A New Phenolic Constituent and a Cyanogenic Glycoside from *Balanophora involucrata* (Balanophoraceae)

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Balanophora involucrata Hook.f. & Thomson (Balanophoraceae) is a parasite plant often growing on the roots of leguminous plants. The whole herb has been used medicinally for the treatment of irregular menstruation, cough, hemoptysis, traumatic injury and bleeding, dizziness and gastralgia in Yunnan Province, China. The 2,2-diphenyl-2-picrylhydrazyl (DPPH) assay on the 60% aq. acetone extract of the fresh whole plant of *B. involucrata* showed considerable radical-scavenging activity (SC_{50} 15.3 μg/ml). Further purification on the extract led to the isolation of one new phenolic glycoside, sieboldin-3′-ketocarboxylic acid (**1**), and one new cyanogenic glycoside, proacacipetalin 6′-*O*-β-D-glucopyranoside (**2**), together with 26 known compounds including three 4″-*O*-galloyl and 2″,3″-*O*-(*S*)-hexahydroxydiphenoyl (HHDP) derivatives of dihydrochalcone glucosides, seven hydrolyzable tannins, and alkane glycosides. The cyanogenic compound isolated from the Balanophoraceae family for the first time might be a signal molecule between *B. involucrata* and its hosts. The free-radical-scavenging activity of the isolated compounds was also examined by DPPH assay.

Introduction. – Balanophoraceae are a small family, with heterotrophic and holoparasitic properties, distributed in the tropical and subtropical areas. The family contains several mono- and polytypic genera, of which *Balanophora* is the largest including *ca.* 80 species [1][2]. So far, many polyphenols, especially hydrolyzable tannins, were isolated from *Balanophora laxiflora* [3], *B. polyandra* [4], *B. harlandii* [2], *B. japonica* [5], *B. abbreviata*, *B. tobiracola* [6][7], and *B. papuana* [8]. In addition, dihydrochalcone glucoside, and its 4″-*O*-galloyl and 2″,3″-*O*-(*S*)-hexahydroxydiphenoyl (HHDP) derivatives occur in several species of the genus *Balanophora*, such as *B. harlandii* [9] *B. japonica* [10], *B. tobiracola* [6][7], *B. papuana* [11], *etc.*

Balanophora involucrata Hook.f. & Thomson, a parasitic plant often growing on the roots of leguminous plants, is distributed mainly in the southwest of China, India, and Nepal [1]. The people living in its growing areas use the whole plant as a folk medicine for the treatment of irregular menstruation, cough, hemoptysis, traumatic injury and bleeding, dizziness, and gastralgia [12][13]. Seven phenylacrylic acid glucosides, eleven flavonoids, and several triterpenoids were reported from *B. involucrata* [12–16]. The anti-inflammatory and analgesic effects were also studied [17].

Continuing our work on the antioxidative constituents of the genus *Balanophora* [2–4][9], we found out, in a preliminary experiment, that the 80% aqueous acetone extract of *B. involucrata* contained significant amounts of phenolic compounds and

exhibited considerable radical scavenging activity (SC_{50} = 15.3 μg/ml) on DPPH assay. Further investigation of the extract led to the isolation of two new glycosides, named sieboldin-3′-ketocarboxylic acid (**1**) and proacacipetalin 6′-*O*-β-D-glucopyranoside (**2**), together with 26 known compounds, **3**–**28** (*Fig. 1*). Here, we report the structure elucidation of the new glycosides, as well as the DPPH radical-scavenging activities of **1**, and **3**–**24**.

Results and Discussion. – *Chemistry.* Repeated column chromatography (CC) of the 80% aqueous acetone extract of the whole fresh plant of *B. involucrata* over *Diaion HP20SS*, *Sephadex LH-20*, MCI-gel *CHP-20P*, and *Toyopearl HW-40F* resulted in the isolation of two new glycosides, **1** and **2**, in addition to 26 known compounds. The known ones were identified as dihydrochalcone glucoside, and its 4″-*O*-galloyl and 2″,3″-*O*-(*S*)-hexahydroxydiphenoyl (HHDP) derivatives, *i.e.*, sieboldin (**3**) [6], 3-hydroxyphloretin 4′-*O*-[3″-*O*-galloyl-4″,6″-*O*-(*S*)-HHDP]-β-D-glucopyranoside (**4**) [6], 3-hydroxyphloretin 4′-*O*-[4″,6″-*O*-(*S*)-HHDP]-β-D-glucopyranoside (**5**) [6], and 3-hydroxyphloretin 4′-*O*-[6″-*O*-galloyl]-β-D-glucopyranoside (**6**) [6], nine hydrolyzable tannins, *i.e.*, 1,2,3,6-tetra-*O*-galloyl- [18], 1-*O*-(*E*)-caffeoyl-, 1-*O*-(*E*)-*p*-coumaroyl-, 1,3-di-*O*-galloyl- [19], 1,3-di-*O*-galloyl-4,6-(*S*)-HHDP- [5], 1-*O*-(*E*)-caffeoyl-4-*O*-galloyl-, and 1-*O*-(*E*)-caffeoyl-3-*O*-galloyl-4,6-(*S*)-HHDP-β-D-glucopyranose (**7**–**13**, resp.), together with 3-*O*- and 6-*O*-galloyl-D-glucopyranose (**14** and **16**, resp.), five phenylpropanoids, *i.e.*, caffeic acid (**16**), *p*-coumaric acid (**17**), ferulic acid (**18**), coniferin (**19**) [20], and methylconiferin (**20** [12]), one gallic acid (**21**), three flavonoids, *i.e.*, eriodictyol-7-*O*-β-D-glucopyranoside (**22**) [21], glucodistylin (**23**) [22], and eriodictyol (**24**), two lignans, *i.e.*, isolariciresinol (**25**) [23] and secoisolariciresinol-4-*O*-β-D-glucopyranoside (**26**) [24], and two alkane glycosides, *i.e.*, isopentyl gentiobioside (**27**) [25], and grandoside (**28**) [26] by TLC comparison with authentic samples and by comparison of their spectroscopic data with those reported in the literatures.

Sieboldin-3′-ketocarboxylic acid (**1**) was obtained as a pale yellow amorphous powder. The molecular formula $C_{23}H_{24}O_{14}$ was deduced from the negative-ion mode HR-FAB-MS (*m*/*z* 523.1083 $[M-H]^-$) in combination with the presence of 23 C-atom signals in ^{13}C-NMR spectrum. The UV visible absorption bands at λ_{max} 203, 269, and 363 nm were suggestive of a chalcone skeleton. The IR spectrum of **1** indicated the presence of OH (3417 cm^{-1}), COO (1618 and 920 cm^{-1}), and phenyl (2923, 1599, 1525, and 920 cm^{-1}) groups. The ^{1}H-NMR spectrum exhibited the signals for one set of *ABX*-type aromatic H-atoms at δ(H) 6.66 (*d*, *J* = 1.9, H–C(2)), 6.66 (*d*, *J* = 8.2, H–C(5)) and 6.45 (*dd*, *J* = 8.2, 1.9, H–C(6))[1]), one *singlet* at higher field of the aromatic region (δ(H) 6.14 (*s*, H–C(5′)), together with two mutually coupled CH_2 signals (δ(H) 3.26 and 2.72 (each 2 H; *t*, *J* = 8.2, H–C(8) and H–C(7))). The data suggested the presence of a dihydrochalcone skeleton with a pentasubstituted *B*-ring in the molecule. In addition, one glucopyranosyl unit (anomeric H- and C-atom signals at δ(H) 4.96 (*d*, *J* = 6.3, H–C(1″)) and δ(C) 102.1 C(1″), resp.) was evidenced by ^{1}H- and ^{13}C-NMR of **1**. The HMBC of glucosyl H–C(1″) (δ 4.96) with C(4′) (δ 166.7) confirmed the location of the glucopyranosyl group at C(4′) in **1**. These NMR features resembled those of the dihydrochalcone glucoside, sieboldin (**3**) [6], except for the presence of an additional

[1]) Atom numbering as indicated in *Fig. 1*. For systematic numbering and name, see the *Exper. Part.*

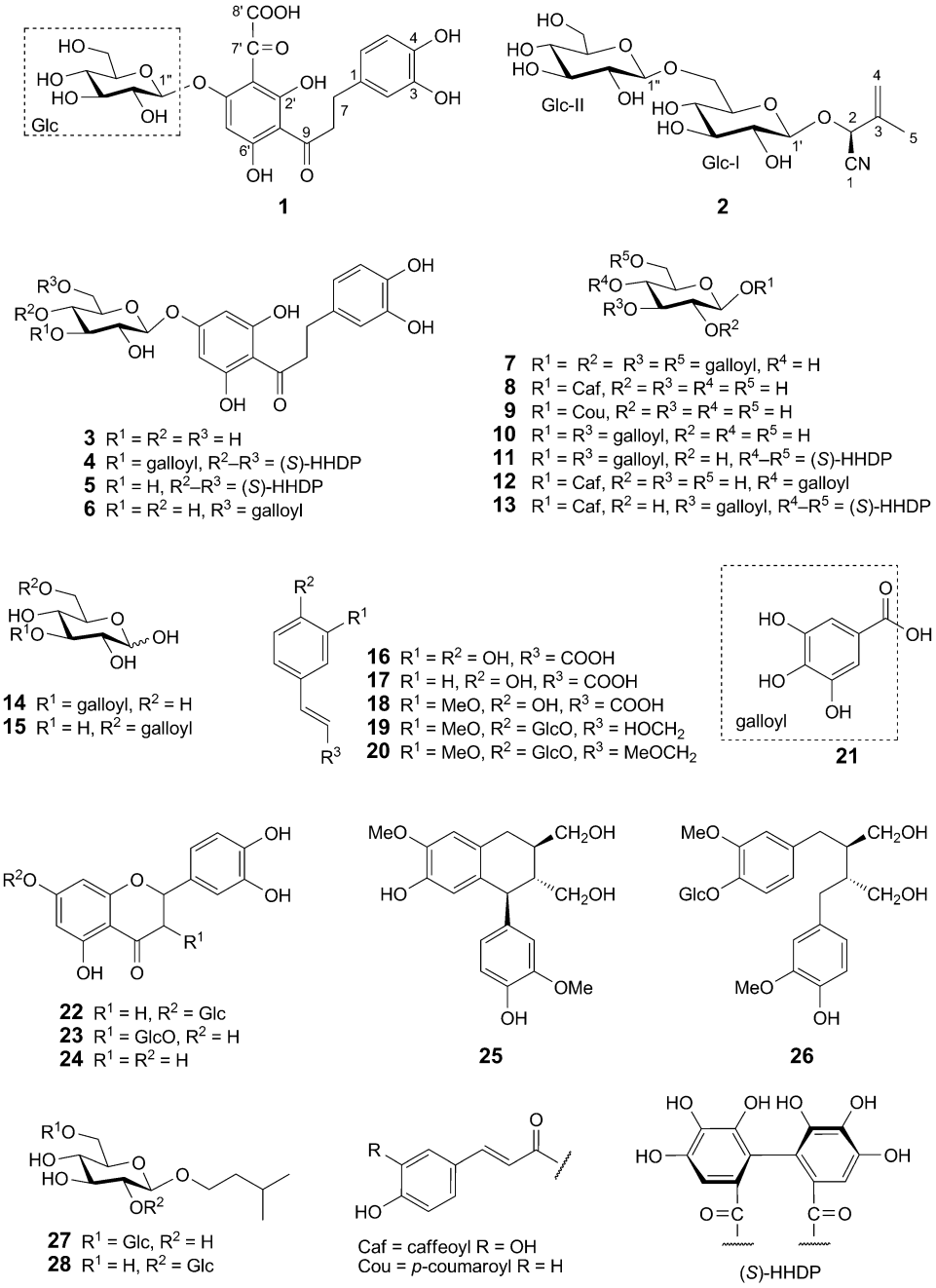

Fig. 1. *Structures of compounds* **1**–**28** *isolated from* B. involucrata

ketocarboxy group (δ(C) 172.0 (COOH) and 197.7 (–CO–)) in **1**. In addition, the aromatic H–C(3′) group in compound **3** ((δ(H) 6.11 (*s*); δ(C) 95.9 (*d*)) was replaced by an aromatic quaternary C-atom in **1** (δ(C) 100.6 (*s*)), indicating that the additional ketocarboxyl group was at C(3′) of **1**. This was further confirmed by the HMBC of H–C(5′) (δ 6.14) with the keto C-atom at δ(C) 197.7. Moreover, other HMBCs of H–C(5′) with C(6′), C(1′), C(4′), C(3′), and C(9) confirmed the structure of compound **1** (*Fig. 2*). Thus, compound **1** was deduced as {3-[3-(3,4-dihydroxyphenyl)propanoyl]-6-(β-D-glucopyranosyloxy)-2,4-dihydroxyphenyl}(oxo)acetic acid, and named sieboldin-3′-ketocarboxylic acid.

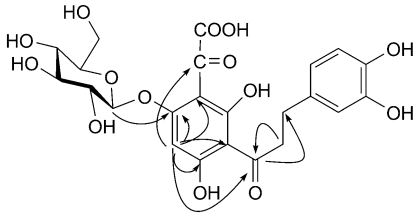

Fig. 2. *Key HMBCs* (H→C) *of compound* **1**

Proacacipetalin 6′-*O*-β-D-glucopyranoside (**2**) was isolated as a brown amorphous powder. Its molecular formula was established as $C_{17}H_{27}NO_{11}$, as deduced from the negative-ion mode HR-FAB-MS (*m*/*z* 420.1508 ($[M-H]^-$)) and ^{13}C-NMR spectrum. Comparison of the NMR data with those of proacacipetalin [27], and the further 2D-NMR spectral data allow elucidation of the structure of compound **2**.

The ^{1}H- and ^{13}C-NMR spectra of **2** revealed the presence of a CN (δ(C) 117.7 (*s*)) and a CH group (δ(C) 70.1 (*d*); δ(H) 5.34), olefinic C-atoms (δ(C) 138.3 (*s*), 117.1 (*t*)), a Me group (δ(C) 18.2 (*q*); δ(H) 1.79), and two β-D-glucopyranosyl moieties (anomeric H-atom signals at δ(H) 4.55 and 4.39 (each 1 H; *d*, *J* = 8.1)), suggesting that **2** was a cyanogenic glycoside. This was supported by the IR spectrum showing a strong band at 2362 cm^{-1} (CN). In the HMBC experiment, the signals at δ(H) 5.34 (br. *s*, H–C(2)) and 1.79 (br. *s*, Me(5)) showed long-range correlations with the signals at δ(C) 117.7 (*s*, C(1)), 138.3 (*s*, C(3)), and 18.2 (*q*, C(5)), and with those at δ(C) 70.1 (*d*, C(2)), 138.3 (*s*, C(3)), and 117.1 (*t*, C(4)), respectively. The HMBCs of glucosyl H–C(1′) (δ(H) 4.55) in **2** with C(2) (δ(C) 70.1) confirmed that the glucopyranosyl groups were at C(2) in **2**. These NMR features resembled those of the proacacipetalin [27][28], except for the presence of an additional set of signals arising from a D-glucopyranosyl group (anomeric H-atom signal at δ(H) 4.39 (*d*, *J* = 8.1)) in **2**. The *J* value (8.1 Hz) of the anomeric H-atom indicated the β-configuration of the glucose moiety. The chemical shift of the glucosyl C(6′) was shifted downfield to δ(C) 69.1 in **2**, indicating that the additional glucosyl group was at C(6′) of the inner glucosyl moiety in **2**. This was further confirmed by the HMBC experiment, in which the correlation of H–C(1″) (δ(H) 4.39) with C(6′) (δ(C) 69.1) of the glucopyranosyl group was observed. The (*S*)-configurations of C(2) in **2** was deduced from comparison of its ^{1}H- and ^{13}C-NMR spectral features with those of the proacacipetalin [27], which contains one glucosyl unit less than **2**, but showed similar negative $[\alpha]_D$ value. Thus the structure of **2** was

determined as (2*S*)-2-{[6-*O*-(*β*-D-glucopyranosyl)-*β*-D-glucopyranosyl]oxy}-3-methylbut-3-enenitrile, and named proacacipetalin 6′-*O*-*β*-D-glucopyranoside.

Cyanogenic glycoside **2** was isolated from the Balanophoraceae family for the first time. It might be a signal molecule between *B. involucrata* and its leguminous hosts, in which cyanogenic glycosides are the characteristic chemical constituents [28].

Radical-Scavenging Activity. Compounds **1** and **3**–**24** were preliminarily evaluated for their radical-scavenging activities by the DPPH assay, with ascorbic acid as positive control. The results are compiled in the *Table*. Most of the isolated compounds showed obvious scavenging activities on DPPH radical. Among them, the hydrolyzable tannins **3**–**7** and **9**–**15**, caffeic acid (**16**) and its derivative **8**, gallic acid (**21**), together with three flavonoids, **22**–**24**, displayed significant activities with the SC_{50} values in the range of 4.0–22.1 μM, which was in accordance with the trend that hydrolyzable tannins with more adjacent OH groups (galloyl, pyrogallol, or catechol group) had higher radical-scavenging activities on DPPH as reported previously [29]. It was further supported by the dihydrochalcone glucosides with galloyl and (*S*)-hexahydroxydiphenoyl (HHDP) moieties in their molecules, (*i.e.* **4**–**6**) showing stronger activities than that of the dihydrochalcone glucoside **5**. Compared to flavonoid glycosides, **22**–**24**, the hydrolyzable tannins, **3**–**7** and **9**–**15**, gallic acid (**21**), caffeic acid (**16**) and its derivative **8** displayed stronger activities than ascorbic acid. As the main constituents, caffeic acid (**16**) and gallic acid (**21**), which were reported to act as a prooxidant in inducing DNA fragmentation and apoptosis of several tumor cells [30][31], may play an important role in the antioxidant activity of *B. involucrata*.

Table. *DPPH Radical-Scavenging Activity of the Compounds Isolated from* B. involucrata

Compounds	SC_{50} [μM][a])[b])	Compounds	SC_{50} [μM][a])[b])
Ascorbic acid[c])	10.5±0.1	**13**	6.4±0.1
1	15.1±0.1	**14**	9.3±0.2
3	10.3±0.1	**15**	8.5±0.1
4	8.6±0.1	**16**	10.4±0.1
5	4.5±0.1	**17**	184±4
6	8.3±0.1	**18**	189±4
7	4.0±0.1	**19**	157±3
8	10.0±0.1	**20**	125±3
9	124±3	**21**	7.9±0.1
10	4.3±0.1	**22**	22.1±0.3
11	5.3±0.1	**23**	21.4±0.3
12	6.1±0.1	**24**	17.5±0.2

[a]) SC_{50}, Radical-scavenging activity (concentration required for 50% reduction of DPPH radical). [b]) Values represent means±S.D. ($n=3$). [c]) Positive control.

The above results provide evidences to evaluate the phytotherapeutic potential of *B. involucrata* and would promote the utilization of this herb in the health care.

The authors are grateful to the staff of the analytical group at State Key Laboratory of Phytochemistry and Plant Resources in West China, Kunming Institute of Botany, Chinese Academy of Sciences, for recording the spectra. This work was supported by the *NSFC* Grant No. 2011CB915503.

Experimental Part

General. DPPH Radical was from *Aldrich Chem. Co*. TLC: silica-gel *G* precoated plates (*Qingdao Haiyang Chemical Co.*) with benzene/HCOOEt/HCOOH: 2:7:1; visualization by spraying with 2% $FeCl_3$ in EtOH. Column chromatography (CC): *Diaion HP 20-SS* (*Mitsuishi Chemical Co.*), *Sephadex LH-20* (*Pharmacia Fine Chemical Co. Ltd.*), *MCI* gel *CHP-20P* (*Mitsubishi Chemical Co.*), and *Toyopearl HW-40F* (*Tosoh Co.*). Optical rotations: *P-1020* Polarimeter (*JASCO*, Tokyo, Japan). UV Spectra: *UV 210A Shimadzu* spectrometer (*Shimadzu*, Kyoto, Japan); λ in nm (log ε). IR Spectra: *IR-450* spectrometer (*Shimadzu*, Kyoto, Japan) with KBr pellets; $\tilde{\nu}$ in cm^{-1}. ^{1}H- and ^{13}C-NMR, HMQC, and HMBC spectra: in (D_6)acetone on a *Bruker AM-400* or *DRX-500* spectrometer operating at 500 and 400 MHz for ^{1}H, and 125 and 100 MHz for ^{13}C, resp; coupling constants *J* in Hz and chemical shifts δ in ppm with Me_4Si as internal standard. FAB-MS and HR-FAB-MS: *AutoSpe 3000* spectrometer (*VG*, Manchester, UK) with glycerol as the matrix; *m/z*. DPPH (*Aldrich Chem. Co.*) radical-scavenging assay: *Emax* precision microplate reader.

Plant Material. The whole fresh plant of *B. involucrata* was collected at Wenshan County, Yunnan Province, P. R. China, and identified by Prof. *X. W. Li*, Taxonomy Department, Kunming Institute of Botany, Chinese Academy of Sciences. The voucher specimen (KUN No. 0622028) was deposited with the KUN Herbarium of Kunming Institute of Botany, Chinese Academy of Sciences.

Extraction and Isolation. The whole fresh plant (3.8 kg) of *B. involucrata* was cut into small pieces and extracted with 80% aq. acetone three times (3×10 l, 24 h each) at r.t. The combined extracts were filtered and concentrated under vacuum to obtain a crude extract (300 g). The extract was subjected to CC (*Diaion HP20SS*; H_2O/MeOH 1:0–0:1 in step gradient) to give nine fractions. *Fr. 1* (11 g) was subjected to CC (*Sephadex LH-20*, MCI gel *CHP-20P*, and *Toyopearl HW-40F* H_2O/MeOH) to give **27** (3 mg) and **28** (4 mg). By the same chromatographic procedures, **2** (12 mg), **9** (64 mg), **19** (7 mg), and **14** (6 mg) from *Fr. 2* (67 g), **9** (50 mg), **15** (10 mg), and **20** (14 mg) from *Fr. 3* (13 g), **1** (12 mg), **3** (23 mg), **6** (13 mg), and **5** (20 mg) from *Fr. 4* (22 g), **4** (15 mg), **7** (16 mg), and **13** (8 mg) from *Fr. 5* (38 g), **12** (9 mg), **11** (24 mg), **18** (8 mg), **21** (100 mg), and **23** (5 mg) from *Fr. 6* (17 g), **22** (7 mg), **24** (64 mg), and **16** (60 mg) from *Fr. 7* (7 g), and **17** (13 mg), **25** (4 mg), **8** (7 mg), and **26** (6 mg) from *Fr. 8* (27 g) were obtained.

Sieboldin-3′-ketocarboxylic Acid (=*{3-[3-(3,4-Dihydroxyphenyl)propanoyl]-6-(β-*D*-glucopyranosyloxy)-2,4-dihydroxyphenyl}(oxo)acetic Acid*; **1**). White amorphous powder. $[\alpha]_D^{21} = -40.7$ ($c = 0.009$, MeOH). UV (MeOH): 363 (3.60), 269 (4.38), 203 (3.64), 196 (4.31). IR: 3417, 2923, 1618, 1599, 1525, 920. ^{1}H-NMR (500 MHz): 2.72 (*t*, *J* = 8.2, H–C(7)); 3.17 (*m*, H–C(2″)); 3.26 (*t*, *J* = 8.2, H–C(8)); 3.46 (*m*, H–C(5″)); 3.51 (*m*, H–C(3″)); 3.55 (*m*, H–C(4″)); 3.63 (*dd*, *J* = 12.0, 7.8, H–C(6″)); 3.82 (*d*, *J* = 12.0, H–C(6″)); 4.96 (*d*, *J* = 6.3, H–C(1″)); 6.14 (*s*, H–C(5′)); 6.45 (*dd*, *J* = 1.9, 8.2, H–C(6)); 6.66 (*d*, *J* = 1.9, H–C(2)); 6.66 (*d*, *J* = 8.2, H–C(5)). ^{13}C-NMR (125 MHz): 29.9 (C(7)); 46.5 (C(8)); 61.6 (C(6″)); 69.6 (C(4″)); 73.2 (C(2″)); 76.7 (C(3″)); 77.1 (C(5″)); 94.9 (C(5′)); 100.6 (C(3′)); 102.1 (C(1″)); 106.0 (C(1′)); 115.9 (C(2)); 116.2 (C(5)); 120.1 (C(6)); 133.4 (C(1)); 143.3 (C(3)); 145.0 (C(4)); 164.4 (C(2′)); 166.7(C(4′)); 170.8 (C(8′)); 171.8 (C(6′)); 197.7 (C(7′)); 206.2 (C(9)). FAB-MS (neg.): 523 ($[M-H]^-$), 361 ($[M-162$ (glucosyl)$]^-$). HR-FAB-MS: 523.1083 ($[M-H]^-$; calc. 523.1087).

*Proacacipetalin 6′-*O*-β-*D*-glucopyranoside* (=*(2*S*)-2-{[6-*O*-(β-*D*-Glucopyranosyl)-β-*D*-glucopyranosyl]oxy}-3-methylbut-3-enenitrile*; **2**). $[\alpha]_D^{21} = -34.0$ ($c = 0.007$, H_2O). UV (MeOH): 265 (3.28), 192 (3.99). IR: 2362, 2349, 2222. ^{1}H-NMR (500 MHz): 1.79 (br. *s*, H–C(5)); 3.22 (*m*, H–C(2′,2″)); 3.27 (*m*, H–C(5″)); 3.29 (*m*, H–C(4′)); 3.40 (*m*, H–C(4″)); 3.43 (*m*, H–C(3″)); 3.45 (*m*, H–C(3′)); 3.54 (*m*, H–C(5′)); 3.61 (*dd*, *J* = 12.0, 7.5, H_a–C(6″)); 3.74 (*dd*, *J* = 12.0, 6.0, H_a–C(6′)); 3.84 (*dd*, *J* = 12.0, 2.1, H_b–C(6″)); 4.13 (*d*, *J* = 12.0, H_b–C(6′)); 4.39 (*d*, *J* = 8.1, H–C(1″)); 4.55 (*d*, *J* = 8.1, H–C(1′)); 5.11 (br. *s*, H_a–C(4)); 5.30 (br. *s*, H_b–C(4)); 5.34 (br. *s*, H–C(2)). ^{13}C-NMR (125 MHz): 18.2 (C(5)); 61.7 (C(6″)); 69.1 (C(6′)); 70.1 (C(2)); 70.2 (C(4″)); 70.5 (C(4′)); 73.9 (C(2″)); 73.5 (C(2′)); 76.1 (C(5′)); 76.6 (C(3′)); 76.8 (C(3″,5″)); 101.2 (C(1′)); 103.9 (C(1″)); 117.1 (C(4)); 117.7 (C(1)); 138.3 (C(3)). FAB-MS (neg.): 420 ($[M-H]^-$), 96 ($[M-162$ (glucosyl)-162 (glucosyl)$]^-$). HR-FAB-MS: 420.1508 ($[M-H]^-$; calc. 420.1584).

DPPH Radical-Scavenging Assay. The DPPH assay was performed as described in [9], and ascorbic acid was used as positive control. Scavenging activity was determined by the following equation (A is absorbance):

$$\text{Scavenging activity } [\%] = 100 \times (A_{\text{control}} - A_{\text{sample}})/A_{\text{control}}$$

The SC_{50} value was obtained through extrapolation from linear regression analysis and denoted the concentration of the sample required to scavenge 50% of DPPH radicals.

REFERENCES

[1] C. Y. Wu, in 'Flora of China', Editorial Board of Flora of China, Chinese Academy of Sciences, Science Press, Beijing, 1988.
[2] R. W. Teng, D. Z. Wang, C. R. Yang, *Acta Bot. Yunnan.* **2000**, *22*, 225.
[3] G. M. She, Y. J. Zang, C. R. Chang, *Chem. Biodiversity* **2009**, *6*, 875.
[4] K. J. Wang, C. R. Yang, Y. J. Zhang, *Chem. Biodiversity* **2006**, *3*, 1317.
[5] Z. H. Jiang, Y. Hirose, H. Iwata, S. Sakamito, T. Tanaka, I. Kouno, *Chem. Pharm. Bull.* **2001**, *49*, 887.
[6] T. Tanaka, R. Uehara, K. Nishida, I. Kouno, *Phytochemistry* **2006**, *66*, 675.
[7] K. Ito, M. Itoigawa, M. Haruna, H. Murata, H. Furukawa, *Phytochemistry* **1980**, *19*, 476.
[8] N. Panthama, S. Kanokmedhakul, K. Kanokmedhakul, *Chem. Pharm. Bull.* **2009**, *57*, 1352.
[9] W. Wang, S. F. Zeng, C. R. Yang, Y. J. Zhang, *Helv. Chim. Acta* **2009**, *92*, 1817.
[10] Z. H. Jiang, X. Y. Wen, T. Tanaka, S. Y. Wu, Z. Q. Liu, H. Iwata, Y. Hirose, S. G. Wu, I. Kouno, *J. Nat. Prod.* **2008**, *71*, 719.
[11] T. Hosoya, A. Nakata, K. Zaima, J. Latip, L. B. Din, N. Muslim, H. Morita, *Chem. Pharm. Bull.* **2010**, *58*, 738.
[12] X. L. Shen, Y. J. Hu, Y. M. Shen, Q. Z. Mu, *Chin. Tradit. Herbal Drugs* **1996**, *27*, 259.
[13] X. Z. Xia, H. X. Han, P. F. Tu, *Chin. Tradit. Herbal Drugs* **2001**, *32*, 6.
[14] J. Y. Pan, Y. Zhou, K. Zou, J. Wu, Q. X. Li, S. Zhang, *Chin. Tradit. Herbal Drugs* **2008**, *39*, 327.
[15] J. Y. Pan, S. Zhang, L. S. Yan, J. D. Tai, Q. Xiao, K. Zou, Y. Zhou, J. Wu, *J. Chromatogr., A* **2008**, *1185*, 117.
[16] B. Luo, K. Zou, Z. Y. Guo, F. J. Dan, J. Z. Wang, H. Wang, *Chem. Nat. Compd.* **2009**, *45*, 371.
[17] H. L. Ruan, J. Li, X. Y. Zhao, Y. H. Zhang, M. Xiang, J. Z. Wu, *Chin. Arch. Tradit. Chin. Med.* **2003**, *21*, 910.
[18] M. A. M. Nawwar, S. A. M. Hussein, I. Merfort, *Phytochemistry* **1994**, *36*, 793.
[19] S. H. Lee, T. Tanaka, G. Nonaka, I. Nishioka, *Phytochemistry* **1989**, *28*, 3469.
[20] C. P. Falshaw, W. D. Ollis, K. L. Ormand, *Phytochemistry* **1969**, *8*, 913.
[21] H. N. El-Sohly, A. Joshi, X. C. Li, S. A. Ross, *Phytochemistry* **1999**, *52*, 141.
[22] Y. H. Pei, X. Li, T. R. Zhu, L. J. Wu, *Acta Pharm. Sin.* **1990**, *25*, 267.
[23] H. L. Liu, L. J. Wu, H. Li, J. Wang, *J. Shenyang Pharm. Univ.* **2002**, *19*, 93.
[24] Z. Yuan, Y. Tezuka, W. Fan, S. Kadota, X. Li, *Chem. Pharm. Bull.* **2002**, *50*, 73.
[25] S. De Rosa, A. De Giulio, G. Tommonaro, *Phytochemistry* **1996**, *42*, 1031.
[26] A. Inada, H. Murata, M. Somekawa, T. Nakanish, *Chem. Pharm. Bull.* **1992**, *40*, 3081.
[27] F. Nartey, L. Brimer, S. B. Christensen, *Phytochemistry* **1981**, *20*, 1311.
[28] B. R. Maslin, J. E. Dunn, E. E. Conn, *Phytochemistry* **1988**, *27*, 421.
[29] T. Yoshida, K. Mori, T. Hatano, T. Okumura, I. Uehara, K. Komagoe, Y. Fujita, T. Okuda, *Chem. Pharm. Bull.* **1989**, *37*, 1919.
[30] M. Inoue, R. Suzuki, T. Koide, N. Sakaguchi, Y. Ogihara, Y. Yabu, *Biochem. Biophys. Res. Commun.* **1994**, *204*, 898.
[31] H. Sakagami, K. Satoh, T. Hatano, T. Yoshida, T. Okuda, *Anticancer Res.* **1997**, *17*, 377.

Received March 29, 2012