acetyl was further identified by the loss of an acetyl unit (*m/z* 735 $[(M - H) - 42]^-$ in the fragmentation patterns of the HR-ESI-MS and treatment of **2** with 0.5% sodium methoxide (NaOMe)–MeOH yielding a deacetyl derivative, exhibiting quasimolecular ion peaks at *m/z* 735 $[M - H]^-$ in the negative-ion ESI-MS. The linkage of the acetyl group to Xyl-C-3 in **2** was characterized from analysis of the HMBC spectrum (Fig. 1), in which key long-range correlation from the Xyl-H-3 [δ_H 4.89 (1H, m)] to the acetyl carbonyl carbon was observed. The correlations of the Xyl-H-1 [δ_H 4.33 (1H, d, J = 7.2 Hz)] with the Ara-C-3 (δ_C 83.7) and the Ara-H-1 [δ_H 4.59 (1H, d, J = 7.8 Hz)] with the C-3 (δ_C 83.5) of the aglycone indicated that the terminal-Xyl moiety was attached to the inner- Ara-C-3 and this disaccharide chain was linked to C-3 in **2**. On the basis of the above-mentioned evidence, compound **2** was determined as hederagenin 3-*O*-(3-*O*-acetyl-*β*-D-xylopyranosyl)-(1→3)-*α*-L-arabinopyranoside.

TABLE 2. ^{13}C NMR Spectroscopic Data of **1–4** (CD_3OD) and **5** (C_5D_5N)

C atom	**1**	**2**	**3**	**4**	**5**	C atom	**2**	**3**	**4**	**5**
1	34.3	39.8	39.8	39.9	39.1		Ara	Ara	Ara	Xyl
2	27.9	26.5	26.5	26.5	26.5	1′	106.0	104.7	104.7	106.9
3	74.3	83.5	82.2	82.3	83.0	2′	72.2	75.3	76.2	75.2
4	45.3	43.9	44.0	44.0	43.7	3′	83.7	74.7	74.1	76.0
5	50.1	48.0	48.0	47.6	47.6	4’	69.4	69.7	69.7	78.7
6	18.2	18.5	18.3	18.2	18.2	5′	66.9	65.6	67.2	63.8
7	34.0	33.6	33.5	33.5	33.5		Xyl	Rha	Rha	Rha
8	40.5	40.5	40.5	40.5	39.8	1″	106.2	101.4	101.3	101.6
9	48.8	48.4	48.4	48.2	48.2	2″	73.4	71.7	71.7	71.6
10	38.3	37.7	37.6	37.6	36.9	3″	78.5	82.4	82.4	81.3
11	24.9	24.3	24.2	24.5	23.9	4″	69.9	73.0	72.8	73.1
12	124.0	123.6	123.6	123.6	122.7	5″	66.8	70.0	69.7	69.8
13	145.7	145.3	145.3	145.2	144.9	6″		18.0	18.1	18.6
14	44.3	42.8	42.8	42.7	42.0			Ara	Ara	Glc
15	29.3	28.8	28.8	28.8	28.9	1‴		106.5	106.5	105.1
16	24.4	24.0	24.0	24.0	23.7	2‴		73.3	72.9	71.8
17	48.2	47.7	47.5	47.0	46.5	3‴		72.8	71.6	78.6
18	41.1	43.0	43.0	43.0	42.2	4‴		72.4	69.9	70.0
19	47.7	47.4	47.3	47.1	46.7	5‴		64.5	64.5	75.6
20	32.1	31.6	31.6	31.6	31.0	6‴				62.6
21	35.3	34.9	34.7	34.8	34.4	Acetyl				
22	33.9	33.8	33.7	33.8	32.9	3‴	172.6			
23	67.7	65.0	64.2	64.5	66.4		21.1			
24	13.2	13.3	13.8	13.8	14.2	4‴		172.6		
25	16.7	16.4	16.4	16.4	16.2			21.3		
26	20.3	17.8	17.8	17.8	17.5					
27	26.9	26.5	26.5	26.5	26.2					
28	182.4	182.0	182.1	181.9	180.3					
29	33.9	33.7	33.6	33.6	33.3					
30	24.5	24.0	24.0	24.0	23.8					

Additionally, four known compounds, hederagenin [7, 8] (**1**), hederagenin 3-*O*-(4-*O*-acetyl-α-L-arabinopyranosyl)-(1→3)-α-L-rhamnopyranosyl-(1→2)-α-L-arabinopyranoside [9] (**3**), hederagenin 3-*O*-α-L-arabinopyranosyl-(1→3)-α-L-rhamnopyranosyl-(1→2)-α-L-arabinopyranoside [9, 10] (**4**), and hederagenin 3-*O*-β-D-glucopyranosyl-(1→3)-α-L-rhamnopyranosyl-(1→4)-β-D-xylopyranoside [11] (**5**), were obtained and their structures were elucidated by comparison of their spectral data with the literature values. This paper is the first isolation report on these constituents from the hull of *Nephelium lappaceum*.

EXPERIMENTAL

General Comments. Optical rotations were measured with a Horiba SEPA-300 polarimeter. A Tenor 27 spectrophotometer was used for scanning IR spectroscopy with KBr pellets. 1D and 2D NMR spectra were recorded on DRX-500 spectrophotometers with TMS as the internal standard. Unless otherwise indicated, chemical shifts (δ) are expressed in ppm with reference to the solvent signals. HR-ESI-MS were performed on a VG Autospec-3000 spectrophotometer. Column chromatography was performed with Si gel (200–300 mesh; Qingdao Marine Chemical Inc., Qingdao, China) and Lichroprep RP-18 gel (40–63 μm; Merck, Darmastadt, Germany). The fractions were monitored by TLC, and spots were visualized by heating Si gel plates sprayed with 5% H_2SO_4 in EtOH.

Plant Materials. The fruit of *Nephelium lappaceum* were purchased from a market in Kunming, China, and identified by Prof. Rong Li, Kunming Institute of Botany, Chinese Academy of Sciences. The specimen (LWJ 2008-12-01) was deposited at the State Key Laboratory of Phytochemistry and Plant Resources in West China, Kunming Institute of Botany, Chinese Academy of Sciences.

Extraction and Isolation. The air-dried fruit hull of *Nephelium lappaceum* (10 kg) was powdered and extracted three times with 95% EtOH under reflux. The combined extracted EtOH solution (18 L) was evaporated under reduced pressure, then suspended in water (1.5 L) and partitioned with petroleum ether, EtOAc, and *n*-BuOH sequentially to yield petroleum ether-soluble (7.5 g), EtOAc-soluble (159.5 g), and *n*-BuOH-soluble (102.5 g) fractions. A portion (154.5 g) of the EtOAc-soluble fraction was separated by silica gel column chromatography (CC, 200–300 mesh, 1.4 kg) and eluted with $CHCl_3$–MeOH (100:1, 98:2, 95:5, 90:10, 80:20, 70:30, 0:100, v:v) gradient solvent system to give ten fractions (l–10). Fraction 3 (8 g) was subjected to CC over silica gel eluted with petroleum ether–EtOAc (1:1) to give four subfractions 3a–3d. Subfraction 3b was chromatographed and eluted with petroleum ether–EtOAc (2:1) to yield compound **1** (10 mg). Fraction 10 (20 g) was chromatographed over a silica gel column with a petroleum ether–EtOAc solvent system (20:1 to pure EtOAc) to give six subfractions (10a–10f). Compounds **2** (8 mg), **3** (34 mg), **4** (500 mg), and **5** (105 mg) were obtained from subfraction 10f (2 g) by repeated silica gel column chromatography with petroleum $CHCl_3$–MeOH (95:15) using an RP-18 column eluted with MeOH–H_2O gradient system (60–100%) and then chromatographed over Sephadex LH-20 column, using $CHCl_3$–MeOH (1:1) as solvent.

Deacetylation of Compound 2. A solution of compound **2** in 0.5% NaOMe–MeOH was stirred at room temperature for 3 h. The reaction mixture was neutralized with Dowex HCR-W2 (H^+ form) and the resin was removed by filtration. Evaporation of the solvent from the filtrate under reduced pressure gave a residue. In the negative-ion ESI-MS of the residue, quasimolecular ion peaks were observed at *m/z* 735 $[M - H]^-$, which was consistent with hederagenin 3-*O*-β-D-xylopyranosyl-(1→3)-α-L-arabinopyranoside [7].

Hederagenin (1). Amorphous powder. ^{1}H NMR (400 MHz, CD_3OD, δ, ppm, J/Hz) 5.24 (t, J = 3.5, H-12), 3.62 (dd, J = 11.2, 4.7, H-3), 3.53 (d, J = 10.9, H-23b), 3.29 (d, J = 10.9, H-23a), 2.84 (dd, J = 12.8, 3.8, H-18), 1.17, 0.97, 0.97, 0.81, 0.69, 0.69 (each s, 24, 25, 26, 27, 29, 30-CH_3). For ^{13}C NMR (100 MHz, CD_3OD, δ) data, see Table 2. ESI-MS *m/z* 472 $[M]^+$.

Hederagenin 3-*O*-(3-*O*-Acetyl-β-D-xylopyranosyl)-(1→3)-α-L-arabinopyranoside (2). Amorphous powder, $[\alpha]_D^{25}$ + 22.9° (*c* 0.26, CD_3OD). IR (KBr, ν, cm^{-1}): 3425, 1730, 1695, 1632, and 1047. For ^{1}H NMR (400 MHz, CD_3OD, δ) and ^{13}C NMR (100 MHz, CD_3OD, δ) spectroscopic data, see Tables 1 and 2. HR-ESI-MS *m/z* 777.4430 $[M - H]^-$ (calcd for $C_{42}H_{65}O_{13}$, 777.4425). ESI-MS *m/z*: 777 $[M - H]^-$, 735 $[(M - H) - Ac]^-$, 471 $[(M - H) - Ac - Xyl - Ara]^-$.

Hederagenin 3-*O*-(4-*O*-Acetyl-α-L-arabinopyranosyl)-(1→3)-α-L-rhamnopyranosyl-(1→2)-α-L-arabinopyranoside (3). Amorphous powder. ^{1}H NMR (400 MHz, CD_3OD, δ, ppm, J/Hz): 5.24 (m, H-12), 4.90 (s, Rha H-1), 4.61 (d, J = 7.2, Ara H-1), 4.52 (d, J = 7.2, terminal Ara H-1), 3.63 (m, H-3), 3.63 (m, H-23b), 3.30 (m, H-23a), 2.85 (m, H-18), 2.07 (s, Me of Acetyl), 1.25 (d, J = 5.9, Rha Me), 1.00 (s, 27-CH_3), 0.97 (s, 25-CH_3), 0.94 (s, 30-CH_3), 0.91 (s, 29-CH_3), 0.82 (s, 26-CH_3), 0.70 (s, 24-CH_3). For ^{13}C NMR (100 MHz, CD_3OD, δ) spectroscopic data, see Table 2. ESI-MS *m/z* 923 $[M - H]^-$.

Hederagenin 3-*O*-α-L-Arabinopyranosyl-(1→3)-α-L-rhamnopyranosyl-(1→2)-α-L-arabinopyranoside (4). Amorphous powder. ^{1}H NMR (400 MHz, CD_3OD, δ, ppm, J/Hz) 5.22 (s, H-12), 4.88 (s, Rha H-1), 4.52 (d, J = 7.2, Ara H-1), 4.44 (d, J = 7.1, terminal Ara H-1), 3.63 (d, J = 8, H-23b), 3.61 (m, H-3), 3.32 (d, J = 10.4, H-23a), 2.83 (m, H-18), 1.24 (d, J = 5.8, Me of Rha), 1.09 (s, 27-CH_3), 0.97 (s, 25-CH_3), 0.93 (s, 30-CH_3), 0.90 (s, 29-CH_3), 0.80 (s, 26-CH_3), 0.69 (s, 24-CH_3). For ^{13}C NMR (100 MHz, CD_3OD, δ) spectroscopic data, see Table 2. ESI-MS *m/z* 881 $[M - H]^-$.

Hederagenin 3-*O*-β-D-Glucopyranosyl-(1→3)-α-L-rhamnopyranosyl-(1→4)-β-D-xylopyranoside (5). Amorphous powder. ^{1}H NMR (400 MHz, C_5D_5N, δ, ppm, J/Hz): 5.47 (d, J = 7.7, Glc H-1), 5.22 (s, H-12), 5.00 (d, J = 6.6, Xyl H-1), 4.95 (s, Rha H-1), 3.63 (d, J = 8, H-23b), 3.61 (m, H-3), 3.32 (d, J = 10.4, H-23a), 2.83 (m, H-18), 1.51 (d, J = 4.7, Me of Rha), 1.09 (s, 27-CH_3), 0.97 (s, 25-CH_3), 0.93 (s, 30-CH_3), 0.90 (s, 29-CH_3), 0.80 (s, 26-CH_3), 0.69 (s, 24-CH_3). For ^{13}C NMR (100 MHz, CD_3OD, δ) spectroscopic data, see Table 2. ESI-MS *m/z* 912 $[M]^+$.

The chemical investigation on the hull of rambutan led to the isolation of a new oleane-type triterpene oligoglycoside, together with four known compounds. All these compounds were obtained from the hull of this plant for the first time. Based on the mass, UV, IR spectrum, and NMR spectroscopic data, the structure of this new compound was determined as hederagenin 3-*O*-(3-*O*-acetyl-β-D-xylopyranosyl)-(1→3)-α-L-arabinopyranoside (Fig. 1), which, when compared with hederagenin 3-*O*-β-D-xylopyranosyl-(1→3)-α-L-arabinopyranoside [7], showed that an acetyl added in C-3 of xylopyranoside. In the present study, only a few compounds isolated from the hull of *Nephelium lappaceum* are reported [1–6]. As for the hull of rambutan, further investigations both of the chemical constituents and their biological activities are necessary to discover if it has any additional value, not simply to be discarded.

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