Eremophilane Glucosides from *Petasites japonicus*

by **Guangyin Wang**[a]), **Junzeng Zhang**[b]), **Marianna Kulka**[c]), **Fujiang Guo***[a]), and **Yiming Li***[a])

[a]) School of Pharmacy, Shanghai University of Traditional Chinese Medicine, Shanghai 201203, P. R. China (phone: +86-21-51322191; fax: +86-21-51322193; e-mail: gfj@shutcm.edu.cn; ymlius@163.com)

[b]) Aquatic and Crop Resource Development, National Research Council of Canada, Halifax, NS, B3 H 3Z1, Canada

[c]) National Institute of Nanotechnology, National Research Council Canada, Edmonton, AB, T6G 2 M9, Canada

Three new eremophilane glucosides, namely, petasitosides A – C, and seven known eremophilane-type sesquiterpenoids were isolated from the roots of *Petasites japonicus*. Their structures were elucidated by spectroscopic techniques including 1D- and 2D-NMR spectroscopy and mass spectrometry. This is the first report on eremophilane glycosides from the genus Petasites.

Introduction. – *Petasites japonicus* (SIEBOLD & ZUCC.) MAXIM., also known as *Butterbur*, is a herbaceous perennial plant in the family of Asteraceae. In China, the whole plant has been used as a traditional Chinese medicine against tonsillitis, carbuncle swollen boils, and poisonous snake bite [1]. It is also cultivated in Japan and South Korea, where it is consumed as a common vegetable. The flower bud is baked and used in traditional medicine as an expectorant or in the treatment of asthma in Japan [2]. Sesquiterpenoids, especially eremophilanes [3 – 6], have been previously reported as the main constituents of this plant. Pharmacological studies have suggested that *P. japonicus* extracts possess a variety of biological features such as neuroprotective [7 – 9], anti-allergic [2][10], antimutagenic, and cytotoxic [11 – 13] activities.

In an *in vivo* model of active systemic anaphylaxis (ASA), our preliminary pharmacological experiments had revealed that the $CHCl_3$-soluble fraction of the 95% EtOH extract taken from the rhizomes blocked type-I and type-IV allergic inflammation [14]. Further chemical investigation of this plant resulted in the isolation of three new eremophilane sesquiterpenoid glucosides, **1** – **3**, along with seven known sesquiterpenoids, **4** – **10** (*Fig. 1*).

Results and Discussion. – The CH_2Cl_2-soluble fraction from the 95% EtOH extract of the roots of *P. japonicus* was subjected to column chromatography on silica gel (200 – 300 mesh), eluting with a gradient of petroleum ether/AcOEt. Further purification by column chromatography using silica gel, *Sephadex LH-20*, and *ODS* yielded **4** – **8**. The BuOH-soluble fraction from the 95% EtOH extract of the roots of *P. japonicus*, was subjected to column chromatography on silica gel (200 – 300 mesh) with a gradient of CH_2Cl_2/MeOH 20 : 1 to MeOH to afford 16 fractions. After further purification on *ODS*, **1** – **3**, **9**, and **10** were obtained. Among the isolated compounds, the known compounds **4** – **10**, which have previously been reported from this genus, were identified as

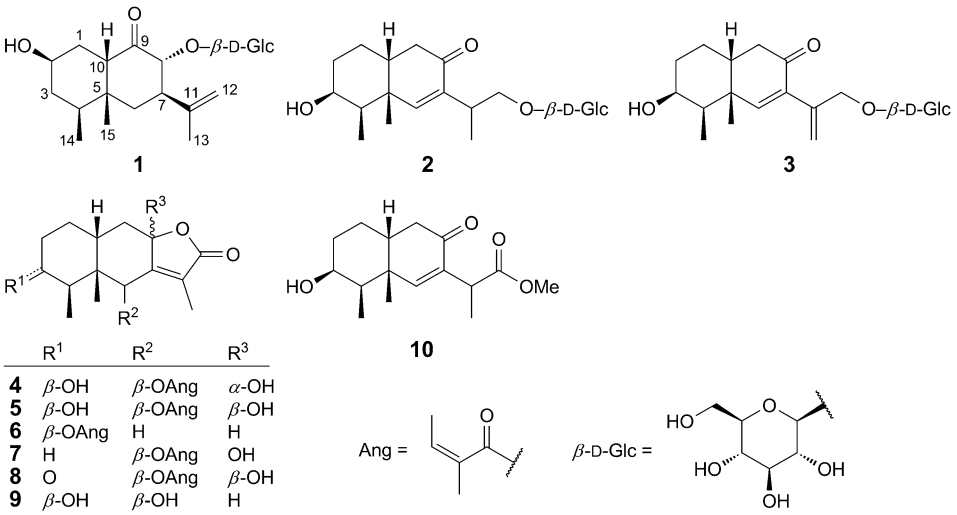


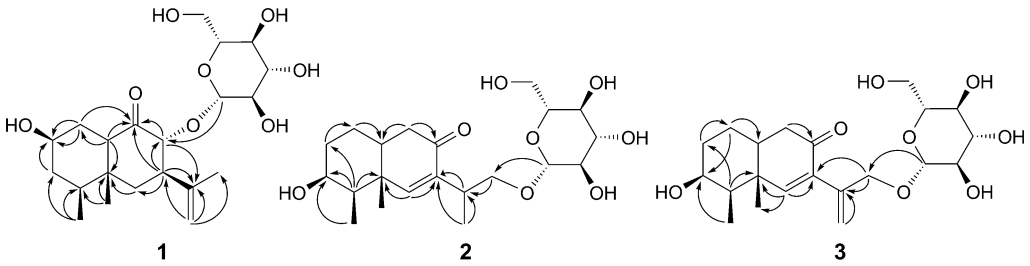
Fig. 1. *Chemical structures of* **1**–**10**

6β-(angeloyloxy)-3β,8α-dihydroxyeremophil-7(11)-en-12,8β-olide (**4**) [4], 6β-(angeloyloxy)-3β,8β-dihydroxyeremophil-7(11)-en-12,8α-olide (**5**) [4], 3β-(angeloyloxy)eremophilenolide (**6**) [15], 6β-(angeloyloxy)-8-hydroxyeremophilenolide (**7**) [16], 6β-(angeloyloxy)-8β-hydroxy-3-oxoeremophil-7(11)-en-12,8α-olide (**8**) [1], 3β,6β-dihydroxyeremophilenolide (**9**) [17], and 3β-hydroxy-8-oxoeremophil-6-en-12-oic acid methyl ester (**10**) [18].

The structures of the new compounds were elucidated by using various spectroscopic methods. Compound **1** was obtained as white amorphous powder with the molecular formula of $C_{21}H_{34}O_8$ deduced from the HR-ESI mass spectrum (*m*/*z* 437.2164 ($[M+Na]^+$)), indicating five degrees of unsaturation. The IR spectrum indicated the presence of OH (3379 cm^{-1}), and C=O (1716 cm^{-1}) groups. In the ^{13}C-NMR spectrum (*Table*), the signals at δ(C) 102.4, 76.9, 76.2, 73.4, 69.9, and 61.3 indicated the presence of one glucosyl moiety. The glucosyl H-atom signals were detected at δ(H) 4.32 (*d*, *J* = 7.6, 1 H), 3.84 (*dd*, *J* = 11.9, 2.0, 1 H), 3.66 (*dd*, *J* = 11.9, 5.8, 1 H), and 3.19–3.32 (overlapped, 4 H) in its ^{1}H-NMR spectrum (*Table*). Acid hydrolysis and GC analysis of **1** confirmed the presence of D-glucose. The ^{13}C-NMR and DEPT-135 data indicated that the aglycon of **1** contained 15 C-atoms including those of three Me, four CH_2, five CH groups, and three quaternary C-atoms. One C=O signal at δ(C) 210.0, two O-bearing C-atom signals at δ(C) 65.5 (CH) and 81.3 (CH), and the signals at δ(C) 144.9 (C) and 112.5 (CH_2), ascribed to the C(11)=C(12) bond, were observed. In the ^{1}H-NMR spectrum, there were three Me signals at high field (δ(H) 1.85 (*s*), 1.09 (*s*), and 0.82 (*d*, *J* = 6.7)). Among them, the signal at δ(H) 1.85 suggested that the corresponding Me group was attached to an olefinic C-atom. These observations and the HMBC analysis (*Fig. 2*) suggested that **1** had a typical eremophilane skeleton. In the HMBC spectrum, long-range correlations were observed between H–C(1), H–C(8), H–C(10), and C(9); H–C(1), H–C(3), and C(2); H–C(12), and C(11),

Table. *^{1}H- and ^{13}C-NMR* (400 and 100 MHz, resp., CD_3OD) *Data of* **1**–**3**. δ in ppm, J in Hz.

Position	**1**		**2**		**3**	
	δ(H)	δ(C)	δ(H)	δ(C)	δ(H)	δ(C)
1	1.44–1.51 (*m*), 2.21–2.26 (*m*)	29.6	1.38–1.46 (*m*), 1.58–1.63 (*m*)	26.4	1.51–1.62 (*m*), 1.63–1.67 (*m*)	26.6
2	3.95–4.04 (*m*)	65.5	1.53–1.60 (*m*)	26.9	1.56–1.61 (*m*)	26.9
3	1.29–1.38 (*m*), 1.68–1.71 (*m*)	38.5	3.64–3.71 (*m*)	69.9	3.73–3.78 (*m*)	69.9
4	1.48–1.54 (*m*)	31.6	1.85–1.91 (*m*)	44.6	1.87–1.95 (*m*)	44.6
5	–	39.8	–	39.8	–	40.2
6	1.82–1.84 (*m*)	39.6	6.61 (*s*)	155.6	6.78 (*s*)	158.8
7	2.56 (*dt*, *J* = 11.9, 4.3)	47.1	–	138.2	–	136.3
8	4.56 (*d*, *J* = 11.9)	81.3	–	199.8	–	199.5
9	–	210.0	2.20 (*dd*, *J* = 17.3, 2.1), 2.74 (*dd*, *J* = 17.3, 4.5)	40.4	2.27 (*dd*, *J* = 17.1, 2.2), 2.77 (*dd*, *J* = 17.3, 4.3)	40.7
10	2.67 (*d*, *J* = 3.2)	55.3	2.03–2.09 (*m*)	35.3	2.06–2.10 (*m*)	35.5
11	–	144.9	2.94–3.03 (*m*)	32.7	–	142.8
12	4.90 (br. *s*), 4.94 (br. *s*)	112.5	3.41 (*dd*, *J* = 7.0, 9.4), 3.92 (*dd*, *J* = 6.5, 9.4)	72.9	4.34 (*d*, *J* = 12.6), 4.54 (*d*, *J* = 12.6)	70.4
13	1.85 (*s*)	18.4	1.11 (*d*, *J* = 7.0)	15.7	5.21 (*d*, *J* = 1.5), 5.34 (*d*, *J* = 1.5)	115.8
14	0.82 (*d*, *J* = 6.7)	20.2	1.00 (*d*, *J* = 7.0)	6.3	1.00 (*d*, *J* = 7.0)	6.3
15	1.09 (*s*)	14.3	1.24 (*s*)	24.4	1.29 (*s*)	24.1
Glc						
1′	4.32 (*d*, *J* = 7.6)	102.4	4.24 (*d*, *J* = 7.8)	103.1	4.27 (*d*, *J* = 7.8)	101.6
2′	3.24 (overlapped)	73.4	3.16 (*dd*, *J* = 9.1, 7.8)	73.8	3.17 (*dd*, *J* = 9.1, 7.8)	73.7
3′	3.32 (overlapped)	76.2	3.26 (overlapped)	76.5	3.24 (overlapped)	76.5
4′	3.30 (overlapped)	69.9	3.25 (overlapped)	70.4	3.24 (overlapped)	70.4
5′	3.19 (overlapped)	76.9	3.34 (overlapped)	76.7	3.34 (overlapped)	76.9
6′	3.66 (*dd*, *J* = 11.9, 5.8), 3.84 (*dd*, *J* = 11.9, 2.0)	61.3	3.67 (*dd*, *J* = 11.9, 5.5), 3.88 (*dd*, *J* = 11.9, 1.6)	61.6	3.64 (*dd*, *J* = 11.9, 5.4), 3.87 (*dd*, *J* = 11.9, 1.4)	61.6



1 **2** **3**

Fig. 2. *Key HMBCs* (H → C) *of* **1**–**3**

C(13), and C(7). These data confirmed the presence of the C(11)=C(12) bond and the C(9)=O group, and the two OH groups were at C(2) and C(8). The position of the sugar residue was also determined from the HMBC experiment, in which there were cross-peaks between the anomeric H-atom signals at δ(H) 4.32 (H–C(1′)) and δ(C)

81.3 (C(8)). The β-anomeric configuration of the D-glucose unit was determined based on its coupling constant ($J = 7.6$). All ^{1}H- and ^{13}C-NMR signals (*Table*) were assigned on the basis of the HMBC, HSQC, and ^{1}H,^{1}H-COSY correlations. The relative configuration of **1** was determined by the NOESY correlations shown in *Fig. 3*. The NOE cross-peak H–C(10)/Me(15) suggested a *cis*-junction of the *A*/*B* rings. The NOE correlations between H_α–C(2) and H_α–C(4), and H_β–C(8) and H_β–C(10) implied that the OH groups at C(2) and C(8) were β- and α-oriented, respectively [19]. The configuration at C(7) was deduced from the coupling constant of 11.9 Hz between H–C(7) and H–C(8), indicating their *trans* diaxial orientation [20]. The structure of **1** was thus elucidated as (2β,8α)-2-hydroxy-9-oxoeremophil-11-en-8-yl β-D-glucopyranoside and named petasitoside A.

Compound **2**, obtained as white amorphous powder, was assigned the molecular formula $C_{21}H_{34}O_8$ according to its HR-ESI-MS (*m*/*z* 437.2150 ($[M + Na]^+$)). The IR spectrum indicated that an OH (3386 cm^{-1}) and a C=C group (1658 cm^{-1}) were present. There was a glucosyl moiety as revealed by ^{1}H- and ^{13}C-NMR (*Table*) and acid hydrolysis. In the ^{1}H-NMR spectrum, signals of three tertiary Me groups were observed δ(H) 1.24, 1.11, and 1.00). The ^{1}H-NMR spectrum also revealed the presence of one CH–O (δ(H) 3.64 – 3.71) and one CH_2O group (δ(H) 3.41 and 3.92). The aglycon structure of **2** was determined as 3,12-dihydroxy-8-oxoeremophil-6-ene according to HMBC analysis (*Fig. 2*). The ^{1}H- and ^{13}C-NMR spectra of the aglycone moiety were similar to those of 3β-hydroxy-8-oxoeremophil-6-en-12-oic acid methyl ester [18], except that the C(12)OOH group was reduced to a primary alcohol in the former. The HMBC between the signals at δ(H) 4.24 (H–C(1′)) and δ(C) 72.9 (C(12)) revealed that the glucosyl moiety was at C(12). All H- and C-atom signals (*Table*) were assigned based on HMBC, HSQC, and ^{1}H,^{1}H-COSY correlations. The relative configuration of **2** was determined by the NOESY correlations shown in *Fig. 3*. In the NOESY spectrum, the correlations H_β–C(10)/Me(15), H–C(6)/H_α–C(3), and H–C(6)/H_α–C(4) suggested that the Me(15) group was *cis* to H–C(10), and the OH group at C(3) was β-oriented [18][20]. Thus, the structure of **2** was elucidated as 3β-hydroxy-8-oxoeremophil-6-en-12-yl β-D-glucopyranoside and named petasitoside B.

Compound **3** was white amorphous powder with a molecular formula $C_{21}H_{32}O_8$ based on the HR-ESI-MS (*m*/*z* 435.1996 ($[M + Na]^+$)), indicating six degrees of unsaturation. The IR spectrum indicated that OH (3386 cm^{-1}) groups and a C=C bond (1662 cm^{-1}) were present. There was a glucosyl moiety revealed by ^{1}H- and ^{13}C-NMR (*Table*) and acid hydrolysis. The ^{1}H- and ^{13}C-NMR spectra of **3** were similar to those of **2**, except that the Me(13) group was replaced by a CH_2(13)= group (δ(C) 115.8). All ^{1}H- and ^{13}C-NMR signals (*Table*) were assigned on the basis of

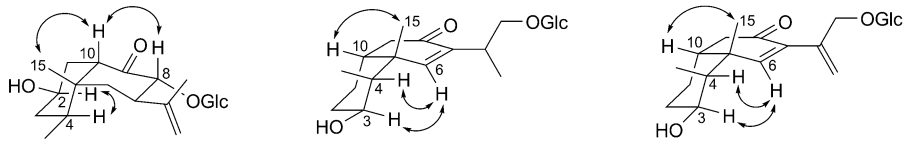


Fig. 3. *Key NOE correlations of* **1**–**3**

HMBC, HSQC, and ^{1}H,^{1}H-COSY correlations. The relative configuration of **3** was determined by the NOESY correlations shown in *Fig. 3*. Therefore, **3** was deduced as 3β-hydroxy-8-oxoeremophila-6,11(13)-dien-12-yl β-D-glucopyranoside, named as petasitoside C.

Eremophilane-type sesquiterpenes belong to the bicyclic sesquiterpene group, whose basic skeletal structure contains two six-membered rings and four Me groups. These compounds often occur in oxygenated forms such as eremophilane alcohols, eremophilane acids, eremophilane lactones, furanoeremophilanes, or rare eremophilane glycosides [21][22] in nature. Some special structures such as noreremophilanes [3], secoeremophilanes [22], and eremophilane dimers [23] also have been found. Many of them possess biological or therapeutic properties including antitumor, antibacterial, and anti-inflammatory activities. Although a series of eremophilane sesquiterpenes were isolated previously, this is the first report of eremophilane glycosides from this genus.

This work was supported by the *National Natural Science Foundation of China* (the Canada–China Joint Health Research Initiatives Grant 81261120567), the *'Xing-lin' Scholar Program* of *SHUTCM*, and the *Eastern Scholar Program* (2012-90).

Experimental Part

General. TLC: *HSGF$_{254}$* silica gel plates (SiO_2; 10–40 μm; *Yantai Jiangyou*, P. R. China). Column chromatography (CC): SiO_2 (100–200, 200–300, or 300–400 mesh; *Qingdao Haiyang Chemical Company*, P. R. China), *Sephadex LH-20* (*GE Healthcare Bio-Sciences AB*, Sweden), and *ODS-A-HG* (S-50 μm; *YMC Co., Ltd.*, Japan). GC: *Thermo TRACE DSQ* apparatus equipped with a *TR-5* column (length, 60 m × 0.25 mm, thickness of liquid phase, 0.25 nm). Optical rotations: *PerkinElmer 341* polarimeter. UV Spectra: *Agilent 8453* spectrometer (*Agilent*, Santa Clara, USA); λ_{max} in nm. IR Spectra: *Nicolet-Magna-750-FT-IR* spectrometer (*ThermoFisher*, Madison, USA); KBr pellets; $\tilde{\nu}$ in cm^{-1}. ^{1}H-, ^{13}C- and 2D-NMR spectra: *Bruker AV-400* instrument (^{1}H: 400 and ^{13}C: 100 MHz); δ in ppm rel. to Me_4Si as internal standard, *J* in Hz. ESI- and HR-ESI-MS: *Finnigan LCQ Deca XP* equipped with an electrospray ionization source mass ion-trap spectrometer and *Waters Micromass Q-TOF ultima Globe* spectrometer, resp.; in *m*/*z*.

Plant Materials. Roots of *P. japonicus* were collected in March 2011 from Bozhou area, Anhui Province, P. R. China, and identified by Prof. *Xiujia Zhou* at Shanghai University of Traditional Chinese Medicine. A voucher sample (20110301) was deposited with the School of Pharmacy, Shanghai University of Traditional Chinese Medicine, P. R. China.

Extraction and Isolation. Dried and milled roots of *P. japonicus* (20.0 kg) were extracted three times (2 h each) under reflux in 95% EtOH (20 l each). The solvent was evaporated under reduced pressure to yield a crude extract (2.4 kg), which was suspended in H_2O (5 l), and then partitioned with petroleum ether (PE; 15 l), CH_2Cl_2 (15 l), and BuOH (15 l), to afford 325 g of CH_2Cl_2-soluble fraction and 100 g of BuOH-soluble fraction.

The CH_2Cl_2-soluble fraction was then subjected to CC (SiO_2 (200–300 mesh); PE/AcOEt 19:1 to 1:1) to give seven fractions, *Frs. 1–7*. Compounds **4** and **5** (15 g) were crystallized as a mixture in CH_2Cl_2/MeOH from *Fr. 5*. *Fr. 3* was subjected repeatedly to CC (SiO_2 (300–400 mesh); PE/AcOEt 10:1 to 1:1), followed by CC (*Sephadex LH-20* (MeOH) and *ODS* (80% MeOH)) to furnish **6** (15 mg), **7** (10 mg), and **8** (12 mg).

The BuOH-soluble fraction was subjected to CC (SiO_2 (200–300 mesh); CH_2Cl_2/MeOH 20:1 to MeOH) to afford 16 fractions, *Frs. 1–16*. *Fr. 4* was decolorized by CC (*MCI* gel (*CHP20P*, *Mitsubishi Chemical Corp.*, Japan). The fraction eluted from 40% MeOH was subjected to CC repeatedly (*Sephadex LH-20* (MeOH) and *ODS* (55% MeOH)) to afford **9** (11 mg). *Fr. 9* also was subjected to CC

on *MCI* for decolorization, and its 20, 40, and 60% MeOH eluting fractions were further purified by a combination of CC (SiO_2 (CH_2Cl_2/MeOH 15:1 to 6:1), *Sephadex LH-20* (MeOH), and *ODS* (40% MeOH)) to yield **10** (27 mg), **1** (29 mg), **2** (5 mg), and **3** (4 mg).

Determination of Sugar Components. Compounds (0.5 mg each) were refluxed in 10% HCl/dioxane 1:1 (2 ml) for 2 h, and the solvent was evaporated under N_2. The residue was dissolved in pyridine (100 µl), 0.1M L-cysteine methyl ester hydrochloride (200 µl) was added, and the mixture was warmed and kept at 60° for 1 h. The trimethylsilylation reagent HMDS-TMCS (hexamethyldisilazane/Me_3SiCl/pyridine 2:1:10) was added, and the mixture was kept at 60° for another 30 min. The thiazolidine derivatives were subjected to GC analysis. D-Glucose (t_R 41.31 min) was identified by comparison with an authentic sample.

Petasitoside A (*=(2β,8α)-2-Hydroxy-9-oxoeremophil-11-en-8-yl β-*D*-Glucopyranoside=(2*R*,3*R*,4a*R*,5*S*,7*R*,8a*S*)-Decahydro-7-hydroxy-4a,5-dimethyl-3-(1-methylethenyl)-1-oxonaphthalen-2-yl β-*D*-Glucopyranoside*; **1**). Amorphous powder. $[\alpha]_D^{25} = +32.3$ ($c = 0.10$, MeOH). UV (MeOH): 212, 242. IR (KBr): 3379, 1716, 1643, 1078, 1030. ^{1}H- and ^{13}C-NMR: see the *Table*. ESI-MS (pos.): 415 ($[M+H]^+$), 437 ($[M+Na]^+$). HR-ESI-MS: 437.2164 ($[M+Na]^+$, $C_{21}H_{34}NaO_8^+$; calc. 437.2151).

Petasitoside B (*=3β-Hydroxy-8-oxoeremophil-6-en-12-yl β-*D*-Glucopyranoside=2-[(4a*R*,7*S*,8*R*,8a*R*)-3,4,4a,5,6,7,8,8a-Octahydro-7-hydroxy-8,8a-dimethyl-3-oxonaphthalen-2-yl]propyl β-*D*-Glucopyranoside*; **2**). Amorphous powder. $[\alpha]_D^{25} = -55.0$ ($c = 0.10$, MeOH). UV (MeOH): 209, 239. IR (KBr): 3386, 1658, 1078, 1032. ^{1}H- and ^{13}C-NMR: see the *Table*. ESI-MS: 415 ($[M+H]^+$). HR-ESI-MS: 437.2150 ($[M+Na]^+$, $C_{21}H_{34}NaO_8^+$; calc. 437.2151).

Petasitoside C (*=3β-Hydroxy-8-oxoeremophila-6,11(13)-dien-12-yl β-*D*-Glucopyranoside=2-[(4a*R*,7*S*,8*R*,8a*R*)-3,4,4a,5,6,7,8,8a-Octahydro-7-hydroxy-8,8a-dimethyl-3-oxonaphthalen-2-yl]prop-2-en-1-yl β-*D*-Glucopyranoside*; **3**). Amorphous powder. $[\alpha]_D^{25} = -70.7$ ($c = 0.09$, MeOH). UV (MeOH): 211, 239. IR (film): 3386, 1662, 1080, 1034. ^{1}H- and ^{13}C-NMR: see the *Table*. ESI-MS (pos.): 413 ($[M+H]^+$), 435 ($[M+Na]^+$). HR-ESI-MS: 435.1996 ($[M+Na]^+$, $C_{21}H_{32}NaO_8^+$; calc. 435.1995).

REFERENCES

[1] Y. Yaoita, M. Kikuchi, *Chem. Pharm. Bull.* **1994**, *42*, 1944.
[2] H. Shimoda, J. Tanaka, E. Yamada, T. Morikawa, N. Kasajima, M. Yoshikawa, *J. Agric. Food Chem.* **2006**, *54*, 2915.
[3] Y. Goto, Y. Kojima, T. Nakayama, M. Terazawa, *Phytochemistry* **2001**, *57*, 109.
[4] Y. Yaoita, K. Nagata, N. Suzuki, M. Kikuchi, *Chem. Pharm. Bull.* **1992**, *40*, 3277.
[5] M. Tori, M. Kawahara, M. Sono, *Tetrahedron Lett.* **1997**, *38*, 1965.
[6] M. Tori, M. Kawahara, M. Sono, *Phytochemistry* **1998**, *47*, 401.
[7] D.-E. Sok, S. H. Oh, Y.-B. Kim, H.-G. Kang, M. R. Kim, *Eur. J. Nutr.* **2006**, *45*, 61.
[8] S. H. Oh, D. E. Sok, M. R. Kim, *J. Med. Food.* **2005**, *8*, 169.
[9] H. S. Cui, M. R. Kim, D. E. Sok, *J. Agric. Food Chem.* **2005**, *53*, 8526.
[10] S. Tobinaga, N. Takeuchi, T. Kasama, J. Yamashita, Y. Aida, Y. Kaneko, *Chem. Pharm. Bull.* **1983**, *31*, 745.
[11] H.-G. Kang, S.-H. Jeong, J.-H. Cho, *J. Vet. Sci.* **2010**, *11*, 51.
[12] H. Y. Cho, J. U. Koh, Y. B. Kwon, K. H. Kong, *IFMBE Proc.* **2007**, *15*, 476.
[13] B.-G. Heo, Y.-S. Park, S.-U. Chon, S.-Y. Lee, J.-Y. Cho, S. Gorinstein, *BioFactors* **2007**, *30*, 79.
[14] Q.-Q. Zheng, P.-J. Kong, X.-M. Wu, H.-L. Li, Y.-M. Li, *Acta Universitatis Traditionis Medicalis Sinensis Pharmacologiaeque Shanghai* **2011**, *4*, 79.
[15] T. Kurihara, S. Suzuki, *Yakugaku Zasshi* **1977**, *97*, 863.
[16] B. Fu, Q. X. Zhu, X. P. Yang, Z. J. Jia, *Pharmazie* **1999**, *54*, 620.
[17] K. Sugama, K. Hayashi, H. Mitsuhashi, *Phytochemistry* **1985**, *24*, 1531.
[18] Y. Yaoita, M. Kikuchi, *Chem. Pharm. Bull.* **1995**, *43*, 1738.
[19] T. Yamada, K. Minoura, R. Tanaka, *J. Antibiot.* **2007**, *60*, 370.
[20] B. Wu, L. Gan, H. Qu, *J. Nat. Prod.* **2010**, *73*, 1069.
[21] A. Mimura, H. Sumioka, K. Matsunami, H. Otsuka, *J. Nat. Med.* **2010**, *64*, 153.

[22] A. Arciniegas, K. González, A.-L. Pérez-Castorena, J. Maldonado, J. L. Villaseñor, A. R. de Vivar, *J. Nat. Prod*. **2011**, *74*, 1584.
[23] M. Tori, K. Otose, H. Fukuyama, J. Murata, Y. Shiotani, S. Takaoka, K. Nakashima, M. Sono, M. Tanaka, *Tetrahedron* **2010**, *66*, 5235.

Received October 10, 2013