Cucurbitane Glycosides from Unripe Fruits of Lo Han Kuo (*Siraitia grosvenori*)

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From the unripe fruits of Lo Han Kuo (*Siraitia grosvenori*), a Chinese medicinal plant, two new cucurbitane triterpene glycosides, 20-hydroxy-11-oxomogroside IA_1 (1) and 11-oxomogroside IIE (2), were isolated along with five known cucurbitane glycosides, 11-oxomogroside IA_1 (3), mogroside IIE (4), mogroside III (5), mogroside IVA (6), and mogroside V (7), and two flavonoid glycosides, kaempferol 7-*O*-α-L-rhamnopyranoside (8) and kaempferol 3,7-di-*O*-α-L-rhamnopyranoside (9). Their structures were determined on the basis of detailed analyses of 1D, 2D-NMR spectroscopic methods and by comparing with literature values. This paper describes the first investigation of unripe bitter Lo Han Kuo fruits.

Key words *Siraitia grosvenori*; Lo Han Kuo; Cucurbitaceae; unripe fruit; bitter principle; cucurbitane-glycoside

Lo Han Kuo is the fruit of the *Siraitia grosvenori* SWINGLE (formerly *Momordica grosvenori* SWINGLE) belonging to Cucurbitaceae species and used as a pulmonary demulcent and emollient for the treatment of dry cough, sore throat, dire thirst, and constipation in traditional Chinese medicine.[1)] Recently, some intriguing pharmacological characteristics such as anti-cancer and anti-hyperglycemic effects, and inhibition of oxidative modification of low density-lipoprotein were reported.[2—4)] Therefore it was suggested that a new kind of cancer chemopreventive agent might be developed. A number of cucurbitane triterpene saponins from the ripe fruits were previously obtained.[5—12)] Some compounds among them are extremely sweet, such as mogroside V (**7**) and mogroside IVA (**6**), and their relative sweetnesses were more than 300 times as high as that of sucrose despite having minimal caloric content. However, it also contains minor tasteless, even bitter principle, such as mogroside III (**5**) and mogroside IIE (**4**). The ripe fruit mainly contains mogroside V (**7**), so it is very sweet. On the basis of these characteristics, its extract is commercially utilized as a sweet component in sugar substitute, that is widely used as additive and ingredient in health foods and beverages. Owing to the influence of cold weather during winter, some fruits cannot mature naturally. The unripe fruits have bitter taste, and at the place of cultivation, these may amount to one quarter of total production. Until now, no chemical constituent studies have been conducted on these fruits. Hence in unripe fruits, a study on the constituents was performed and provided two new cucurbitane triterpene glycosides, 20-hydroxy-11-oxomogroside IA_1 (**1**) and 11-oxomogroside IIE (**2**), along with five known cucurbitane glycosides, 11-oxomogroside IA_1 (**3**), mogroside IIE (**4**), mogroside III (**5**), mogroside IVA (**6**), mogroside V (**7**), and two flavonoid glycosides, kaempferol 7-*O*-α-L-rhamnopyranoside (**8**) and kaempferol 3,7-di-*O*-α-L-rhamnopyranoside (**9**). Their structures were determined on the basis of detailed analyses of 1D, 2D-NMR spectroscopic methods and by comparing with literature values.[4—11)] Compounds **2** and **4** are the main constituents of unripe fruits and contribute to bitter taste. This paper deals with the first investigation of unripe bitter Lo Han Kuo fruits.

Fresh unripe fruits were extracted with methanol. A suspension of methanol-extract in water was subjected to a high-porous polystynene gel, Diaion HP-20, which was successively eluted with H_2O and 30%, 80%, and 100% methanol. The 80% methanolic eluate was chromatographed on silica gel, Sephadex LH-20 and reverse phase silica gel to afford nine glycosides, compounds **1**—**9**, in yields of 0.0002%, 0.0068%, 0.00064%, 0.0081%, 0.0024%, 0.00019%, 0.0005%, 0.00081% and 0.0011%, respectively.

Compound **1**, a white amorphous powder, $[\alpha]_D$ +113.3° (MeOH), showed a quasi-molecular ion peak at *m/z* 654 $[M+H]^+$ and 654.4398 $[M+H]^+$ in the positive HR-FAB-MS, corresponding to the molecular formula $C_{36}H_{62}O_{10}$, which was supported by ^{13}C-NMR spectrum and its distortionless enhancement by polarization transfer (DEPT) measurement (Table 1). The ^{13}C-NMR spectrum displayed signals due to eight methyls, nine methylenes, eleven methines, and eight quaternary carbons. The ^{1}H-NMR spectrum (Table 1) of **1** exhibited signals due to eight tertiary methyls at δ 1.10, 1.15, 1.23, 1.26, 1.35, 1.43, 1.45 and 1.46 (each 3H), two oxygen-bearing methines at δ 3.72 (1H, br s, $W_{1/2}$=7.2 Hz) and 3.93 (1H, d, J=8.0 Hz) and one olefinic proton signal at δ 5.52 (1H, d, J=5.2 Hz), which correlated with the carbon signals at δ 18.5, 28.0, 19.2, 20.2, 27.0, 26.1, 26.3, 25.4, 75.6, 91.1 and 119.1, respectively, in the heteronuclear multiple quantum coherence (HMQC). It also showed a doublet signal at δ 4.99 (1H, d, J=7.9 Hz), ascribable to an anomeric proton, along with other ^{1}H signals at δ 4.01, 4.20, 4.18, 3.95, 4.30, and 4.50 (each 1H), which correlated with the carbon signals at δ 105.8, 75.4, 78.6, 71.8, 78.4, and 62.7, respectively, in HMQC. After acid hydrolysis of **1**, D-glucose was detected on TLC. The J=7.9 Hz indicated β-glycosidic linkage. On the comparative spectroscopic investigation with those of 11-oxomogroside IA_1 (**3**), the molecular ion of **1** was bigger by 16 mass units than that of **3** in the positive FAB-MS spectrum, suggesting that **1** had one more hydroxyl group than **3**. One hydroxyl-bearing quaternary carbon signal was observed at δ 74.4 in the ^{13}C-NMR spectrum of **1**. How-

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ever in the ^{1}H-NMR spectrum, **1** lacked a doublet methyl signal observed at δ 0.93 (3H, d, J=6.8 Hz) in the spectrum of **3**, and it was replaced by a singlet tertiary methyl signal at δ 1.45. This indicated a hydroxyl group attached to C-20 on the aglycone moiety. In the ^{13}C-NMR spectrum, on going from **3** to **1**, the signal due to C-20 at δ 36.4 was replaced by that of quaternary carbon with a tertiary hydroxyl group at δ 74.4, and the signals due to the carbons around the C-20 position were somewhat displaced: signals due to C-16 at δ 28.1 and C-23 at δ 28.1 were shifted upfield by 6.9 and 0.9 ppm (γ-effect), respectively; those due to C-17 (δ 50.3), C-21 (δ 18.8) and C-22 (δ 33.4) were shfited downfield by 2.4, 7.5, 8.0 ppm, respectively, while other carbon signals remained almost unshifted (Table 1). It follows that **1** could be formulated as 20-hydroxy-11-oxomogroside IA$_1$. In the heteronuclear multiple bonds correlation (HMBC) was observed between H_3-21 and C-17, C-22; H-17 and C-14, C-18. The ^{1}H–^{1}H shift correlation (COSY) and HMQC measurements enabled the assignment of the respective signals on the side chain at C-17, that is, CH_2-22: δ_H 2.55, δ_C 41.4; CH_2-23: δ_H 2.08, δ_C 27.2; CH-24: δ_H 3.93, δ_C 91.1. The nuclear Overhauser exchange spectroscopy (NOESY) (Fig. 1) showed correlations between H-6 and H_3-29; H_3-19 and H-8; H-8 and H-12; H-12 and H_3-18 on the β-face of the molecule, and on the other hand, between H-3 and H_3-28; H-10 and H-3; H-7 and H_3-30; H-17 and H_3-21; H-24 and glucosyl anomeric proton on the α-face. This accords with the skeleton of cucurbitane triterponoid. Hence, **1** was formulated as 3β,20,24,25-tetra-hydroxy-(24*R*)-cucurbit-5-en-11-one 24-*O*-β-D-glucopyranoside (20-hydroxy-11-oxomogroside IA$_1$) as shown in Fig. 2. This is the first time that a 20-hydroxylated aglycone has been isolated from the fruits of Lo Han Kuo.

Compound **2**, a white amorphous powder, $[\alpha]_D$ +64.8° (MeOH), showed a quasi-molecular ion peak at *m/z* 800 $[M+H]^+$ and 799.7955 $[M+H]^+$ in the positive HR-FAB-MS, corresponding to the molecular formula $C_{42}H_{70}O_{14}$, which was also supported by the ^{13}C-NMR and its DEPT spectra. It was composed of eight methyl carbons, ten methylene carbons, seventeen methine carbons, and seven quaternary carbons. The ^{1}H-NMR spectrum (Table 1) of **2** exhibited signals due to seven tertiary methyls at δ 0.74, 0.93, 1.12, 1.16, 1.40, 1.46, and 1.53 (each 3H), one secondary methyl at 0.89 (3H, d, J=6.7 Hz), two oxygen-bearing methines at 3.65 (1H, br s), and 3.85 (1H, d, J=9.2 Hz), and one olefinic group at 5.52 (1H, d, J=5.2 Hz), which correlated with the carbon signals at δ 16.9, 18.5, 28.3, 20.2, 26.9, 25.4, 25.8, 18.2, 87.1, 90.5 and 118.5, respectively, in the HMQC. In the ^{1}H-NMR spectrum (Table 1) of **2**, two anomeric protons at δ 4.84 (1H, d, J=7.7 Hz) and 4.97 (1H, d, J=7.9 Hz) were observed along with other signals at δ 4.01, 4.19, 4.16, 3.92, 4.29, 4.53, 4.03, 4.21, 4.18, 3.95, 4.36, and 4.51 (each 1H), which correlated with the carbon signals at δ 107.2, 75.3, 78.6, 71.8, 78.2, 63.0, 105.8, 75.5, 78.7, 72.0, 78.4, and 62.8, respectively, in the HMQC (Table 1). Acid hydrolysis of **2** yield only D-glucose on TLC. The J=7.7, 7.9 Hz indicated β-glycosidic linkages. When the ^{1}H- and ^{13}C-NMR spectra of **2** were compared with those of **3**, signals ascribable to the aglycone moiety were identical. The HMBC was observed between the amomeric proton at δ 4.84 and the C-3 at δ 87.1; another amomeric proton at δ 4.97 and C-24 at δ 90.5. Consequently, the structure of **2** was characterized as 3,24-*O*-β-D-glucopynanosyl 11-oxomogrol (11-oxomogroside IIE).

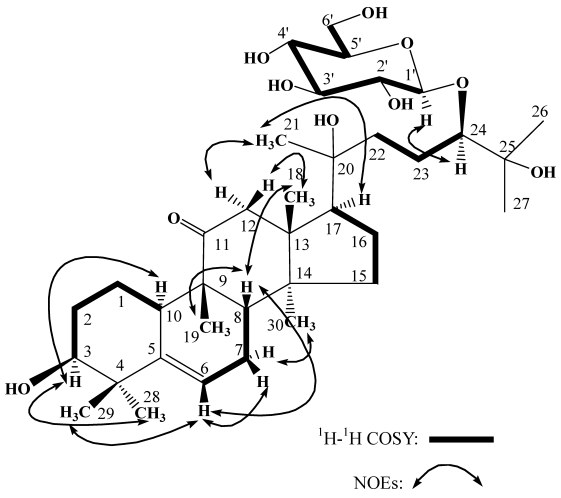
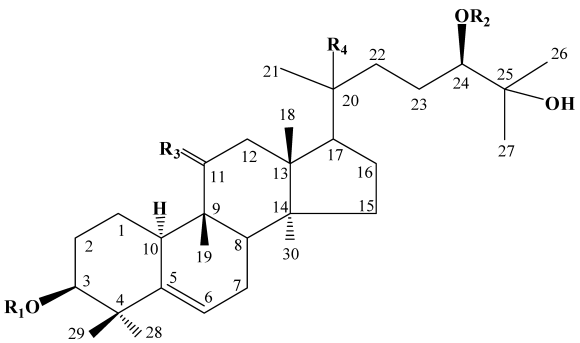
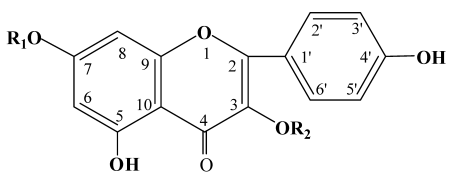


Fig. 1. ^{1}H–^{1}H COSY and Key NOESY Correlations in Compound **1**



	R_1	R_2	R_3	R_4
20-hydroxy-11-oxomogroside ⅠA$_1$ (1)	—H	—Glc	=O	—OH
11-oxomogroside ⅡE (2)	—Glc	—Glc	=O	—H
11-oxomogroside ⅠA$_1$ (3)	—H	—Glc	=O	—H
mogroside ⅡE (4)	—Glc	—Glc	OH / H	—H
mogroside Ⅲ (5)	—Glc	—Glc^{6}Glc	OH / H	—H
mogroside Ⅳ (6)	—Glc^{6}Glc	—Glc^{6}Glc	OH / H	—H
mogroside Ⅴ (7)	—Glc^{6}Glc	—Glc^{6}Glc (2 Glc)	OH / H	—H



	R_1	R_2
kaempferol 7-O-α-L- rhamnopyranoside (8)	−Rha	−H
kaempferol 3,7-di-O-α-L-rhamnopyranoside (9)	−Rha	−Rha

Fig. 2. Structures of Compounds **1**—**9** from the Unripe Fruit of *Siraitia grosvenori*

Table 1. ^{13}C, ^{1}H, and HMBC NMR Spectral Data for Cucurbitane Glycosides, **1** and **2**, from the Unripe Fruits of Lo Han Kuo (in C_5D_5N)

C No.	20-hydroxy-11-oxomogroside IA_1 (**1**)			11-oxo-mogroside IIE (**2**)		
	δ_C	δ_H [a)]	HMBC(H–C)	δ_C	δ_H [a)]	HMBC(H–C)
1	22.4	1.61 (α), 2.08 (β)	2, 10	22.1	1.58 (α), 1.98 (β)	2, 10
2	29.8	1.88 (α), 1.70 (β)	4	29.4	1.91 (α), 1.75 (β)	4
3	75.6	3.72 (br s, $W_{1/2}$=7.2)	1, 5	87.1	3.65 (br s, $W_{1/2}$=5.2)	1, 2, 4
4	41.9			42.0		
5	141.4			141.3		
6	119.1	5.52 (d, 5.2)	8, 10	118.5	5.52 (d, 5.2)	4, 7, 8, 10
7	24.2	2.25 (α), 1.82 (β)	8, 9	24.1	2.20 (α), 1.75 (β)	8, 9
8	43.5	1.97	7, 9, 15, 30	44.0	1.81	7, 14, 19, 30
9	49.0			49.0		
10	36.0	2.55	9, 11	36.0	2.46	9, 11
11	214.2			213.7		
12	49.4	3.07 (α), 2.51 (β)	11, 13, 18	48.7	2.91 (α), 2.49 (β)	13, 14, 18
13	49.3			49.0		
14	50.4			49.7		
15	34.2	1.30 (α), 1.37 (β)	16, 17	34.6	1.18 (α), 1.30 (β)	14, 16, 17
16	21.2	2.31 (α), 1.92 (β)	13, 14	28.4	1.92 (α), 1.82 (β)	14, 15
17	52.7	2.29	14, 18	49.9	1.78	15, 18
18	19.2	1.23 (3H, s)	12, 13, 17	16.9	0.74 (3H, s)	12, 13, 17
19	20.2	1.26 (3H, s)	8, 9, 10	20.2	1.16 (3H, s)	1, 8, 9, 10
20	74.4			36.2	1.45	17, 21
21	26.3	1.45 (3H, s)	17, 20, 22	18.2	0.89 (3H, d, 6.7)	17, 18, 20
22	41.4	1.99 (d, 8.7), 2.55 (d, 8.6)	23	33.3	1.81, 1.92	20, 21
23	27.2	1.87, 2.08	22	28.0	2.36, 2.46	
24	91.1	3.93 (d, 8.0)	23, 25, G1′	90.5	3.85 (d, 9.2)	23, 25, G-1″
25	72.2			72.0		
26	25.4	1.46 (3H, s)	24, 25, 27	25.4	1.46 (3H, s)	24, 25, 27
27	27.0	1.35 (3H, s)	24, 25, 26	26.9	1.40 (3H, s)	24, 25, 26
28	28.0	1.15 (3H, s)	3, 4, 5, 29	28.3	1.12 (3H, s)	3, 4, 5, 29
29	26.1	1.43 (3H, s)	3, 4, 5, 28	25.8	1.53 (3H, s)	2, 3, 4, 5, 28
30	18.5	1.10 (3H, s)	8, 14, 15	18.5	0.93 (3H, s)	8, 9, 13, 14
G-1′	105.8	4.99 (d, 7.9)	24, G2′, G5′	107.2	4.84 (d, 7.7)	3
2′	75.4	4.01 (dd, 7.9, 8.0)	G1′, G3′	75.3	4.01 (*t*-like, 7.7)	G1′, G3′
3′	78.6	4.20 (dd, 7.9, 8.0)	G2′, G4′	78.6	4.19*	G2′, G4′
4′	71.8	4.18 (dd, 7.9, 8.0)	G3′, G5′	71.8	4.16*	G2′, G3′
5′	78.4	3.95 (m)	G1′, G6′	78.2	3.92 (m)	G1′, G3′
6′	62.7	4.51 (dd, 5.5, 9.8); 4.31 (d, 9.8)	G5′	63.0	4.29 (dd, 5.5, 11.6); 4.53 (d, 11.6)	G4′
G-1″				105.8	4.97 (d, 7.9)	G3″, G5″
				75.5	4.03 (*t*-like, 7.9)	G1″, G3″
				78.7	4.21*	G2″, G4″
4″				72.0	4.18*	G3″, G5″
5″				78.4	3.95 (m)	G1″, G6″
6″				62.8	4.36 (dd, 5.5, 12.0); 4.51 (d, 12.0)	G4″, G5″

Numbers in parentheses denote *J* values (Hz); * overlapped.

Experimental

General Experimental Procedures Optical rotations were measured with a P-1010 polarimeter (JASCO, Japan) at 25 °C. TLC was performed on precoated silica gel 60 F_{254} plate (Merck), and detection was by spraying 10% aq. H_2SO_4. Column chromatographies were carried out on Kiesel gel (40—100 mesh and 230—400 mesh, Kanto Chem.), Diaion HP-20 (Mitsubishi Chemical Ind.). Sephadex LH-20 (25—100 mm, Pharmacia Fine Chemicals), Wakogel 50C18 (36—212 mm, Wako Pure Chemical Industuies, Ltd.), Chromatorex ODS (30—50 μm, Fuji Silysia Chemical Ltd.). FAB-MS were measured by JEOL JMS-DX303HF spectrometer (Xe atom beam, accel. voltage 2—3 kV, matrix glycerol), 200—300 mA. NMR spectra were recorded at 500 MHz for ^{1}H and 125 MHz for ^{13}C by JNC-A500 NMR spectrometer and chemical shifts were given on a δ (ppm) scale with tetramethylsilane as internal standard. Standard pulse sequences were employed for DEPT, HMQC, and HMBC experiments. NOESY spectra were measured with mixing times of 600 ms. Acid hydrolysis of the triterpene glycoside was performed with 1 M H_2SO_4–MeOH for 2 h under reflux on a water bath.

Plant Material Unripe fruits of *Siraitia grosvenori* (40—50 d of growing) were obtained from Lingui county, Guilin city of Guangxi province, China, in October 2004 and identified by Professor Wei Huanan. A voucher specimen (SG05820) of the plant is deposited at the Herbarium of Guangxi Institute of Botany, China.

Extraction and Isolation Fresh unripe fruits (5 kg) of *Siraitia grosvenori* were extracted with methanol (8 l×3) at room temperature for 10 d. The extract was evaporated under reduced pressure to afford methanol extract (205 g). The extract was chromotograped on Diaion HP-20, with successive elution with H_2O and 30%, 80%, and 100% methanol. The 80% methanol eluate (30.5 g) was submitted to silica gel column and eluted with $CHCl_3$–MeOH–H_2O (8 : 2 : 0.2; 7 : 3 : 0.5; 6 : 4 : 1, v/v), gradiently, to afford ten fractions. Fr. 5 (1.13 g) was then subjected to a Wakogel C18 column chromatography (50—60% MeOH) to afford **4** (405.6 mg) and **8** (40.6 mg). Fr. 2—3 (880 mg) were repeatedly subjected to silica gel column chromatography with $CHCl_3$–MeOH–H_2O (8 : 2 : 0.2, v/v), followed by further purification with Sephadex LH-20 (30% MeOH) to afford **2** (342 mg) and **3** (32 mg). Fr. 4 (400 mg) was chromotograped on a Wakogel C18 column followed by further purification with Sephadex LH-20 (30—50% MeOH) to provide **1** (10.1 mg) and **9** (55 mg). Fr. 7—9 (1.2 g) were repeatedly subjected to silica gel column chromatography with $CHCl_3$–MeOH–H_2O (8 : 2 : 0.2; 7 : 3 : 0.5, v/v) followed by further purification with Chromatorex ODS (55—65% MeOH) to give **5** (128 mg), **6** (9.4 mg), and **7** (25.2 mg).

20-Hydroxy-11-oxomogroside IA_1 (1) A white amorphous powder, $[\alpha]_D$ +113.3° (c=0.2, MeOH). Positive FAB-MS (m/z): 654 $[M+H]^+$. Positive HR-FAB-MS (m/z): 654.4398 $[M+H]^+$ (Calcd for $C_{36}H_{62}O_{10}$, 654.4377). ^{1}H- and ^{13}C-NMR (in pyridine-d_5) given in Table 1.

11-Oxomogroside IIE (2) A white amorphous powder, $[\alpha]_D$ +64.8° (c=0.3, MeOH). Positive FAB-MS (m/z): 800. Positive HR-FAB-MS (m/z): 799.7955 $[M+H]^+$ (Calcd for $C_{42}H_{70}O_{14}$, 799.7971). ^{1}H- and ^{13}C-NMR (in pyridine-d_5) given in Table 1.

11-Oxomogroside IA$_1$ (3) A white amorphous powder, $[\alpha]_D^{25}$ +2.8° (c=0.1, MeOH). Positive FAB-MS (m/z): 675.5 $[M+Na]^+$, ^{1}H-NMR (in pyridine-d_5) δ: 0.93 (3H, d, J=6.8 Hz H_3-21), 1.08 (3H, s, H_3-30), 1.10 (3H, s, H_3-28), 1.18 (3H, s, H_3-18), 1.40 (3H, s, H_3-19), 1.43 (3H, s, H_3-27), 1.45 (3H, s, H_3-26), 1.46 (3H, s, H_3-29), 1.95 (1H, m, H-8), 2.64 (1H, t, H-10), 2.96 (1H, s, H-12), 3.70 (1H, br s, $W_{1/2}$=6.2 Hz, H-3), 3.85 (1H, d, J=8.2 Hz, H-24), 4.98 (1H, d, J=7.9 Hz, glc H-1), 4.04 (1H, dd, J=8.0, 9.5 Hz, glc H-2), 4.22 (2H, dd, J=8.7, 6.1 Hz, glc H-3, 4), 3.97 (1H, t, J=5.5 Hz, glc H-5), 4.53 (1H, dd, J=8.8, 12.0 Hz, glc H-6), 5.57 (1H, d, J=5.5 Hz, H-6); ^{13}C-NMR (in pyridine-d_5) δ: aglycone moiety 20.5 (C1), 29.5 (C2), 75.6 (C3), 42.0 (C4), 141.4 (C5), 120.1 (C6), 24.0 (C7), 43.5 (C8), 54.2 (C9), 36.0 (C10), 212.8 (C11), 49.1 (C12), 48.9 (C13), 49.5 (C14), 35.1 (C15), 28.1 (C16), 50.3 (C17), 16.1 (C18), 20.2 (C19), 36.4 (C20), 18.8 (C21), 33.4 (C22), 28.1 (C23), 90.7 (C24), 72.0 (C25), 25.4 (C26), 26.2 (C27), 27.8 (C28), 26.9 (C29), 18.6 (C30). β-D-glucopy-ranosyl moiety 105.9 (C1), 75.4 (C2), 78.6 (C3), 71.8 (C4), 78.5 (C5), 62.8 (C6).

Mogroside IIE (4) A white amorphous powder, $[\alpha]_D^{25}$ +13.2° (c=0.1, MeOH), Positive FAB-MS (m/z): 823.6 $[M+Na]^+$, ^{1}H-NMR (in pyridine-d_5) δ: 0.86 (3H, s, H_3-30), 0.92 (3H, s, H_3-18), 0.97 (3H, d, J=6.7 Hz, H_3-21), 1.16 (3H, s, H_3-28), 1.31 (3H, s, H_3-19), 1.39 (3H, s, H_3-27), 1.44 (3H, s, H_3-26), 1.54 (3H, s, H_3-29), 3.68 (1H, br s, H-3), 3.85 (1H, d, J=7.9 Hz, H-24), 4.05 (1H, dd, J=5.0, 11.2 Hz, H-11), 5.50 (1H, d, J=5.2 Hz, H-6), anomeric proton: 4.85 (1H, d, J=7.9 Hz), 4.97 (1H, d, J=7.8 Hz). ^{13}C-NMR (in pyridine-d_5) δ: aglycone moiety 26.7 (C1), 29.5 (C2), 87.8 (C3), 42.3 (C4), 144.2 (C5), 118.5 (C6), 24.5 (C7), 43.5 (C8), 40.1 (C9), 36.8 (C10), 77.8 (C11), 41.0 (C12), 47.4 (C13), 49.7 (C14), 34.5 (C15), 28.3 (C16), 50.9 (C17), 17.0 (C18), 26.9 (C19), 36.4 (C20), 18.8 (C21), 33.4 (C22), 28.3 (C23), 90.6 (C24), 72.1 (C25), 25.3 (C26), 26.2 (C27), 27.7 (C28), 26.3 (C29), 19.3 (C30), anomeric C: 107.2, 105.8.

Mogroside III (5) A white amorphous powder, $[\alpha]_D^{25}$ +3.6° (c=0.1, MeOH), Positive FAB-MS (m/z): 986.0 $[M+Na]^+$, ^{1}H-NMR (in pyridine-d_5) δ: 0.86 (3H, s, H_3-30), 0.93 (3H, s, H_3-18), 0.94 (3H, d, J=9.8 Hz, H_3-21), 1.16 (3H, s, H_3-28), 1.32 (6H, s, H_3-19, H_3-27), 1.43 (3H, s, H_3-26), 1.55 (3H, s, H_3-29), 3.68 (1H, br s, H-3), 5.49 (1H, d, J=5.2 Hz, H-6), 3.75 (1H, d, J=9.2 Hz, H-24), 4.02 (1H, d, J=8.9 Hz, H-11), anomeric proton: 4.82 (1H, d, J=7.3 Hz), 4.88 (1H, d, J=7.9 Hz), 4.94 (1H, d, J=8.2 Hz). ^{13}C-NMR (in pyridine-d_5) δ: 26.7 (C1), 29.5 (C2), 87.9 (C3), 42.4 (C4), 144.3 (C5), 118.5 (C6), 24.6 (C7), 43.5 (C8), 40.1 (C9), 36.8 (C10), 77.8 (C11), 41.2 (C12), 47.4 (C13), 49.7 (C14), 34.6 (C15), 28.2 (C16), 51.1 (C17), 17.1 (C18), 27.0 (C19), 36.2 (C20), 18.8 (C21), 33.1 (C22), 28.2 (C23), 92.7 (C24), 72.7 (C25), 24.3 (C26), 26.2 (C27), 27.7 (C28), 26.3 (C29), 19.3 (C30), anomeric C: 107.3, 104.8, 106.3.

Kaempferol 7-*O*-α-L-Rhamnopyranoside (8) A pale yellow needles, $[\alpha]_D^{25}$ −142.8° (c=0.1, MeOH), Positive FAB-MS (m/z): 289.2 $[M+H]^+$, ^{1}H-NMR (in DMSO-d_6) δ: 1.13 (3H, d, J=6.1 Hz Rha Me), 5.52 (1H, d, J=2.0 Hz, Rha H-1), 6.42 (1H, d, J=1.8 Hz, H-8), 6.82 (1H, d, J=2.5 Hz, H-6), 6.92 (2H, d, J=8.5 Hz, H-3′, 5′), 8.09 (2H, d, J=9.2 Hz, H-2′, 6′). ^{13}C-NMR (in DMSO-d_6) δ: 148.0 (C2), 136.5 (C3), 176.6 (C4), 160.9 (C5), 99.3 (C6), 161.9 (C7), 94.9 (C8), 156.3 (C9), 105.2 (C10), 121.0 (C-1′), 130.1 (C-2′, 6′), 116.0 (C-3′, 5′), 159.9 (C-4′). Rha: 98.9, 70.5, 70.8, 72.1, 70.4, 18.4.[13,14]

Kaempferol 3,7-Di-*O*-α-L-rhamnopyranoside (9) A pale yellow powder, $[\alpha]_D^{25}$ −25.6° (c=0.1, MeOH), Positive FAB-MS (m/z): 455.2 $[M+Na]^+$, 433.2 $[M+H]^+$, ^{1}H-NMR (in pyridine-d_5) δ: 1.42 (3H, br s, Rha Me-6), 1.47 (3H, d, Rha′ Me), 6.21 (1H, d, J=2.0 Hz, Rha H-1), 6.26 (1H, d, J=2.0 Hz, Rha′ H-1), 6.77 (1H, d, J=2.4 Hz, H-8), 6.94 (1H, d, J=1.8 Hz, H-6), 7.27 (2H, d, J=8.6 Hz, H-3′, 5′), 8.05 (2H, d, J=9.1 Hz, H-2′, 6′). ^{13}C-NMR (in DMSO-d_6) δ: 156.1 (C2), 134.5 (C3), 177.9 (C4), 160.9 (C5), 99.4 (C6), 161.7 (C7), 94.6 (C8), 157.7 (C9), 105.8 (C10), 120.3 (C-1′), 130.6 (C-2′, 6′), 115.4 (C-3′, 5′), 160.1 (C-4′). 3-Rha: 101.8, 70.2, 70.6, 71.6, 70.0, 17.4; 7-Rha: 98.5, 70.3, 70.6, 71.1, 69.8, 17.8.[13,14]

References

1) "The Pharmacopoeia of the People's Republic of China," Part I, The Pharmacopoeia Commission of PRC, Chemical Industry Publishing Press, Beijing, 2005, pp. 147—148.
2) Takasaki M., Konoshima T., Murata Y., Sugiura M., Nishino H., Tokuda H., Matsumoto K., Kasai R., Yamasaki K., *Cancer Lett.*, **198**, 37—42 (2003).
3) Suzuki Y. A., Murata Y., Inui H., Sugiura M., Nakano Y., *J. Agric. Food Chem.*, **53**, 2941—2946 (2005).
4) Takeo E., Yoshida S., Tada S., Shingu T., Matsuura H., Murata Y., Yoshikawa S., Ishikawa T., Nakamura H., Ohsuzu F., Kohda H., *J. Atheroscler. Thromb.*, **9**, 114—120 (2002).
5) Takemoto T., Arihara S., Nakajima T., Okuhira M., *Yakugaku Zasshi*, **103**, 1151—1173 (1983).
6) Kasai R., Nie R. L., Nashi K., Ohtani K., Zhou J., Tao G. D., Tanaka O., *Agric. Biol. Chem.*, **53**, 3347—3349 (1989).
7) Matsumoto K., Kasai R., Ohtani K., Tanaka O., *Chem. Pharm. Bull.*, **38**, 2030—2032 (1990).
8) Si J. Y., Chen D. H., Chang Q., Shen L. G., *Acta Pharm. Sinica*, **29**, 158—160 (1994).
9) Chang Q., Chen D. H., Si J. Y., Shen L. G., *Chin. J. Mag. Res.*, **11**, 43—48 (1994).
10) Si J. Y., Chen D. H., Shen L. G., *Acta Botanica Sinica*, **38**, 489—494 (1996).
11) Ukiya M., Akihisa T., Tokuda H., Toriumi M., Mukainaka T., Banno N., Kimura Y., Hasegawa J., Nishino H., *J. Agric. Food Chem.*, **50**, 6710—6715 (2002).
12) Zhang J. Y., Yang X. W., *J. Chin. Pharm. Sci.*, **12**, 196—200 (2003).
13) Si J. Y., Chen D. H., Chang Q., Shen L. G., *Acta Pharm. Sinica*, **29**, 158—160 (1994).
14) Nakano K., Takatani M., Tomimatsu T., Nohara T., *Phytochemistry*, **22**, 2831—2833 (1983).