Iridoid Glycosides from *Globularia trichosantha*

İhsan Çalış,*,† Hasan Kırmızıbekmez,† and Otto Sticher‡

Department of Pharmacognosy, Faculty of Pharmacy, Hacettepe University, TR-06100 Ankara, Turkey, and Department of Applied BioSciences, Swiss Federal Institute of Technology (ETH) Zurich, CH-8057 Zürich, Switzerland

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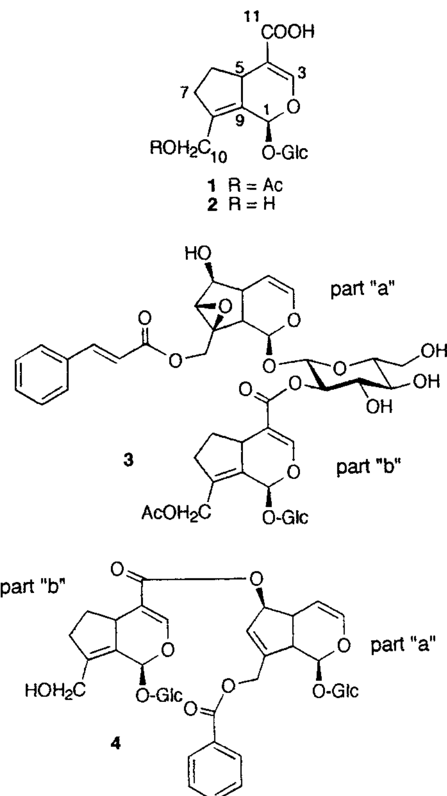
A new iridoid glycoside, deacetylalpinoside (**2**), was isolated from the aerial parts of *Globularia trichosantha* together with nine known iridoid glycosides: catalpol, 10-*O*-benzoyl-catalpol, aucubin, asperuloside, deacetylasperuloside, asperulosidic acid, scandoside, geniposidic acid, and alpinoside (**1**). From the underground parts of the same plant, two new bisiridoid glycosides, globulosides A (**3**) and B (**4**); a known iridoid glycoside, globularidin; a lignan glycoside, liriodendrin; and seven phenylethanoid glycosides, arenarioside, verbascoside (= acteoside), isoacteoside, crenatoside, isocrenatoside, and trichosanthosides A and B, were isolated. Compounds **2**−**4** are new iridoids containing an 8,9 double bond representing a rare carbon skeleton. Their structures were established by spectroscopic methods.

Our previous studies have resulted in the isolation of five phenylethanoid glycosides: crenatoside, verbascoside, rossicaside A, and trichosanthosides A and B from the aerial parts of *Globularia trichosantha* Fisch. & C. A. Meyer (Globulariaceae).[1] The present studies on the aerial and underground parts of the same plant resulted in the isolation of several iridoid, phenylethanoid, and lignan glycosides. Among the isolated iridoid glycosides, alpinoside (**1**) has a rare skeleton with an 8,9 double bond.[2] In this work, we further report a new representative (**2**) of the rare alpinoside-type iridoids, as well as two new bisiridoid glycosides, globulosides A (**3**) and B (**4**).



Results and Discussion

The water-soluble part of the methanolic extracts of the aerial and underground parts of *G. trichosantha* were separately fractionated by vacuum liquid chromatography (VLC). After repeated chromatography (medium-pressure liquid chromatography = MPLC) of these fractions, three new compounds (**2**−**4**) were isolated.

The positive- and negative-ion ESIMS of compounds **1** and **2** exhibited pseudomolecular ions $[M + Na]^+$, $[2M + Na]^+$, $[M - H]^-$, $[2M - H]^-$ at *m*/*z* 439, 855, 415, and 831 for **1**, and at *m*/*z* 397, 771, 373, and 747 for **2**, which are compatible with the molecular formulas $C_{18}H_{24}O_{11}$ and $C_{16}H_{22}O_{10}$, respectively. Their UV spectra (λ_{max} 233 nm for **1** and 232 for **2**) were characteristic for C-4-substituted iridoids. The ^{1}H NMR spectra (δ_H 7.34, d, $J = 1.6$ Hz; δ_H 7.21 d, $J = 1.8$ Hz; for H-3 of **1** and **2**, respectively) indicated the presence of a 4-substituted enol−ether system typical of iridoids. The ^{1}H and ^{13}C NMR spectroscopic findings were consistent with **1** and **2** bearing a C-10-iridoid monoglucosidic moiety. On the basis of ^{1}H and ^{13}C NMR data secured by 2D NMR experiments, compound **1** was identified as alpinoside, previously isolated from *Plantago alpina*.[2] When comparing their NMR data, a striking resemblance was noticed between **1** and **2**. The only difference was the absence of the acetyl signals in the spectra of **2**. Additionally, the resonances of 10-oxy-methylene protons (δ_H 4.26 and 4.17, $J_{AB} = 14.6$ Hz) were at a higher field than the corresponding protons of **1** (δ_H 4.70 and 4.80, $J_{AB} = 14.6$ Hz), supporting the disappearance of acetyl group at C-10. The common structural feature of **1** and **2** was a sharp singlet at δ_H 6.27, which was assigned to the protons at C-1, indicating the absence of a proton at C-9 in both compounds. These conclusions were confirmed by 2D NMR experiments (COSY, HSQC, and HMBC). We, therefore, concluded that the new compound **2** is deacetylalpinoside.

Globuloside A (**3**) proved to have the molecular formula $C_{42}H_{50}O_{21}$, as seen from the negative- and positive-ion ESIMS (*m*/*z* 889 $[M - H]^-$ and 913 $[M + Na]^+$, respectively) combined with ^{1}H and ^{13}C NMR data (Table 1). The FTIR spectrum showed absorption bands at 3400 (br OH), 1708 (ester), 1627 (C=C−O), and 1508 cm^{-1} (aromatic ring), and the UV spectrum exhibited maxima at 208 (sh), 216, 222 (sh), 238, and 278 nm. Analysis of the ^{1}H NMR spectrum of **3** revealed the feature of a bisiridoid glycoside with two acyl moieties. The signals in the region of δ_H 3.15−5.00

* To whom correspondence should be addressed. Tel: 90 312-3051089. Fax: 90 312-3114777. E-mail: acalis@dominet.in.com.tr.
† Hacettepe University.
‡ ETH Zurich.

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Table 1. ^{1}H and ^{13}C NMR Spectroscopic Data and HMBC Correlations for Globuloside A (**3**) (^{1}H NMR, 500 MHz; ^{13}C NMR, 75.5 MHz)[a]

part "a"					part "b"				
C/H		δ_C	δ_H ppm, J (Hz)	HMBC (C→H)	C/H		δ_C	δ_H ppm, J (Hz)	HMBC (C→H)
1	CH	95.4	5.05 d (9.7)	H-3, H-9, H-1′	1	CH	91.9	6.26 s	H-3, H-1′
3	CH	141.8	6.35 dd (6.0 and 1.8)	H-1, H-5	3	CH	152.2	7.30 d (1.8)	H-1
4	CH	103.8	5.07 dd (6.0 and 4.7)	H-3, H-5, H-6	4	C	113.9		H-1, H-3
5	CH	38.9	2.28 m	H-3, H-4, H-6, H-7	5	CH	39.0	3.57 m	H-1, H-3, H_2-6
6	CH	79.4	3.90 br s	H-5, H-7, H-9	6	CH_2	32.1	2.51 and 1.49 m	H_2-7
7	CH	62.8	3.49 br s	H-9, H_2-10	7	CH_2	35.0	2.42 m	H_2-10
8	C	63.5		H-7, H-9, H_2-10	8	C	134.1		H_2-6, H_2-7, H_2-10
9	CH	43.5	2.57 dd (9.7 and 7.6)	H-4, H-5, H_2-10	9	C	137.6		H-1, H_2-6, H_2-7, H_2-10
10	CH_2	64.8	4.97 d (12.5)		10	CH_2	60.9	4.80 d (12.9)	$COC\mathit{H}_3$
			4.21 d (12.5)					4.68 d (12.9)	
					11	C	167.4		H-3, H-2′ (part "a")
1′	CH	97.9	4.99 d (8.1)	H-1, H-2′	$\mathit{C}OCH_3$	C	172.2		$COC\mathit{H}_3$, H_2-10
2′	CH	74.6	4.77 dd (8.1 and 9.5)	H-3′	$CO\mathit{C}H_3$	CH_3	20.7	2.07 s	
3′	CH	76.4	3.53 t (9.5)	H-2′					
4′	CH	71.7	3.36[b]	H-3′, H-6′	1′	CH	99.9	4.67 d (7.9)	H-1, H-2′
5′	CH	78.7	3.37[b]	H-1′	2′	CH	74.7	3.16 dd (7.9 and 9.0)	H-3′
6′	CH_2	62.9	3.94 br d (12.0)		3′	CH	78.0	3.36[b]	H-2′
			3.69 dd (12.0 and 5.5)		4′	CH	71.4	3.29 t (9.5)	H-3′, H-6′
					5′	CH	78.3	3.37[b]	H-1′
1″	C	136.0			6′	CH_2	62.6	3.90 dd (12.0 and 2.0)	
2″	CH	129.5	7.65 m	H-α, H-3″, H-4″				3.69 dd (12.0 and 5.5)	
3″	CH	129.9	7.40 m						
4″	CH	131.4	7.40 m	H-2″, H-6″					
5″	CH	129.9	7.40 m						
6″	CH	129.5	7.65 m	H-α, H-4″, H-5″					
α	CH	119.0	7.70 d (16.0)	H-β					
β	CH	146.4	6.58 d (16.0)	H-α, H-2″, H-6″					
C=O	C	168.6		H-α, H-β, H_2-10					

[a] All proton and carbon assignments are based on 2D NMR (DQF−COSY, HSQC and HMBC). [b] Signal patterns are unclear due to overlapping.

comprised two anomeric proton resonances at δ_H 4.67 (d, J = 7.9 Hz) and 4.99 (d, J = 8.1 Hz), which suggested the presence of two β-glucopyranoside units. The complete assignments of all proton and carbon resonances were based on the DQF−COSY, HSQC, and HMBC experiments. Thus, the vicinally coupled olefinic protons at δ_H 6.35 (dd, J = 6 and 1.8 Hz) and 5.07 (dd, J = 6.0 and 4.7 Hz) were ascribed to H-3 and H-4, respectively, indicating the presence of an iridoid moiety with a nonconjugated enol−ether system, part "a". On the other hand, the proton and carbon signals at δ_H 7.30 (d, J = 1.8 Hz, H-3) and δ_C 152.2 (C-3) suggested the presence of a second iridoid moiety with a conjugated enol−ether system, part "b". Apart from these signals, the relevant proton and carbon resonances of two iridoid moieties were completely assigned by the help of 2D NMR experiments (Table 1). These NMR data clearly supported that the structure of part "a" is like that of catalpol, while part "b" is similar to that of alpinoside (**1**). The remaining signals indicated the presence of two ester functionalities. Two olefinic protons observed as an AX system at δ_H 6.58 and 7.70 (J_{AX} = 16 Hz) and five aromatic protons at δ_H 7.40 (3H) and 7.65 (2H) were consistent with the presence of an *trans*-cinnamoyl moiety. The second acyl moiety was established as an acetoxyl group (δ_H 2.07, 3H, s). The HMBC and NOESY correlations between C-1 (δ_C 95.4) and H-1′ (δ_H 4.99) for part "a", and C-1 (δ_C 91.9) and H-1′ (δ_H 4.67) for part "b", as well as long-range reverse correlations between C-1′ and H-1 for both iridoid moieties led to the assignments of the glucose units of each, parts "a" and "b". Thus, the downfield shift for the H-2′ (δ_H 4.77, dd, J = 8.1, 9.5 Hz) signal of the glucose unit of part "a" showed the first acylation site as C-2′(OH). Furthermore, the downfield shifts for both 10-oxymethylene protons of parts "a" and "b", which were located at δ_H 4.97 and 4.27 (J_{AX} = 12.5 Hz) and at δ_H 4.80 and 4.68 (J_{AX} = 12.9 Hz), respectively, revealed the other acylation sites. The significant ^{1}H−^{13}C HMBC cross-peaks between the carbonyl carbons (C=O) of cinnamoyl (δ_C 168.6), acetoxyl (δ_C 172.2), and C-11 of part "b" (δ_C 167.4) and the related protons established all connectivities. The HMBC cross-peaks observed from the carbonyl carbon signal of the cinnamoyl moiety to the H_2-10 of part "a" and from the carbonyl carbon signal of the acetoxyl group to H_2-10 of the part "b" secured the assignments of the acylation sites. Finally, the ^{1}H−^{13}C long-range correlations observed between C-11 of part "b" (alpinoside moiety) and H-2′ (δ_H 4.77) of the glucose moiety of part "a" (catalpol moiety), as well as C-11/H-3 (δ_H 7.30) established the connectivity between the two iridoid parts "a" and "b", to be via an ester linkage. Consequently, the structure of compound **3** was determined as a bisiridoid glycoside composed of acylated catalpol and alpinoside iridoid units. For this novel structure we propose the trivial name globuloside A.

Globuloside B (**4**) proved to have the elemental composition $C_{38}H_{46}O_{19}$ as determined by negative- and positive-ion ESIMS (m/z 805 $[M - H]^-$ and 829 $[M + Na]^+$, respectively) combined with ^{1}H and ^{13}C NMR data (Table 2). The FTIR spectrum showed absorption bands at 3392 (br OH), 1704 (ester), 1625 (C=C−O), and 1541 and 1508 cm^{-1} (aromatic ring), and the UV spectrum exhibited maxima at 207, 230, and 281 nm. The ^{1}H and ^{13}C NMR spectra of **4** clearly showed its dimeric nature by the duplication of the signals typical of an iridoid glucoside. One-half of the molecule, part "a" was easily assigned to an aucubin-type iridoid due to the signals at δ_H 6.35 (dd, J = 6.2, 2.0 Hz; H-3) and 5.08 (dd, J = 6.2, 3.6 Hz; H-4). The second part "b" was indicated to be a C-4 substituted iridoid structure on the basis of the resonances at δ_H 7.39 (d, J = 1.8 Hz) assigned as H-3, and δ_C 152.4, 114.2, and 168.5, which were assigned as C-3, C-4, and C-11, respec-

Table 2. ^{1}H and ^{13}C NMR Spectroscopic Data and HMBC Correlations for Globuloside B (**4**) (^{1}H NMR, 500 MHz; ^{13}C NMR, 75.5 MHz)[a]

part "a"					part "b"				
C/H		δ_C	δ_H ppm, J (Hz)	HMBC (C→H)	C/H		δ_C	δ_H ppm, J (Hz)	HMBC (C→H)
1	CH	96.9	5.18 d (6.4)	H-1′, H-3, H-9	1	CH	92.3	6.37 s	H-3, H-1′
3	CH	142.1	6.35 dd (6.2 and 2.0)	H-1, H-4	3	CH	152.4	7.39 d (1.8)	H-1
4	CH	104.8	5.08 dd (6.2 and 3.6)	H-3, H-6	4	C	114.2		H-1, H-3, H-6
5	CH	42.6	2.98 m	H-1, H-3, H-4, H-7	5	CH	39.0	3.60 m	H-1, H-3, H$_2$-7
6	CH	84.6	5.32 br s	H-4, H-5, H-7, H-9	6	CH$_2$	32.4	2.55 and 1.45 m	H$_2$-7
7	CH	128.6	5.91 t-like (1.7)	H-9, H$_2$-10	7	CH$_2$	34.8	2.50 m	H$_2$-6, H$_2$-10
8	C	146.0		H-6, H-7, H-9, H$_2$-10	8	C	134.5		H-1, H$_2$-7, H$_2$-10
9	CH	49.0	3.15[b]	H-4, H-7	9	C	142.7		H-1, H$_2$-7, H$_2$-10
10	CH$_2$	63.7	5.03 br d (13.5)	H-7	10	CH$_2$	59.1	4.19 dd (12.5 and 1.0)	
			5.15 br d (13.5)					4.27 br d (12.5)	
					11	C	168.5		H-3, H-6 of part "a"
1′	CH	100.0	4.70 d (7.9)	H-1, H-2′					
2′	CH	74.8	3.24 dd (7.9 and 8.0)		1′	CH	100.1	4.68 d (7.9)	H-1, H-2′
3′	CH	77.9	3.38[b]		2′	CH	74.6	3.15 dd (7.9 and 9.0)	
4′	CH	71.5	3.29[b]		3′	CH	77.9	3.38[b]	
5′	CH	78.3	3.30[b]		4′	CH	71.4	3.29[b]	
6′	CH$_2$	62.8	3.86[b] and 3.68[b]		5′	CH	78.3	3.30[b]	
					6′	CH$_2$	62.6	3.86[b] and 3.68[b]	
1″	C	131.0		H-3″, H-5″					
2″	CH	130.7	8.06 m	H-4″, H-6″					
3″	CH	129.7	7.50 t-like (8.0)	H-4″, H-5″					
4″	CH	134.5	7.62 m	H-2″, H-6″					
5″	CH	129.7	7.50 t-like (8.0)	H-3″, H-4″					
6″	CH	130.7	8.06 m	H-4″, H-6″					
C=O		167.6		H$_2$-10, H-2″, H-6″					

[a] All proton and carbon assignments are based on 2D NMR (DQF–COSY, HSQC and HMBC). [b] Signal patterns are unclear due to overlapping.

tively. Additional aromatic proton signals at δ_H 8.06 (2H), 7.62 (1H), and 7.50 (2H), together with the corresponding carbon resonances, supported the presence of a benzoyl moiety. Two anomeric proton signals at δ_H 4.70 and 4.68 (both d, $J = 7.9$ Hz) were consistent with the presence of two β-glucose units within **4**, supporting the proposed dimeric structure. The COSY, HSQC, and HMBC experiments allowed the assignments of all proton and carbon resonances of part "a" to constitute a substituted aucubin moiety (Table 2). Furthermore, the proton signals assigned to H-6 (δ_H 5.32, br s) and H$_2$-10 (δ_H 5.03 and 5.15, J_{AB} = 13.5 Hz) of the aucubin moiety were found to be shifted downfield due to acylations. The HMBC correlations between the carbonyl carbon (δ_C 167.6) of the benzoyl moiety and hydroxymethylene protons (H$_2$-10) of aucubin (part "a") showed C-10 to be the site of benzoylation. The remaining proton and carbon resonances were consistent with an iridoid moiety similar to that of deacetylalpinoside (**2**). The connectivity between parts "a" and "b" was found to be an ester linkage between the C-6(OH) of part "a" (aucubin moiety) and the carboxyl group (C-11) of part "b" (deacetylalpinoside moiety). In comparison to that of aucubin, the downfield shift for H-6 (δ_H 5.32 in **4** and 4.43 in aucubin) of part "a" due to acylation clearly supported the site of linkage between parts "a" and "b". This observation was also evident by the presence of a HMBC correlation between C-11 (δ_C 168.5) of part "b" and H-6 of part "a". Thus, compound **4** belongs to the dimeric iridoids, and we propose the trivial name globuloside B.

Alpinoside (**1**) and **2** present a rare iridoid skeleton with an 8,9 double bond. These compounds are also part of the structure of the two bisiridoids, globulosides A and B (**3**, **4**). There are only a few reports of iridoids with an 8,9 double bond. Anagalloside,[3] majoroside,[4] 10-hydroxymajoroside,[5] hookerioside,[6] deacetylhookerioside,[2] and 10-acetoxymajoroside[7] are the other examples of this type of iridoid. Except anagalloside, which has been isolated from *Veronica anagallis-aquatica* (Scrophulariaceae),[3] all of them have been isolated from *Plantago* species (Plantaginaceae). On the other hand, *Globularia* species (Globulariaceae) have been reported to contain a rare type of phenylethanoid glycosides, crenatoside (= oraposide)[8,9] and isocrenatoside.[10] These compounds were also isolated from *Orobanchae* species (Orobanchaceae). Thus, the results presented in this study might be of significance for the chemotaxonomy of Globulariaceae.

Experimental Section

General Experimental Procedures. Optical rotations were measured on a Perkin-Elmer 141 polarimeter using a sodium lamp operating at 589 nm. UV spectra were performed on a Shimadzu UV-160A spectrophotometer. IR spectra were measured on a Perkin-Elmer 2000 FT-IR spectrometer in KBr pellets. NMR measurements in CD$_3$OD were performed on Bruker AMX 300 and DRX 500 spectrometers operating at 300 and 500 MHz for ^{1}H and 75.5 MHz for ^{13}C, respectively, using the XWIN NMR software package for the data acquisition and processing. Negative- and positive-mode ESIMS were recorded on a Finnigan TSQ 7000 instrument.

Plant Material. *G. trichosantha* was collected from Sivas, between Akdagmadeni and Yildizeli, Central Anatolia, Turkey, in June 1998, at an altitude of ca. 1800 m. Voucher specimens (98–001) have been deposited at the herbarium of the Department of Pharmacognosy, Faculty of Pharmacy, Hacettepe University, Ankara, Turkey.

Extraction and Isolation (Aerial Parts). Extraction and fractionation of the air-dried, aerial parts (stems, leaves, and flowers, 100 g) of *G. trichosantha* were reported in our previous study.[1] Fraction D (1242 mg) eluted with 10–15% MeOH in H$_2$O was subjected to MPLC using reversed-phase material (LiChroprep C$_{18}$; column dimensions: 2.6 × 40 cm), and H$_2$O (250 mL), H$_2$O–MeOH mixtures with increasing amount of MeOH in H$_2$O (10–50%, 2050 mL) as solvents to yield three fractions, D$_1$ (195 mg), D$_2$ (290 mg), and D$_3$ (200 mg). Fraction D$_2$ was rechromatographed on a Si gel (27 g) column eluting with CHCl$_3$–MeOH–H$_2$O (90:10:1; 200 mL; 80:20:2; 600 mL; 61:32:7; 100 mL) to give 10-*O*-benzoylcatalpol (93 mg). Fraction B (3316 mg), eluted with H$_2$O was similarly subjected to MPLC, employing H$_2$O (300 mL), H$_2$O–MeOH mixtures (1–40% MeOH, 1600 mL) as eluents to yield catalpol (20 mg) and

additional four fractions B_2 (210 mg), B_3 (125 mg), B_4 (77 mg), and B_5 (690 mg). Fraction B_5 was rechromatographed on a Si gel (70 g) column using the mixtures of $CHCl_3$−MeOH−H_2O to yield asperuloside (238 mg), asperulosidic acid (4 mg), and a crude deacetylalpinoside (**2**, 36 mg). The latter was further purified on a Si gel (9 g) column eluting with $CHCl_3$−MeOH−H_2O mixtures (61:32:7, 100 mL, 55:35:10, 75 mL) to give compound **2** (12 mg). Fraction B_4 was applied to a Si gel (13 g) column eluting with $CHCl_3$−MeOH−H_2O mixtures (80:20:2, 100 mL, 70:30:3, 100 mL) to give deacetylasperuloside (4 mg) and aucubin (9 mg). Fraction A (6591 mg), eluted with H_2O, was dissolved in H_2O and partitioned with *n*-BuOH. The butanol phase was evaporated to dryness in vacuo (1 g) and subjected to Si gel (70 g) column eluting with $CHCl_3$−MeOH−H_2O mixtures (80:20:2, 200 mL, 70:30:3, 500 mL; 61:32:7, 200 mL; 55:35:10, 200 mL) to give asperuloside (20 mg) and a mixture of geniposidic acid and scandoside. The mixture of these compounds was combined with fraction B_2 and subjected to a Si gel (12 g) column chromatography using the same solvent mixtures to give pure scandoside (10 mg) and geniposidic acid (5 mg). Fraction E (2860 mg) was subjected to MPLC using reversed-phase material employing H_2O (250 mL), H_2O−MeOH mixtures with increasing amount of MeOH in H_2O (10−80%, 1800 mL), and MeOH (200 mL) as eluents to give three fractions, E_1 (195 mg), E_2 (780 mg), and E_3 (534 mg). Fraction E_1 was rechromatographed on a Si gel column eluting with $CHCl_3$−MeOH−H_2O mixtures (70:30:3, 200 mL; 61:32:7, 50 mL) to give alpinoside (**1**, 27 mg).

Extraction and Isolation (Underground Parts). The air-dried, underground parts (roots and epigeal stolons, 190 g) of *G. trichosantha* were extracted with 80% MeOH in H_2O (600 mL × 2) for 6 h at 45 °C and filtered. The filtrate was concentrated to dryness in vacuo (18.5 g, yield 9.7%). The extract was dissolved in H_2O and partitioned with $CHCl_3$. The H_2O phase was lyophilized (17.5 g) and subjected to VLC using reversed-phase material (Sepralyte 40 μm, 150 g), employing H_2O (200 mL), H_2O−MeOH mixtures with increasing amount of MeOH in H_2O (5-80% MeOH), and MeOH to give 10 main fractions, A−J: A (540 mg), B (1.742 g) and C (190 mg), D (654 mg), E (735 mg), F (3.9 g), G (2.741 g), H (5.320 g), I (350 mg) and J (930 mg). Fraction F was subjected to a Si gel (100 g) column using the mixtures of $CHCl_3$−MeOH−H_2O (80:20:2, 400 mL; 70:30:3, 200 mL; 61:32:7, 600 mL; 60:40:4, 200 mL) to yield seven fractions: F_1 (230 mg), F_2 (300 mg), F_3 (497 mg), F_4 (810 mg), F_5 (400 mg), F_6 (520 mg), and F_7 (113 mg). Fraction F_5 was further subjected to MPLC (18.5 × 352 mm), employing H_2O−*i*-PrOH mixtures with increasing amounts of *i*-PrOH in H_2O (5−30%, 700 mL) as solvents to yield arenarioside (13 mg) and trichosanthoside A (44 mg). Fraction F_6 was likewise subjected to MPLC employing H_2O−MeOH−*i*-PrOH mixtures (80:15:5, 500 mL; 75:20:5, 200 mL) to give trichosanthoside B (11.16 mg). Fraction G was subjected to MPLC (26 × 480 mm) and H_2O−*i*-PrOH mixtures with increasing amount of *i*-PrOH in H_2O (10−50%, 1450 mL) as solvents to give six fractions, G_1 (116 mg), G_2 (370 mg), G_3 (634 mg), G_4 (250 mg), G_5 (413 mg), and G_6 (65 mg). Fraction G_1 was rechromatographed on a Si gel (20 g) column eluting with CH_2Cl_2−MeOH−H_2O (80:20:2, 200 mL) to give liriodendrin (21 mg). Fraction G_2 was subjected to a Si gel (40 g) column using CH_2Cl_2−MeOH−H_2O (61:32:7, 300 mL) to yield verbascoside (66 mg) and trichosanthoside B (35 mg). Fraction G_4 was also applied to a Si gel column (30 g) and using CH_2Cl_2−MeOH−H_2O (70:30:3, 300 mL; 61:32:7, 100 mL) to give crenatoside (9 mg) and trichosanthoside A (79 mg). Fraction G_5 was first subjected to a Si gel (35 g) column and eluted with CH_2Cl_2−MeOH−H_2O (80:20:1, 250 mL; 80:20:2, 500 mL; 61:32:7, 250 mL) to yield two main fractions: G_{5a} (180 mg) and G_{5b} (56 mg). Repeated chromatography of fraction G_{5a} afforded crenatoside (52 mg), isocrenatoside (7 mg), and isoacteoside (13 mg). Fraction G_6 was applied to a Si gel (12 g) column using CH_2Cl_2−MeOH−H_2O (80:20:2, 200 mL) to yield globularidin (14 mg) and isocrenatoside (14 mg). Fraction I was subjected to a Si gel (30 g) column eluting with CH_2Cl_2−MeOH−H_2O (80:20:2, 200 mL; 70:30:3, 200 mL) to yield two main fractions, I_1 (35 mg) and I_2 (45 mg). Repeated chromatography of fractions I_1 and I_2 on Si gel (8 g; for each) columns, separately, using CH_2Cl_2−MeOH−H_2O (80:20:2, 200 mL; for each) gave globulosides A (**3**, 13 mg) and B (**4**, 15 mg), respectively.

Alpinoside (1): $[\alpha]^{20}_D$ −57.4° (*c* 0.5, MeOH); UV (MeOH) λ_{max} 233 nm; IR (KBr) ν_{max} 3390 (OH), 1717 (ester), 1706 (C=O), 1626 cm^{-1} (C=C); ^1H NMR (300 MHz, CD_3OD) δ 7.34 (1H, d, J = 1.6 Hz, H-3), 6.27 (1H, s, H-1), 4.80 (1H, d, J = 14.6 Hz, H-10b), 4.70 (1H, d, J = 14.6 Hz, H-10a), 4.68 (1H, d, J = 8.0 Hz, H-1′), 3.88 (1H, dd, J = 11.9, 1.5 Hz, H-6′b), 3.68 (1H, dd, J = 11.9, 5.1 Hz, H-6′a), 3.58 (1H, m, H-5), 3.36 (1H, t, J = 8.8 Hz, H-3′), 3.33 (1H, m, H-5′), 3.30 (1H, overlapped, H-4′), 3.16 (1H, dd, J = 8.0, 8.8 Hz, H-2′), 2.56 (1H, m, H-6b), 2.47 (2H, m, H_2-7), 2.05 (3H, s, OCO*CH*$_3$), 1.47 (1H, m, H-6a); ^{13}C NMR (75.5 MHz, CD_3OD) δ 172.7 (C, O*C*OCH$_3$), 171.1 (C, C-11), 151.4 (CH, C-3), 137.4 (C, C-9), 134.6 (C, C-8), 115.0 (C, C-4), 99.9 (CH, C-1′), 91.7 (CH, C-1), 78.3 (CH, C-5′), 78.0 (CH, C-3′), 74.7 (CH, C-2′), 71.5 (CH, C-4′), 62.7 (CH_2, C-6′), 60.9 (CH_2, C-10), 39.3 (CH, C-5), 35.1 (CH_2, C-7), 32.1 (CH_2, C-6), 20.7 (CH_3, OCO*C*H$_3$); HMBC data C-1/H-3, H-1′, C-3/H-1, C-4/H-3, C-4/H-6a, C-5/H-1, C-5/H-3, C-5/H_2-7, C-6/H_2-7, C-7/H_2-6, C-7/H_2-10, C-8/H-6b, C-8/H_2-7, C-8/H_2-10, C-9/H-1, C-9/H-6b, C-9/H_2-7, C-9/H_2-10, C-10/CO*C*H$_3$, C-11/H-3, *C*OCH$_3$/H_2-10, C-1′/H-1; ESIMS: *m/z* 439 $[M + Na]^+$, 855 $[2M + Na]^+$, 415 $[M - H]^-$, 831 $[2M - H]^-$.

Deacetylalpinoside (2): $[\alpha]^{20}_D$ −52° (*c* 0.56, MeOH); UV (MeOH) λ_{max} 232 nm; IR (KBr) ν_{max} 3370 (OH), 1690 (C=O), 1632 cm^{-1} (C=C); ^1H NMR (300.13 MHz, CD_3OD) δ 7.21 (1H, d, J = 1.8 Hz, H-3), 6.27 (1H, s, H-1), 4.68 (1H, d, J = 8.0 Hz, H-1′), 4.26 (1H, d, J = 13.9 Hz, H-10b), 4.17 (1H, d, J = 14.6 Hz, H-10a), 3.88 (1H, dd, J = 11.9, 1.7 Hz, H-6′b), 3.68 (1H, dd, J = 11.9, 5.1 Hz, H-6′a), 3.58 (1H, m, H-5), 3.37 (1H, t, J = 8.6 Hz, H-3′), 3.30 (2H, overlapped, H-4′ and H-5′), 3.16 (1H, dd, J = 7.9, 8.6 Hz, H-2′), 2.57 (1H, m, H-6b), 2.47 (2H, m, H_2-7), 1.46 (1H, m, H-6a); ^{13}C NMR (75.5 MHz, CD_3OD) δ 173.7 (C, C-11), 149.3 (CH, C-3), 141.7 (C, C-9), 132.4 (C, C-8), 117.5 (C, C-4), 100.1 (CH, C-1′), 92.0 (CH, C-1), 78.2 (CH, C-5′), 77.9 (CH, C-3′), 74.7 (CH, C-2′), 71.5 (CH, C-4′), 62.7 (CH_2, C-6′), 59.1 (CH_2, C-10), 39.7 (CH, C-5), 34.8 (CH_2, C-7), 32.2 (CH_2, C-6); ESIMS *m/z* 397 $[M + Na]^+$, 775 $[2M + Na]^+$, 373 $[M - H]^-$, 747 $[2M - H]^-$.

Globuloside A (3): $[\alpha]^{20}_D$ −72.5° (*c* 0.1, MeOH); UV (MeOH) λ_{max} 208 (sh), 216, 222 (sh), 238, and 278 nm; IR (KBr) ν_{max} 3400 (OH), 1708 (ester), 1627 (C=C−O), and 1508 cm^{-1} (aromatic ring); ^1H NMR (500 MHz, CD_3OD) and ^{13}C NMR (125 MHz, CD_3OD), see Table 1; ESIMS (*m/z* 889 $[M - H]^-$ and 913 $[M + Na]^+$.

Globuloside B (4): $[\alpha]^{20}_D$ −81.5° (*c* 0.1, MeOH); UV (MeOH) λ_{max} 207, 230 and 281 nm; IR (KBr) ν_{max} 3392 (OH), 1704 (ester), 1625 (C=C−O), and 1541, 1508 cm^{-1} (aromatic ring); ^1H NMR (500 MHz, CD_3OD) and ^{13}C NMR (125 MHz, CD_3OD), see Table 2; ESIMS (*m/z* 805 $[M - H]^-$ and 829 $[M + Na]^+$.

1D and 2D NMR spectroscopic data and FABMS or ESIMS data for catalpol,[11] 10-*O*-benzoylcatalpol,[12] aucubin,[13] asperuloside,[14] deacetylasperuloside,[14,15] asperulosidic acid,[14,15] scandoside,[13,14,16] geniposidic acid,[13,17] globularidin,[11,18] verbascoside,[19] isoacteoside,[20] crenatoside,[8,9] isocrenatoside,[10] trichosanthosides A and B,[1] arenarioside,[21] and liriodendrin[11] were identical with published data.

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