Quadranosides VI—XI, Six New Triterpene Glucosides from the Seeds of *Combretum quadrangulare*

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Six new triterpene glucosides, quadranosides VI—XI (1—6), belonging to three different [ursane- (1—4), oleanane- (5) and lupane-type (6)] triterpene classes, have been isolated from a MeOH extract of the seeds of *Combretum quadrangulare* KURZ (Combretaceae), together with nine known compounds, rosamutin (7), 28-*O*-β-D-glucopyranosyl-6β,23-dihydroxytormentic acid (8), arjunetin (9), arjunglucoside II (10), combreglucoside (11), chebuloside II (12), vitexin (13), (+)-catechin (14) and (−)-epigallocatechin (15). The structures of these compounds were elucidated by spectroscopic analysis.

Key words *Combretum quadrangulare*; Combretaceae; triterpene glucoside; quadranoside; Vietnamese folk medicine; Tram bau

Combretum (*C.*) species (Combretaceae) are widely used in folk medicine for the treatment of hepatitis, malaria, respiratory infections and cancer in different parts of Asia and Africa.[1)] *Combretum quadrangulare* is a tree indigenous to eastern Asia that is commonly known as "Tram bau" in Vietnam. The seeds, leaves and stem bark of the plant have been used in Vietnamese folk medicine as an antipyretic, antidysenteric, antihepatitis and anthelmintic agent. The seeds are administrated orally together with ripe bananas as an anthelmintic for ascariasis and oxyuriasis.[2)] In our study of the bioactive constituents of *C. quadrangulare*, we identified thirty cycloartane-type triterpenes, including twenty-eight new ones, and seven known flavonoids from the leaves.[3)] Recently, we have also examined the constituents of the seeds and isolated five new triterpene glucosides, quadranosides I—V, from a MeOH extract.[4)] In a continuing study of the constituents of the seeds, we further examined the MeOH extract and isolated six new triterpene glucosides, named quadranosides VI—XI (**1**—**6**), together with nine known compounds. In this paper, we report the isolation and structure elucidation of the new triterpene glucosides by spectroscopic techniques.

The dried seeds of *C. quadrangulare* were extracted with MeOH and evaporation under reduced pressure yielded a light brown MeOH extract which exhibited a potent hepatoprotective effect on D-galactosamine (D-GalN)/tumor necrosis factor (TNF)-α-induced cell death in primary cultured mouse hepatocytes.[4)] By repeated column chromatography over Sephadex LH-20, Cosmosil 75C_{18}-OPN and silica gel, followed by preparative TLC and HPLC, the MeOH extract gave a further six new triterpene glucosides, quadranosides VI—XI (**1**—**6**), together with nine known compounds, rosamutin (**7**),[5)] 28-*O*-β-D-glucopyranosyl-6β,23-dihydroxytormentic acid (**8**),[6)] arjunetin (**9**),[7)] arjunglucoside II (**10**),[8)] combreglucoside (**11**),[9)] chebuloside II (**12**),[10)] vitexin (**13**),[11)] (+)-catechin (**14**)[12)] and (−)-epigallocatechin (**15**).[13)] These known compounds were identified by comparison of their spectral data with that in the literature.

Quadranoside VI (**1**) was isolated as a colorless amorphous solid. The molecular ion peak at *m/z* 673.3923 in the high-resolution FAB-MS (HR-FAB-MS) of **1** indicated its molecular formula to be $C_{36}H_{56}O_{11}$. Absorption bands at 3450, 1730 and 1640 cm^{-1} in the IR spectrum of **1** suggested the presence of a hydroxyl, carbonyl and olefinic group, respectively. The ^{1}H-NMR spectrum of **1** displayed signals corresponding to six tertiary methyls (δ_H 1.00, 1.57, 1.63, 1.69, 1.73, 1.80), an olefin (δ_H 5.72, t, J=2.5 Hz), three oxygenated methines (δ_H 4.23, 4.39, 5.43) and an oxygenated methylene (δ_H 4.03, 4.39, each d, J=10.5 Hz), together with seven oxygenated methine and methylene protons ascribable to a sugar unit (Table 1). The ^{13}C-NMR spectrum of **1**, on the other hand, showed thirty-six carbon signals including six primary, nine secondary, eleven tertiary, and six quaternary sp^3 carbons (Table 1), and one tri- and one tetra-substituted olefin, including typical signals (δ_C 128.1 and 137.3) for a double-bond at C-12(13) of ursane-type triterpenes.[14)] Thus, **1** was considered to be an ursane-type triterpene bearing a sugar, three oxygenated methine, an oxygenated methylene and an olefin at C-12(13). The ^{1}H- and ^{13}C-NMR data for **1** were similar to that for 2α,3β,23-trihydroxyurs-12,19-dien-28-oic acid 28-*O*-β-D-glucopyranoside (**16**) isolated from the same extract,[4)] but they were characterized by disappearance of the methylene signal assigned to C-6 and appearance of oxygenated methine signals (δ_H 5.43; δ_C 67.4). Thus, **1** appeared to be a 6-hydroxyl derivative of **16** and this was confirmed by analysis of ^{1}H–^{1}H shift correlation spectroscopy (COSY), heteronuclear multiple quantum coherence (HMQC) and heteronuclear multiple bond correlation (HMBC) spectra. The HMBC spectrum (Fig. 1a) showed long-range correlations between the quaternary carbon at δ_C 44.5 (C-4) and the protons at δ_H 4.39 (H-2), 4.23 (H-3), 5.43 (H-6) and 1.73 (H_3-24), indicating the position of the additional hydroxyl group to be at C-6. The sugar moiety of **1** was supposed to be glucose based on the coupling constants of each proton and the ^{13}C-NMR chemical shifts and this was confirmed by GC analysis of a chiral derivative of an acid hydrolysate.[15)] Furthermore, GC analysis indicated that the glucose has a D configuration. The chemical shifts of the anomeric proton (δ_H 6.31, d, J=8.1 Hz) and carbon (δ_C 95.9) revealed that the glucose is attached to the carboxyl group

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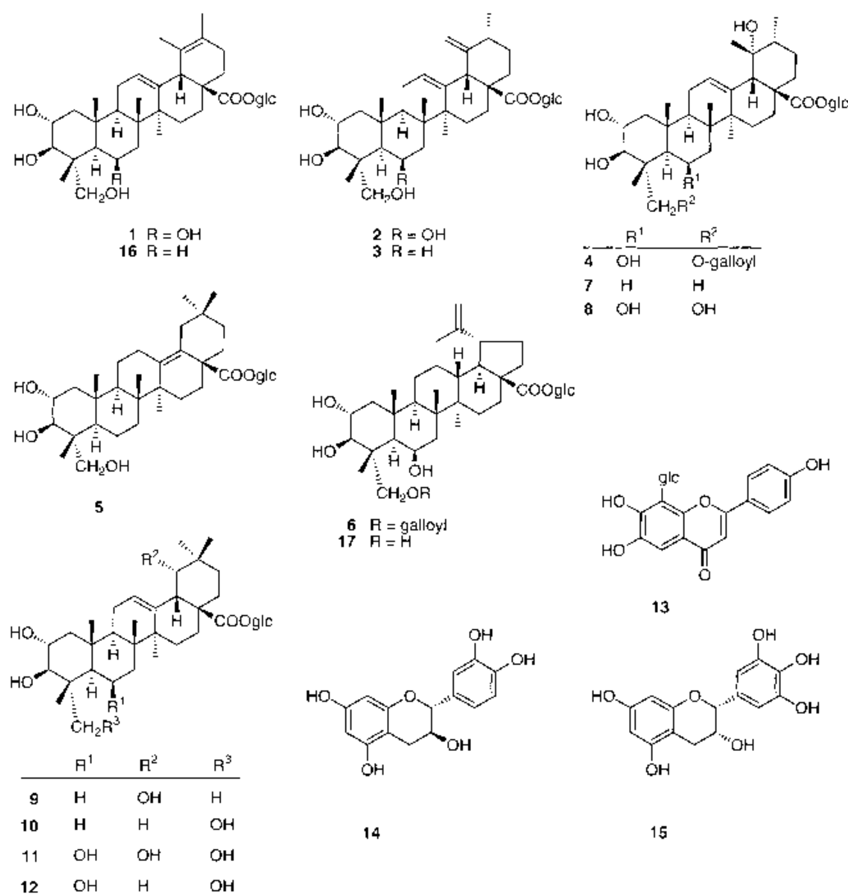


Chart 1

(C-28). This was confirmed by a long-range correlation between the anomeric proton and the carboxyl carbon (δ_C 176.2) in the HMBC spectrum (Fig. 1a). Accordingly, the planar structure of quadranoside VI was determined as 2,3,6,23-tetrahydroxyurs-12,19-dien-28-oic acid 28-*O*-β-D-glucopyranoside.

The stereochemistry of **1** was determined from the ROESY spectrum (Fig. 1b). The spectrum showed correlations between H-2 and the methyl protons (H_3-24 and H_3-25) and between H-3 and H-5, indicating the orientation of the hydroxyl groups to be 2α, 3β and 4α (4α-CH_2OH). The broad singlet of H-6 and the ROESY correlation between H-5 and H-6 indicated the configuration of 6-OH to be β. Thus, the structure of quadranoside VI was determined to be 2α,3β,6β,23-tetrahydroxyurs-12,19-dien-28-oic acid 28-*O*-β-D-glucopyranoside (**1**).

Quadranoside VII (**2**) was isolated as a colorless amorphous solid and its molecular formula was determined to be $C_{36}H_{56}O_{11}$ by HR-FAB-MS. The IR spectrum of **2** also indicated the presence of hydroxyl, carbonyl and olefinic groups. The ^{1}H- and ^{13}C-NMR spectra of **2** were similar to **1**, except for the presence of signals due to an *exo*-olefin (δ_H 5.05, 5.20; δ_C 110.5), a secondary methyl (δ_H 1.05; δ_C 19.4) and a methine (δ_H 1.81; δ_C 37.5) group instead of the signals of two vinyl methyls (δ_H 1.63, 1.57; δ_C 17.3, 20.4) and a tetrasubstituted olefin (δ_C 123.6, 128.9). Thus, **2** was a glucoside of an ursane-type triterpene having a double bond at C-19(29). This was confirmed by the HMBC spectrum, which showed a long-range correlation between the *exo*-olefinic protons and C-18 (Fig. 2). Accordingly, the planar structure of quadranoside VII was determined to be 2,3,6,23-tetrahydroxyurs-12,19(29)-dien-28-oic acid 28-*O*-β-D-glucopyranoside. In the ROESY spectrum of **2**, ROESY correlations were observed between H-2 and H_3-24 and between H-3 and H-5, indicating that the stereochemistry of ring A was 2α-OH, 3β-OH and 4α-CH_2OH. The broad singlet of H-6, identical with that of **1**, and a ROESY correlation between H-6 and H_2-23 suggested that 6-OH has a β-orientation. Thus, the structure of quadranoside VII was determined to be 2α,3β,6β,23-tetrahydroxyurs-12,19(29)-dien-28-oic acid 28-*O*-β-D-glucopyranoside (**2**).

Quadranoside VIII (**3**) was also obtained as a colorless amorphous solid whose molecular formula was determined to be $C_{36}H_{56}O_{10}$ by HR-FAB-MS. The IR spectrum of **3** indicated the presence of hydroxyl (3400 cm^{-1}), carbonyl (1710 cm^{-1}) and olefinic (1640 cm^{-1}) groups. The ^{1}H- and ^{13}C-NMR spectra of **3** were almost identical to **2** except for the absence of the oxygenated methine signal at C-6 (Table 1). Thus, the structure of quadranoside VIII appeared to be 2α,3β,23-trihydroxyurs-12,19(29)-dien-28-oic acid 28-*O*-β-D-glucopyranoside (**3**), which was confirmed by the ^{1}H–^{1}H COSY, HMQC, HMBC and ROESY spectra.

Quadranoside IX (**4**) showed a *quasi*-molecular ion peak at *m/z* 857.3937 in the HR-FAB-MS, corresponding to the molecular formula $C_{43}H_{62}O_{16}$. The IR spectrum of **4** showed absorption bands at 3400 and 1710 cm^{-1}, corresponding to a hydroxyl and carbonyl group, respectively. The ^{1}H- and ^{13}C-NMR spectra of **4** were similar to 28-*O*-β-D-glucopyranosyl-

Table 1. ^{1}H- and ^{13}C-NMR Data of **1**—**4** in C_5D_5N[a)]

Position	**1**		**16**		**2**	
	^{13}C	^{1}H	^{13}C	^{1}H	^{13}C	^{1}H
1	50.7	1.47 m, 2.42 dd (12.7, 5.5)	48.3	1.38 m, 2.34 dd (12.2, 3.9)	50.3	1.49 m, 2.37 dd (12.5, 4.1)
2	69.1	4.39 m	68.9	4.27 m	69.1	4.42 m
3	78.2	4.23 d (9.3)	78.1	4.24 m	78.3	4.25 m
4	44.5		43.6		44.5	
5	48.4	1.98 m	48.0	1.78 m	48.8	1.97 m
6	67.4	5.43 br s	18.4	1.68 m	67.6	5.08 br s
7	41.7	1.81 m, 2.01 m	33.9	1.36 m	41.3	1.88 m, 1.98 m
8	44.3		43.8		39.3	
9	48.9	1.87 m	48.3	1.72 m	48.8	2.13 m
10	38.1		39.9		38.2	
11	24.1	2.15 m, 2.28 m	23.9	2.02 m	24.1	2.15 m, 2.30 m
12	128.1	5.72 t (2.5)	127.7	5.63 t (2.5)	128.9	5.62 t (2.6)
13	137.3		137.8		136.8	
14	39.3		38.3		43.5	
15	28.7	1.26 m, 2.49 m	28.7	1.13 m, 2.34 m	29.1	1.15 m, 2.49 m
16	23.7	2.00 m	23.6	1.99 m	25.9	1.75 m, 1.85 m
17	47.4		47.3		49.8	
18	50.5	3.55 s	50.4	3.51 s	52.2	3.81 s
19	123.6		123.8		153.4	
20	128.9		128.8		37.5	1.81 m
21	28.5	1.72 m, 1.75 m	28.5	1.74 m, 2.18 m	30.6	1.43 m
22	32.9	1.93 m	32.9	1.66 m	37.1	1.81 m, 1.98 m
23	66.2	4.03 d (10.5), 4.39 d (10.5)	66.5	3.70 d (10.5), 4.23 d (10.5)	66.2	4.06 d (10.4), 4.39 d (10.4)
24	16.0	1.73 s	14.4	1.05 s	16.0	1.76 s
25	19.5	1.80 s	18.0	1.10 s	19.2	1.82 s
26	20.1	1.69 s	18.3	1.15 s	18.8	1.74 s
27	22.2	1.00 s	22.1	0.98 s	26.2	1.18 s
28	176.2		176.2		176.0	
29	17.3	1.63 s	17.3	1.60 s	110.5	5.05 br s, 5.20 br s
30	20.4	1.57 s	20.4	1.57 s	19.4	1.05 d (5.8)
Glucose						
1′	95.9	6.31 d (8.1)	95.8	6.33 d (8.0)	96.0	6.28 d (8.0)
2′	74.2	4.18 dd (8.8, 8.1)	74.2	4.19 m	74.1	4.18 dd (8.7, 8.0)
3′	78.7	4.27 dd (9.0, 8.8)	78.8	4.28 m	78.7	4.26 dd (8.9, 8.7)
4′	71.2	4.37 m	71.1	4.38 m	71.2	4.34 dd (9.2, 8.9)
5′	79.2	3.98 m	79.2	4.00 m	79.2	4.02 m
6′	62.2	4.39 m, 4.43 m	62.2	4.42m, 4.45 m	62.2	4.35 m, 4.45 m
Galloyl						
1″						
2″						
3″						
4″						
5″						
6″						
7″						

6β,23-dihydroxytormentic acid (**8**),[6)] but a set of signals ascribable to a galloyl group [δ_H 7.77, s, 2H; δ_C 110.0 (2C), 121.5, 140.9, 147.6 (2C), 167.2] in the spectra of **4** led to the conclusion that **4** was a gallate of **8**. The presence of a galloyl group was confirmed by TLC analysis of an acid hydrolysis product. The galloyl moiety was located at C-23 because the oxygenated methylene protons of **4** resonated at a lower field (δ_H 4.73, 4.88) than those of **8** (δ_H 4.04, 4.38). From these data and analysis of the HMBC spectrum (Fig. 3), the structure of quadranoside IX was concluded to be 23-*O*-galloyl-2α,3β,6β,19α-tetrahydroxyurs-12-en-28-oic acid 28-*O*-β-D-glucopyranoside (**4**).

Quadranoside X (**5**) showed IR absorptions of hydroxyl (3400 cm^{-1}) and carbonyl (1710 cm^{-1}) groups, and its molecular formula was determined to be $C_{36}H_{58}O_{11}$ by HR-FAB-MS. The ^{1}H-NMR spectrum of **5** showed signals of six tertiary methyls (δ_H 0.78, 0.90, 0.98, 1.05, 1.09, 1.13), an anomeric proton (δ 6.34, d, J=8.0 Hz), and eight oxygenated methine and methylene protons, while the ^{13}C-NMR spectrum of **5** revealed thirty-six carbon signals including one double-bond (Table 2). Thus, **5** was also thought to be a triterpene monoglycoside. The sugar unit was determined to be D-glucose attached to a carboxyl group (C-28), based on comparison of the ^{1}H- and ^{13}C-NMR data with that of **1**—**4** and GC analysis of a chiral derivative of an acid hydrolysate. Moreover, the ^{1}H- and ^{13}C-NMR spectra of **5** were found to be similar to arjunglucoside II (**10**)[8)] obtained from the same extract, suggesting that **5** is a glucoside of an oleanane-type triterpene. The absence of an olefinic proton signal in the ^{1}H-NMR spectrum of **5** and the long-range correlations between H_3-27 and C-13, between H_2-19 and C-13 and C-18 in the HMBC spectrum (Fig. 4a) led to the conclusion that **5** has a

Table 1. Continued

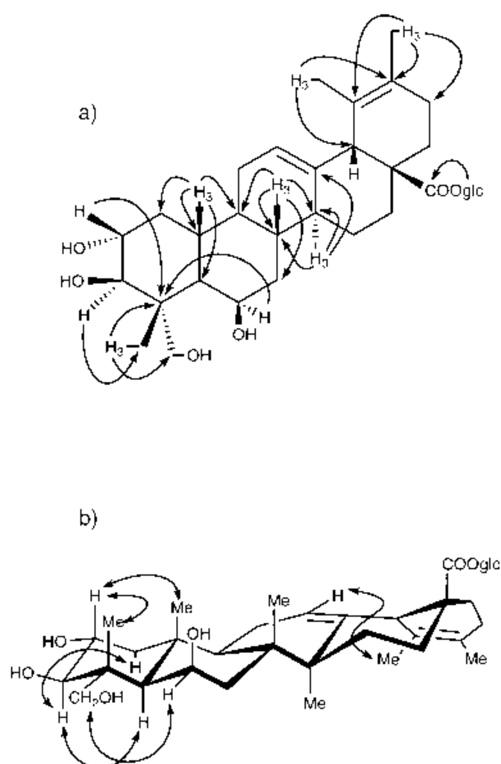
Position	3		4	
	^{13}C	^{1}H	^{13}C	^{1}H
1	47.9	1.38 m, 2.27 dd (12.5, 3.6)	50.1	1.11 m, 2.29 dd (11.0, 3.6)
2	68.9	4.18 m	68.5	4.33 m
3	78.2	4.17 m	78.1	3.92 d (9.5)
4	43.6		43.8	
5	48.1	1.81 m	49.8	1.88 m
6	18.6	1.68 m	67.9	4.86 br s
7	33.1	1.36 m, 1.65 m	41.7	1.86 m, 2.07 m
8	39.9		40.0	
9	48.2	1.96 m	48.6	2.02 m
10	38.5		38.0	2.09 m
11	24.0	2.05 m	24.8	
12	128.5	5.50 t (2.6)	128.7	5.59 t (2.5)
13	137.5		138.6	
14	42.9		42.7	
15	29.1	1.38 m, 2.38 m	29.0	1.15 m, 2.45 td (12.5, 4.6)
16	25.8	1.69 m, 1.86 m	26.3	1.49 m, 2.96 td (13.4, 4.6)
17	49.8		48.6	
18	52.2	3.76 s	54.6	2.92 s
19	153.3		72.7	
20	37.5	1.79 m	42.1	1.36 m
21	30.7	1.25 m, 1.43 m	26.7	1.74 m
22	37.2	1.79 m, 1.97 m	37.5	1.76 m, 2.03 m
23	66.5	3.69 d (9.6), 4.17 d (9.6)	67.2	4.73 d (11.2), 4.88 d (11.2)
24	14.3	1.05 s	15.6	1.73 s
25	17.6	1.09 s	19.1	1.77 s
26	17.5	1.15 s	18.7	1.72 s
27	26.2	1.14 s	24.9	1.69 s
28	176.1		176.8	
29	110.4	5.00 br s, 5.12 br s	27.1	1.38 s
30	19.4	1.03 d (6.7)	16.7	1.05 d (6.6)
Glucose				
1′	95.9	6.29 d (8.2)	95.9	6.20 d (8.1)
2′	74.1	4.18 m	74.0	4.15 dd (8.5, 8.1)
3′	78.9	4.27 t (9.2)	78.7	4.22 dd (8.8, 8.5)
4′	71.2	4.33 t (9.2)	71.3	4.30 dd (9.3, 8.8)
5′	79.3	4.02 ddd (9.2, 4.4, 2.6)	79.1	3.97 m
6′	62.3	4.37 m, 4.45 m	62.3	4.35 m, 4.42 dd (12.0, 2.4)
Galloyl				
1″			121.5	
2″			110.0	7.77 s
3″			147.6	
4″			140.9	
5″			147.6	
6″			110.0	7.77 s
7″			167.2	

a) *J* values (in Hz) in parentheses.

double-bond at C-13(18) instead of C-12(13) in **10**. Thus, the planar structure of quadranoside X was determined to be 2,3,23-trihydroxyolean-13(18)-en-28-oic acid 28-*O*-β-D-glucopyranoside. Then, the orientations of the three hydroxyl groups were determined to be the same as **2**, 2α-OH, 3β-OH and 4α-CH_2OH (C-23), from the ROESY correlations between H-2 and H_3-24 and between H-3 and H_2-23 (Fig. 4b). Thus, the structure of quadranoside X was determined to be 2α,3β,23-trihydroxyolean-13(18)-en-28-oic acid 28-*O*-β-D-glucopyranoside (**5**).

Quadranoside XI (**6**), having the molecular formula $C_{43}H_{62}O_{15}$, showed an $[\alpha]_D^{25}$ of +7.9° (c=0.045, MeOH). The IR spectrum of **6** showed absorption bands at 3350 and 1725 cm^{-1} corresponding to a hydroxyl and carbonyl group, respectively. The ^{1}H- and ^{13}C-NMR spectra of **6** were similar to quadranoside II (**17**), isolated from the same extract,[4] except that **6** showed additional signals corresponding to a galloyl group, as in the case of **4**. The presence of a gallic acid moiety and also a D-glucose was confirmed by TLC or GC analysis of an acid hydrolysate. The oxygenated methylene proton signals of **6** (δ_H 4.72, 4.89, H_2-23) appeared downfield compared with those of **17** (δ_H 4.06, 4.40),[4] suggesting that the galloyl moiety was located at C-23, and this was confirmed by the long-range correlations observed in the HMBC spectrum (Fig. 5a). The stereochemistry of **6**, on the other hand, was determined from the ROESY correlations (Fig. 5b), and the structure of quadranoside XI was determined to be 23-*O*-galloyl-2α,3β,6β-trihydroxylup-20(29)-en-28-oic acid 28-*O*-β-D-glucopyranoside (**6**).

The triterpenes isolated in this study all have a 2α,3β-di-



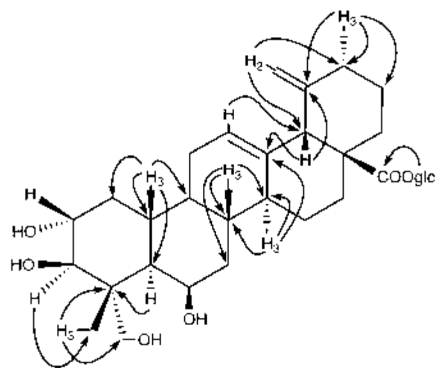


Fig. 1. Significant Correlations Observed in the HMBC (a) and in the ROESY Spectra of **1** (b, Mixing Time 500 ms)

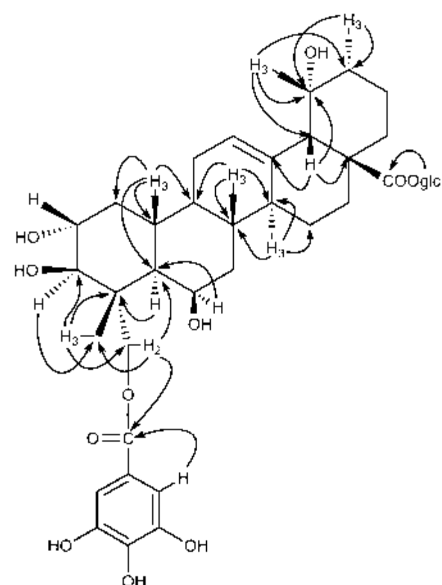


Fig. 3. Significant Correlations Observed in the HMBC Spectrum of **4**

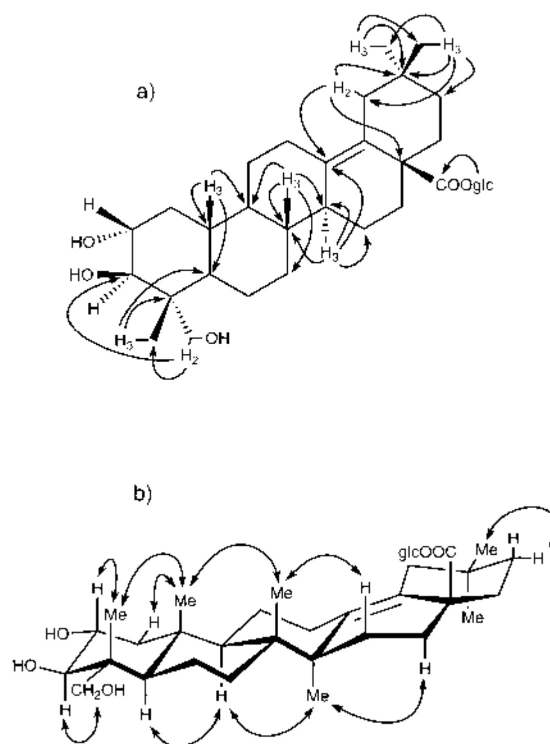


Fig. 4. Significant Correlations Observed in the HMBC (a) and in the ROESY Spectra of **5** (b, Mixing Time 500 ms)

Fig. 2. Significant Correlations Observed in the HMBC Spectrum of **2**

hydroxyl group even though they belong to three different (lupane-, oleanane- and ursane-type) triterpene classes. Oleanane-type triterpenes with a double-bond at C-13(18) and ursane-type triterpenes with two double-bonds at C-12(13) and C-19(29) are very rare,[5,6] and **4** and **6** are the first examples of triterpenes bearing a galloyl unit from a *Combretum* species. Furthermore, among the nine known compounds, six (**7**—**12**) have been isolated for the first time from *C. quadrangulare.*

Experimental

General Experimental Procedures Optical rotations were determined in MeOH on a JASCO DIP 140 digital polarimeter at 25 °C. IR spectra were recorded in KBr disks on a Shimadzu IR-408 spectrophotometer. NMR spectra were recorded in C_5D_5N or CD_3OD containing tetramethylsilane (TMS) as internal standard on a JEOL JNM-GX400 spectrometer. FAB-MS measurements were performed on a JEOL JMS-700T spectrometer using glycerol as a matrix. GC analysis was performed on a Shimadzu GC-14AH system, and preparative HPLC was conducted on Shimadzu LC-5A system. Analytical and preparative TLC were conducted on precoated Merck Kieselgel $60F_{254}$ (0.25 and 0.5 mm) and RP-$18F_{254}$ (0.25 mm) plates.

Plant Material Seeds of *C. quadrangulare* KURZ were collected in Ho Chi Minh City, Vietnam in January 1998. A voucher sample (TMPW 19000) is preserved in the Museum for Materia Medica, Toyama Medical and Pharmaceutical University, Toyama, Japan.

Extraction and Isolation The dried seeds (2.25 kg) of *C. quadrangulare* were extracted with MeOH (7 l, 3 h×2) at 80 °C and the water-soluble fraction (400 g) of the MeOH extract (700 g) was subjected to Sephadex LH-20 column chromatography with a H_2O–MeOH gradient system to afford seven fractions.[4]

Fraction 2 (20 g) was chromatographed on Cosmosil $75C_{18}$-OPN (Nacalai Tesque, Kyoto, Japan) with a H_2O–MeOH gradient system to give eight subfractions. Subfraction 2 was separated by HPLC (column: Discovery™,

Table 2. ^{1}H- and ^{13}C-NMR Data of **5** and **6** in C_5D_5N[a)]

Position	**5**		**6**	
	^{13}C	^{1}H	^{13}C	^{1}H
1	48.1	1.35 m, 2.42 dd (12.7, 4.6)	50.1	1.18 m, 2.31 dd (12.4, 4.4)
2	69.1	4.28 m	69.0	4.35 m
3	78.3	4.20 m	78.0	3.98 d (9.3)
4	43.6		43.7	
5	48.1	1.77 m	49.9	1.79 m
6	25.5	1.84 m, 2.74 dd (12.9, 4.8)	67.8	4.77 br s
7	34.9	1.29 m	42.3	1.77 m
8	44.7		42.8	
9	51.1	1.72 m	52.0	1.49 m
10	38.7		38.3	
11	18.5	1.68 m	21.3	1.40 m, 1.52 m
12	22.1	1.58 m	26.1	1.18 m, 1.88 m
13	138.7		37.4	2.74 ddd (11.8, 2.7)
14	41.9		40.6	
15	27.5	1.01 m, 2.08 m	29.9	1.12 m, 2.02 m
16	33.3	1.55 m, 2.25 m	32.1	1.38 m, 2.57 br d (12.4)
17	48.9		56.9	
18	128.3		50.0	1.67 m
19	41.4	2.19 d (13.4), 2.54 d (13.4)	47.3	3.37 td (4.9, 10.7)
20	32.9		150.9	
21	36.1	1.35 m, 2.52 m	30.8	1.39 m, 2.02 m
22	37.1	1.22 m, 1.62 m	36.9	1.41 m, 2.15 m
23	66.5	3.71 d (10.2), 4.23 d (10.2)	67.0	4.72 d (11.2), 4.89 d (11.2)
24	14.3	1.05 s	15.3	1.66 s
25	18.0	0.98 s	19.6	1.55 s
26	18.5	1.13 s	17.0	1.68 s
27	21.2	1.09 s	15.0	0.85 s
28	175.8		174.9	
29	32.2	0.90 s	109.9	4.74 br s, 4.85 br s
30	24.4	0.78 s	19.6	1.74 s
Glucose				
1′	96.2	6.34 d (8.0)	95.3	6.28 d (8.3)
2′	74.2	4.16 dd (8.8, 8.0)	74.1	4.07 dd (8.5, 8.3)
3′	79.0	4.25 dd (9.0, 8.8)	78.7	4.25 dd (9.0, 8.5)
4′	71.3	4.32 dd (9.0, 8.9)	71.1	4.32 dd (9.3, 9.0)
5′	79.4	4.01 ddd (8.9, 4.7, 2.2)	79.2	3.95 m
6′	62.4	4.35 dd (11.7, 2.2), 4.43 dd (11.7, 4.7)	82.1	4.33 m, 4.40 m
Galloyl				
1″			121.4	
2″			109.9	7.22 s
3″			147.5	
4″			140.0	
5″			147.5	
6″			109.9	7.22 s
7″			167.2	

a) *J* values (in Hz) in parentheses.

250×21.2 mm; mobile phase: MeCN–MeOH–H_2O, 15 : 15 : 75; flow rate: 15 ml/min; detection: UV 210 nm) to give combreglucoside (**11**, 5 mg) and 28-*O*-*β*-D-glucopyranosyl-6*β*,23-dihydroxytormentic acid (**8**, 7 mg).

Fraction 3 (20 g) was subjected to silica gel column chromatography with $CHCl_3$–MeOH–H_2O (14 : 6 : 1) and nine subfractions were collected. Further Cosmosil 75C_{18}-OPN column chromatography (MeCN–MeOH–H_2O, 1 : 1 : 2) and preparative TLC (MeCN–MeOH–H_2O, 1 : 1 : 1.5) of subfraction 7 yielded **8** (60 mg), while the same treatment of subfraction 8 gave quadranosides VI (**1**, 5 mg) and VII (**2**, 5 mg) and chebuloside II (**12**, 7 mg).

Fraction 5 (10 g) was chromatographed on a silica gel column with $CHCl_3$–MeOH–H_2O (14 : 6 : 1) and nine subfractions were collected. Subfraction 3 underwent preparative TLC (MeCN–MeOH–H_2O, 1 : 1 : 1.5) to yield (+)-gallocatechin (3.4 mg),[4)] (−)-epicatechin (10 mg)[4)] and a mixture, which was further separated by HPLC (column: Discovery™, 250×21.2 mm; mobile phase: MeOH–H_2O, 60 : 40; flow rate: 15 ml/min; detection: UV 210 nm) to give quadranosides VIII (**3**, 3 mg) and X (**5**, 5 mg). On the other hand, Cosmosil 75C_{18}-OPN column chromatography (MeCN–MeOH–H_2O, 1 : 1 : 2) and preparative TLC (MeCN–MeOH–H_2O, 1 : 1 : 1.5) of subfraction 4 yielded quadranoside IV (27.3 mg),[4)] 2*α*,3*β*,23-trihydroxyurs-12,19-dien-28-oic acid 28-*O*-*β*-glucopyranoside (19.6 mg)[4)] and a mixture, which was separated by HPLC (column: Discovery™, 250×21.2 mm; mobile phase: MeOH–H_2O, 60 : 40; flow rate: 15 ml/min; detection: UV 210 nm) to afford rosamutin (**7**, 6 mg) and arjunetin (**9**, 7 mg). The same treatment of subfraction 7 gave quadranosides V (17.0 mg)[4)] and IX (**4**, 17 mg).

Fraction 6 (45 g) was again chromatographed on a Cosmosil 75C_{18}-OPN column with a H_2O–MeOH gradient system and twelve subfractions were collected. Subfractions 3, 6 and 9 were subjected to silica gel column chromatography (MeOH–acetone–$CHCl_3$, 2 : 1 : 7) and preparative TLC (MeOH–acetone–$CHCl_3$, 2 : 1 : 7) to give (+)-catechin (**14**, 591 mg), (−)-epigallocatechin (**15**, 70.4 mg) and vitexin (**13**, 27.1 mg), respectively. On the other hand, Cosmosil 75C_{18}-OPN column chromatography (MeCN–MeOH–H_2O, 1 : 1 : 2), followed by preparative TLC (MeCN–MeOH–H_2O, 1 : 1 : 1.5) of subfractions 10 and 11 gave quadranoside XI (**6**, 17.8 mg) and arjunglucoside II (**10**, 16 mg), respectively.

Quadranoside VI (**1**): Colorless amorphous solid. $[\alpha]_D^{25}$ +23.8° (c=0.036, MeOH). IR (KBr) cm^{-1}: 3450, 1730, 1640. ^{1}H- and ^{13}C-NMR, see Table 1. HR-FAB-MS *m/z*: 687.3712 [Calcd for $C_{36}H_{56}O_{11}Na$: 687.3720 $(M+Na)^+$].

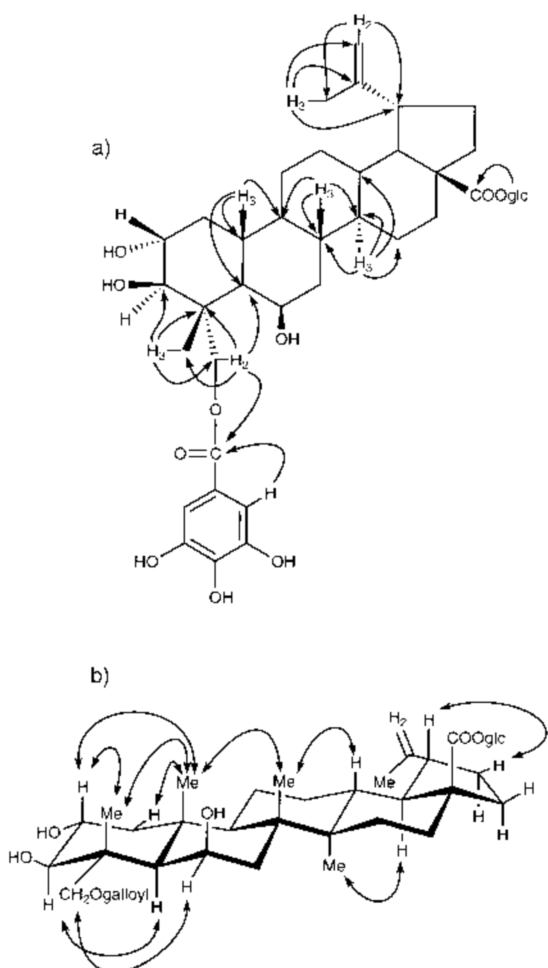


Fig. 5. Significant Correlations Observed in the HMBC (a) and in the ROESY Spectra of **6** (b, Mixing Time 500 ms)

Quadranoside VII (**2**): Colorless amorphous solid. $[\alpha]_D^{25}$ +80.4° (c=0.020, MeOH). IR (KBr) cm^{-1}: 3450, 1730, 1645. ^{1}H- and ^{13}C-NMR, see Table 1. HR-FAB-MS m/z: 687.3726 [Calcd for $C_{36}H_{56}O_{11}Na$: 687.3721 (M+Na)$^+$].

Quadranoside VIII (**3**): Colorless amorphous solid. $[\alpha]_D^{25}$ +73.2° (c=0.028, MeOH). IR (KBr) cm^{-1}: 3400, 1710, 1640. ^{1}H- and ^{13}C-NMR, see Table 1. HR-FAB-MS m/z: 671.3774 [Calcd for $C_{36}H_{50}O_{10}Na$: 671.3771 (M+Na)$^+$].

Quadranoside IX (**4**): Colorless amorphous solid. $[\alpha]_D^{25}$ +24.4° (c=0.045, MeOH). IR (KBr) cm^{-1}: 3400, 1710, 1645. ^{1}H- and ^{13}C-NMR, see Table 1. HR-FAB-MS m/z: 857.3937 [Calcd for $C_{43}H_{62}O_{16}Na$: 857.3935 (M+Na)$^+$].

Quadranoside X (**5**): Colorless amorphous solid. $[\alpha]_D^{25}$ +15.6° (c=0.030, MeOH). IR (KBr) cm^{-1}: 3500, 1740, 1660. ^{1}H- and ^{13}C-NMR, see Table 2. HR-FAB-MS m/z: 673.3896 [Calcd for $C_{36}H_{58}O_{10}Na$: 673.3927 (M+Na)$^+$].

Quadranoside XI (**6**): Colorless amorphous solid. $[\alpha]_D^{25}$ +7.9° (c=0.045, MeOH). IR (KBr) cm^{-1}: 3400, 1710, 1640. ^{1}H- and ^{13}C-NMR, see Table 2. HR-FAB-MS m/z: 841.3972 [Calcd for $C_{43}H_{62}O_{15}Na$: 841.3986 (M+Na)$^+$].

Sugar Analysis Each compound (1 mg) was hydrolyzed with 1 N HCl-dioxane (1 : 1, 2 ml) at 80 °C for 4 h. The reaction mixture was neutralized with Amberlite IRA67 (OH$^-$ form), and the filtrate was concentrated to dryness *in vacuo.* To the residue, 0.1 M L-cysteine methyl ester hydrochloride in pyridine (2 ml) was added and the mixture was heated at 60 °C for 2 h. After concentration to dryness in a stream of argon gas, trimethylsilylimidazole (0.2 ml) was added and the mixture was heated at 60 °C for 1.5 h. The reaction mixture was partitioned between hexane and H_2O (0.3 ml each), and the hexane layer was analyzed by GC; column, Shimadzu CBJ17-S30-025, 0.32×30 m; coloumn temperature, 230 °C; detector temperature, 270 °C; injection temperature, 270 °C. Standard D- and L-glucose gave one peak at t_R 6.04 and 6.59 min, respectively.

Analysis of Galloyl Group The hydrolysate of compound **4** or **6** was analyzed by TLC using two solvent systems, BuOH–acetone–H_2O (6 : 4 : 3) and MeCN–H_2O (85 : 15), with a standard sample of gallic acid (*Rf* 0.77 and 0.64, respectively).

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