Cardiac Glycosides and Pregnanes from *Adenium obesum* (Studies on the Constituents of *Adenium*. I)

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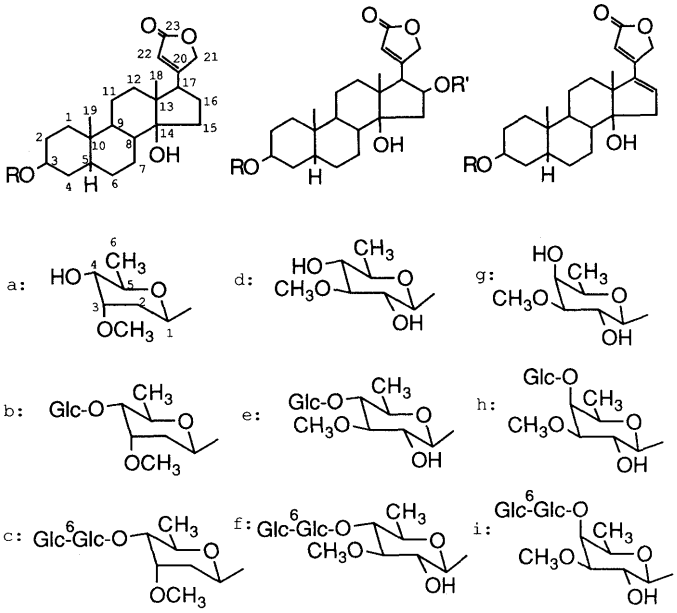
Cardiac glycosides and pregnanes from the roots and the stems of *Adenium obesum* ROEM. *et* SCHULT. were investigated. Among 30 cardiac glycosides including 15 known glycosides and 15 new combinations of the known aglycones and sugars, the structures of 11 glycosides were elucidated. Oleandrigenin β-gentiobiosyl-β-D-thevetoside was the main glycoside. Neridienone A and 16,17-dihydroneridienone A, common pregnanes in Apocynaceae, were also isolated.

Keywords *Adenium obesum*; Apocynaceae; cardiac glycoside; D-thevetoside; obeside; obebioside; obetrioside; pregnane; neridienone A

Cardiac glycosides of five *Adenium* species have been investigated by Frerejacque and Hasenfratz[1] and Reichstein's group,[2] and 14 glycosides were isolated. Recently *Adenium obesum* ROEM. *et* SCHULT. was examined by two groups.[3,4] Cardenolides of *Adenium* include digitoxigenin, oleandrigenin, gitoxigenin and Δ^{16}-digitoxigenin, while D-cymarose, D-thevetose and D-digitalose are known as component deoxysugars. During our investigations on the constituents of Apocynaceae plants, cardiac glycosides from the roots and the stems of *A. obesum* were examined and 30 glycosides including 15 new combinations of the known cardenolides and component sugars were isolated. In this paper, 11 glycosides having the new combinations are described along with two known pregnanes.



1: R=a **2**: R=a, R′=Ac **3**: R=a
4: R=d **5**: R=d, R′=Ac **6**: R=d, R′=H **7**: R=d
8: R=g, R′=Ac **9**: R=g, R′=H
10: R=glucosyl, R′=Ac
11: R=b, R′=Ac
12: R=e **13**: R=e, R′=Ac **14**: R=e, R′=H **15**: R=e
16: R=h **17**: R=h, R′=Ac **18**: R=h, R′=H **19**: R=h
20: R=c **21**: R=c, R′=Ac **22**: R=c
23: R=f **24**: R=f, R′=Ac
25: R=i **26**: R=i, R′=Ac

Chart 1

The isolation and fractionation of the cardiac glycosides and the pregnanes were carried out in the usual manner described for other Apocynaceae plants,[5] and 30 cardiac glycosides presented in Chart 1 and two pregnanes were obtained. Compounds **1**—**4**, **8**—**11**, **16**—**20**, **25**, **26** were identified as known glycosides by analyses of the proton nuclear magnetic resonance (^{1}H-NMR) spectra, carbon-13 nuclear magnetic resonance (^{13}C-NMR) spectra and the fast atom bombardment mass spectra (FAB-MS). Some of the identifications were confirmed by direct comparisons of the compounds with authentic samples by thin layer chromatography (TLC) and high-performance liquid chromatography (HPLC), as well as comparisons of spectral data.

Compound **5** showed an $[M+Na]^+$ peak at *m/z* 615.314 ($C_{32}H_{48}NaO_{10}$) in the FAB-MS, 58 mass units (m.u.) more than honghelin (digitoxigenin β-D-thevetoside, **4**),[1] and the signals due to the sugar portion showed the same pattern as those of **4** in the ^{1}H- and ^{13}C-NMR spectra (Table I). The presence of the 16-*O*-acetyl group was suggested by the 3H singlet signal at δ 1.85 and H-16 at lower field (δ 5.69). The ^{13}C-NMR signals were assignable as those of an oleandrigenin glycoside. Compound **5** was therefore considered to be oleandrigenin β-D-thevetoside. In order to confirm the component sugar, **5** was hydrolyzed with 0.7 N HCl–30% dioxane, and the resultant sugar was identified as D-thevetose by its optical rotation value and its identical *Rf* value with authentic L-thevetose on TLC. Compound **5** was named obeside B.

Compounds **6** and **7** were obtained as minor glycosides. Compound **6** showed a carbinyl proton signal assignable to H-16 at δ 4.96 and an $[M+Na]^+$ peak at *m/z* 573.305 ($C_{30}H_{46}NaO_9$), 42 m.u. less than **5**, suggesting **6** to be a gitoxigenin glycoside. In the ^{1}H-NMR spectrum of **7**, an olefinic proton signal was observed at δ 6.16, which was ascribable to H-16 in a Δ^{16}-cardenolide, and FAB-MS afforded an $[M+Na]^+$ peak at *m/z* 555.290 ($C_{30}H_{44}NaO_8$), 18 m.u. less than in the case of **6**. The signals due to the sugar moieties in **6** and **7** were identical with those of **5**. Compounds **6** and **7** were therefore determined to be gitoxigenin β-D-thevetoside and Δ^{16}-digitoxigenin β-D-thevetoside, respectively, and were named obesides C and D.

Compounds **12**, **13**, **14** and **15** were considered to be biosides composed of the same β-D-glucosyl-β-D-thevetosyl moiety, based on two anomeric proton signals (δ 4.71—4.73, 5.12—5.14) and signals of one methoxyl and one *sec*-

TABLE I. ^{13}C Chemical Shifts of Cardiac Glycosides from *Adenium obesum*

C	5	9	13	19	21	24	25
1	30.5[a]	30.6[a]	30.6	30.5[a]	30.6[a]	30.6	30.4[a]
2	27.0	27.1	27.0	27.0	27.0	27.0	27.0[b]
3	74.5	74.4	74.5	74.4	73.2	74.4[a]	74.4
4	30.6[a]	30.7[a]	30.6	30.7[a]	30.7[a]	30.6	30.6[a]
5	36.6[b]	36.6[b]	36.6[a]	36.7[b]	36.9[b]	36.6[b]	36.6[c]
6	27.0	27.1	27.0	27.0	27.0	27.0	27.2[b]
7	21.1[c]	21.2[c]	21.1[b]	20.2[c]	21.1[c]	21.1[c]	21.5[d]
8	41.9	42.1	41.9	41.6	41.9	41.9	41.9
9	35.8[b]	35.9[b]	35.8[a]	36.5[b]	35.8[b]	35.8[b]	35.9[c]
10	35.3	35.4	35.3	35.3	35.4	35.3	35.4
11	21.6[c]	21.8[c]	21.6[b]	21.6[c]	21.6[c]	21.6[c]	21.9[d]
12	38.9	40.1	38.9	38.5	38.9	38.9	39.7
13	50.4	50.5	50.4	52.6	50.4	50.4	50.1
14	83.4	84.2	83.2	84.8	83.4	83.0	84.6
15	41.2	43.9	41.2	40.9	41.2	41.2	33.1
16	74.9	72.3	74.9	133.6	74.9	74.9	27.3[b]
17	56.7	59.3	56.8	144.4	56.8	56.8	51.5
18	16.2	17.0	16.2	16.8	16.2	16.2	16.1
19	23.9	23.7	23.7	23.9	23.4	23.7	23.6
20	170.1	172.3	170.1	159.7	170.1	170.1	175.9
21	76.1	76.6	76.2	71.9	76.2	76.2	73.7
22	121.5	120.1	121.3	111.9	121.5	121.5	117.6
23	174.0	174.5	174.1	174.6	174.1	174.0	175.9
-OAc	20.6		20.6		20.6	20.6	
	169.6		169.6		169.7	169.6	
1′	102.9	103.5	102.7	103.3	96.7	102.7	103.3
2′	75.0	70.8	74.8	70.4	37.2	74.5[a]	70.5
3′	88.1	85.0	86.2	85.5	78.4[d]	86.1	85.6
4′	76.0	68.7	83.4	76.8	83.7	83.4	75.8[c]
5′	72.6	71.0	72.0[c]	71.4	69.4	71.9[d]	71.3[f]
6′	18.6	17.4	18.8	17.7	18.7	18.7	17.9
-OMe	60.7	57.2	60.4	58.9	58.9	60.5	58.8
1″			104.7	105.5	106.5	104.5	105.0
2″			75.8	76.0	75.2	75.6[f]	75.7[e]
3″			78.6	78.5[d]	78.4[d]	78.5[e]	78.5[g]
4″			71.6[c]	71.9	71.9[e]	71.8[d]	71.8[f]
5″			78.0	78.3[d]	77.0	77.2	77.6
6″			63.1	63.1	70.8	70.4	70.4
1‴					105.6	105.3	105.5[g]
2‴					75.2	75.4[f]	75.2[e]
3‴					78.4[d]	78.3[e]	78.4[g]
4‴					71.7[e]	71.7[d]	71.7[f]
5‴					78.2[d]	78.2[e]	78.3[g]
6‴					62.8	62.8	62.8

a—*g*) Signal assignments marked *a*—*g*) in each column may be reversed. δ (ppm) from TMS in pyridine-d_5.

methyl groups, and the other signals due to the sugar portions in the ^1H-NMR spectra. The linkage of D-glucose to D-thevetose was assigned as the 4-OH of D-thevetose, based on the glycosylation shift of C-4 of D-thevetose (+7.4 ppm) in **13** in comparison with that of **5**. In the FAB-MS of these biosides, $[M+Na]^+$ peaks were observed at *m/z* 719.359 (**12**), 777 (**13**), 735 (**14**) and 717.346 (**15**). Since the characteristic signals due to digitoxigenin, oleandrigenin, gitoxigenin and Δ^{16}-digitoxigenin were observed in the ^1H-NMR spectra of **12**, **13**, **14** and **15**, respectively, and the ^{13}C-NMR signals of **12**, **13** and **15**, were consistent with the assignments by ^1H-NMR, the structures were determined to be β-D-glucosyl(1→4)-β-D-thevetoside of each cardenolide. Compounds **12**—**15** were named obebiosides A (**12**), B (**13**), C (**14**) and D (**15**), respectively.

Compound **21** afforded an $[M+Na]^+$ peak at *m/z* 923, suggesting it to be a trioside. In the ^1H-NMR spectrum, the presence of a 16-*O*-acetyl group and H-16 (δ 5.68) in the aglycone moiety was observed along with 3′-*O*-methyl and 6′-methyl groups and three anomeric protons, of which one anomeric proton at δ 5.19 formed a doublet of doublets. The signals due to the sugar portion were in good agreement with those of echujin (digitoxigenin β-gentiobiosyl-β-D-cymaroside, **20**), and the aglycone was assignable as oleandrigenin from the ^{13}C-NMR spectrum. The structure of **21** was thus determined to be oleandrigenin β-gentiobiosyl-β-D-cymaroside and **21** was named honghelotrioside A. Compound **22** also showed the presence of the same sugar moiety as **20** and **21**, and the aglycone was identified as Δ^{16}-digitoxigenin based on the ^1H-NMR spectra and on the $[M+Na]^+$ peak at *m/z* 863. The structure was therefore determined to be Δ^{16}-echujin.

Compounds **23** and **24** were obtained as solids and afforded $[M-1]^-$ peaks at *m/z* 857 ($C_{42}H_{66}O_{18}$) and 915 ($C_{44}H_{68}O_{20}$), respectively, in the negative FAB-MS, 162 m.u. more than those of **12** and **13**, respectively. In the ^1H-NMR spectra, signals due to three anomeric protons of β-linked hexoses, and protons of one methoxyl and one *sec*-methyl groups of the sugar portions were observed at almost the same chemical shifts, suggesting that **23** and **24** have the same sugar moieties. Anomeric proton signals both observed at δ 4.72 in **23** and **24** were assignable to those of β-D-thevetosyl groups in comparison with those of **5** and **6**, and two others to those of gentiobiosyl units. The β-gentiobiosyl (1→4)-β-D-thevetosyl moiety was confirmed by examination of the ^{13}C-NMR spectra, and the structures of **23** and **24** were assigned as β-gentiobiosyl-β-D-thevetosides of digitoxigenin and oleandrigenin; these compounds were named obetriosides A and B, respectively.

Pregnanes obtained from the benzene extractives of the roots and the stems were identified as neridienone A (12β-hydroxypregna-4,6,16-triene-3,20-dione, **31**) and 16,17-dihydroneridienone A (**32**) based on NMR considerations and by comparison with authentic samples. Neridienone A was first isolated from the root bark of *Nerium odorum*[6] and then from *Anodendron affine*,[7] *Apocynum venetum* var. *basikurumon*[8] in Apocynaceae, and recently from *Periploca sepium*[9] in Asclepiadaceae.

The roots and the stems contain the same cardiac glycosides, with similar amounts in the two sources. Most of the known cardiac glycosides so far obtained from *Adenium* spp. are D-cymarosides, D-digitalosides, and their glucosides or gentiobiosides, except for digitoxigenin β-D-thevetoside (honghelin, **4**) from *A. honghel* A. DC.[1] In *A. obesum*, however, the main glycoside is oleandrigenin β-D-glucosyl-(1→4)-β-D-thevetoside, and oleandrigenin glycosides predominate over digitoxigenin glycosides.

The structures of **27**—**30** will be published elsewhere.

Experimental

Melting points were measured on a hot stage and are uncorrected. Specific rotations were measured with a JASCO DIP 360 polarimeter. ^1H- and ^{13}C-NMR spectra were recorded on a JEOL GX-400 spectrometer in pyridine-d_5. Chemical shifts are given in δ values referred to internal tetramethylsilane (TMS), and the following abbreviations are used: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = doublet of doublets, dt = doublet of triplets, br s = broad singlet, br d = broad doublet. The following solvent systems were used for silica gel column chromatographies and TLC: solvent 1, benzene–acetone; solvent 2, EtOAc–hexane; solvent 3, $CHCl_3$–MeOH–H_2O (bottom layer); solvent 4, EtOAc–MeOH–

H_2O (top layer); solvent 5, MeCN–H_2O. Detection of the spots was carried out by spraying diluted H_2SO_4 onto the TLC plates, followed by heating the plates. HPLC was carried out on a Waters ALC 200 equipped with Radial Pack C_{18} eluted with solvent 5.

Extraction and Isolation of Cardiac Glycosides Fresh roots (4.5 kg) and stems (3.0 kg) of *A. obesum* ROEM *et* SCHULT., purchased at a garden shop in Manila in October 1988, were homogenized separately with MeOH. The homogenized mixtures were then transferred into columns and eluted with MeOH. The MeOH percolates from the roots and the stems were concentrated to 5 l *in vacuo* and filtered. The filtrates were partitioned between benzene and $CHCl_3$. The MeOH in the water layers was evaporated *in vacuo* and the water layers were partitioned with BuOH.

The benzene extracts (4.9 g from roots; 1.9 g from stems) were then subjected to chromatographies on silica gel columns with solvent 1 (10:1—5:1), solvent 2 (3:1—1:1) and solvent 3 (7:1:1) to give compounds **5** (140 mg from roots; 90 mg from stems), **7** (2 mg, 15 mg), **27** (13 mg from roots), and **28** (50 mg from roots), along with neridienone A (**31**, mp 203—205 °C, 10 mg; 10 mg), 16,17-dihydroneridienone A (**32**, mp 164—165 °C, 10 mg; 10 mg), somalin (digitoxigenin β-D-cymaroside, **1**, mp 115—125 °C, 29 mg; 14 mg), hongheloside A (oleandrigenin β-D-cymaroside, **2**, mp 207—214 °C, 164 mg; 20 mg), Δ^{16}-somalin (**3**, 5 mg from roots) and honghelin (digitoxigenin β-D-thevetoside, **4**, 12 mg; 35 mg).

The $CHCl_3$ extracts (1.64 g from roots; 2.0 g from stems) were subjected to silica gel column chromatography with solvent 3 and HPLC to afford **6** (11 mg from roots), **13** (20 mg; 90 mg), along with 16-*O*-acetylstrospeside (**8**, 76 mg; 20 mg), strospeside (**9**, mp 252—253 °C, 32 mg from roots), hongheloside C (**11**, mp 159—162 °C, 40 mg; 45 mg), and oleandrigenin β-D-glucosyl(1→4)-β-D-digitaloside (16-*O*-acetyldigitalinum verum) (**17**, 33 mg; 328 mg).

The BuOH extracts (14.5 g from roots; 17.9 g from stems) were dissolved in H_2O and chromatographed on a polystyrene column (MCI gel, Mitsubishi Chem. Co.) with H_2O, 20%, 40%, 60% and 80% MeOH. The eluates with 60% and 80% MeOH were subjected to silica gel column chromatography with solvents 3 and 4, C_{18} column chromatography with solvent 5, and HPLC for some glycosides, finally affording **12** (245 mg; 57 mg), **13** (1.1 g; 1.16 g), **14** (15 mg from roots), **15** (16 mg; 24 mg), **21** (147 mg; 27 mg), **22** (10 mg from roots), **23** (2 mg, 9 mg), **24** (5 mg; 33 mg), **29** (30 mg; 25 mg) and **30** (240 mg; 65 mg), along with oleandrigenin glucoside (**10**, 12 mg; 23 mg), odorobioside G (**16**, 40 mg from roots), digitalinum verum (**18**, mp 245—247 °C, 62 mg from roots), Δ^{16}-digitalinum verum (**19**, mp 199—202 °C, 27 mg from roots), echujin (**20**, 184 mg; 20 mg), odoroside G (**25**, 80 mg; 17 mg), and oleandrigenin β-gentiobiosyl-β-D-digitaloside (16-*O*-acetylneogitostin) (**26**, 27 mg; 3 mg).

Obeside B (Oleandrigenin β-D-Thevetoside, 5) Prisms from MeOH, mp 198—200 °C, $[\alpha]_D^{28}$ −25.3° (*c*=0.50, MeOH). FAB-MS *m/z*: 615.314, Calcd for $C_{32}H_{48}NaO_{10}$: 615.314. ^{1}H-NMR δ: 0.83, 1.07 (3H each, s, H-18,19), 1.60 (3H, d, *J*=6 Hz, H-6′), 1.85 (3H, s, –OAc), 3.38 (1H, d, *J*=9 Hz, H-17), 3.61 (1H, t, *J*=8 Hz, H-3′), 3.64 (1H, dt, *J*=4, 8 Hz, H-4′), 3.71 (1H, m, H-5′), 3.89 (3H, s, 3′-OMe), 3.97 (1H, dt, *J*=5, 8 Hz, H-2′), 4.33 (1H, br s, H-3), 4.79 (1H, d, *J*=8 Hz, H-1′), 5.21, 5.40 (1H each, dd, *J*=18, 2 Hz, H-21a,b), 5.69 (1H, td, *J*=9, 2 Hz, H-16), 6.32 (1H, br s, H-22), 6.82 (1H, d, *J*=5 Hz, 2′-OH), 6.88 (1H, d, *J*=4 Hz, 4′-OH). After reflux of **5** (100 mg) with 3 ml of 0.7 N HCl in 30% dioxane for 3 h, the mixture was diluted with H_2O, and partitioned with BuOH. The H_2O layer was then de-acidified with IR-410A and the H_2O layer was concentrated *in vacuo*. The residue (13 mg) showed one spot, which was identical with that of authentic L-thevetose on TLC (solvent 3, 25:17:3). $[\alpha]_D^{27}$ +38.9° (*c*=0.65, H_2O) (lit. +35.5°).[10]

Obeside C (Gitoxigenin β-D-Thevetoside, 6) Solid, $[\alpha]_D^{28}$ +2.00° (*c*=0.30, MeOH). FAB-MS *m/z*: 573.305, Calcd for $C_{30}H_{46}NaO_9$: 573.304. ^{1}H-NMR δ: 0.84, 1.11 (3H each, s, H-18,19), 1.59 (3H, d, *J*=6 Hz, H-6′), 3.25 (1H, d, *J*=8 Hz, H-17), 3.61 (1H, t, *J*=8 Hz, H-3′), 3.65 (1H, t, *J*=8 Hz, H-4′), 3.72 (1H, m, H-5′), 3.89 (3H, s, 3′-OMe), 4.31 (1H, br s, H-3), 4.78 (1H, d, *J*=8 Hz, H-1′), 4.96 (1H, t, *J*=8 Hz, H-16), 5.52, 5.66 (1H each, dd, *J*=18, 2 Hz, H-21a,b), 6.23 (1H, br s, H-22).

Obeside D (Δ^{16}-Digitoxigenin β-D-Thevetoside, 7) Prisms from MeOH, mp 238—240 °C, $[\alpha]_D^{25}$ +50.3° (*c*=0.30, MeOH). FAB-MS *m/z*: 555.290, Calcd for $C_{30}H_{44}NaO_8$: 555.293. ^{1}H-NMR δ: 0.90, 1.47 (3H each, s, H-18,19), 1.60 (3H, d, *J*=6 Hz, H-6′), 2.51 (1H, dd, *J*=18, 3 Hz, H-15a), 2.74 (1H, br d, *J*=18 Hz, H-15b), 3.63 (1H, t, *J*=8 Hz, H-3′), 3.66 (1H, t, *J*=8 Hz, H-4′), 3.73 (1H, m, H-5′), 3.90 (3H, s, 3′-OMe), 3.99 (1H, t, *J*=8 Hz, H-2′), 4.35 (1H, br s, H-3), 4.80 (1H, d, *J*=8 Hz, H-1′), 4.82, 5.07 (1H each, d, *J*=16 Hz, H-21a,b), 6.16 (1H, br s, H-16), 6.27 (1H, br s, H-22).

Obebioside A (Digitoxigenin β-D-Glucosyl(1→4)-β-D-thevetoside, 12) Prisms from MeOH, mp 267—270 °C, $[\alpha]_D^{25}$ −2.9° (*c*=0.96, MeOH). FAB-MS *m/z*: 719.359, Calcd for $C_{36}H_{56}NaO_{13}$: 719.362. ^{1}H-NMR δ: 0.83, 1.00 (3H each, s, H-18,19), 1.76 (3H, d, *J*=6 Hz, H-6′), 2.79 (1H, dd, *J*=8, 6 Hz, H-17), 3.72 (1H, t, *J*=8 Hz, H-3′), 3.77 (1H, m, H-5′), 3.94 (3H, s, 3′-OMe), 4.27 (1H, br s, H-3), 4.33 (1H, dd, *J*=12, 5 Hz, H-6″a), 4.49 (1H, dd, *J*=12, 2 Hz, H-6″b), 4.71 (1H, d, *J*=8 Hz, H-1′), 5.13 (1H, d, *J*=8 Hz, H-1″), 5.01, 5.29 (1H each, dd, *J*=18, 1 Hz, H-21a,b), 6.12 (1H, br s, H-22).

Obebioside B (Oleandrigenin β-D-Glucosyl(1→4)-β-D-thevetoside, 13) Prisms from MeOH, mp 178—182 °C. $[\alpha]_D^{24}$ −15.0° (*c*=1.45, MeOH). *Anal.* Calcd for $C_{38}H_{58}O_{15}\cdot 3H_2O$: C, 56.42; H, 7.98. Found: C, 56.37; H, 7.98. FAB-MS *m/z*: 777 $[M+Na]^+$. ^{1}H-NMR δ: 0.83, 1.07 (3H, s, H-18,19), 1.76 (3H, d, *J*=6 Hz, H-6′), 1.85 (3H, s, –OAc), 3.37 (1H, d, *J*=9 Hz, H-17), 3.72 (1H, t, *J*=8 Hz, H-3′), 3.76 (1H, m, H-5′), 3.93 (3H, s, 3′-OMe), 4.27 (1H, br s, H-3), 4.32 (1H, dd, *J*=12, 5 Hz, H-6″a), 4.48 (1H, dd, *J*=12, 3 Hz, H-6″b), 4.71 (1H, d, *J*=8 Hz, H-1′), 5.12 (1H, d, *J*=8 Hz, H-1″), 5.21, 5.40 (1H each, dd, *J*=18, 1 Hz, H-21a,b), 5.68 (1H, td, *J*=9, 2 Hz, H-16), 6.32 (1H, br s, H-22).

Obebioside C (Gitoxigenin β-D-Glucosyl-(1→4)-β-D-thevetoside, 14) Solid, $[\alpha]_D^{23}$ +29.6° (*c*=0.84, MeOH). *Anal.* Calcd for $C_{36}H_{56}O_{14}\cdot H_2O$: C, 59.16; H, 8.00. Found: C, 59.16; H, 8.55. FAB-MS *m/z*: 735 $[M+Na]^+$. ^{1}H-NMR δ: 0.84, 1.11 (3H each, s, H-18,19), 1.76 (3H, d, *J*=6 Hz, H-6′), 3.25 (1H, d, *J*=8 Hz, H-17), 3.72 (1H, t, *J*=8 Hz, H-3′), 3.76 (1H, m, H-5′), 3.94 (3H, s, 3′-OMe), 4.25 (1H, br s, H-3), 4.34 (1H, dd, *J*=12, 5 Hz, H-6″a), 4.50 (1H, dd, *J*=12, 2 Hz, H-6″b), 4.71 (1H, d, *J*=8 Hz, H-1′), 4.95 (1H, dd, *J*=8, 7 Hz, H-16), 5.14 (1H, d, *J*=8 Hz, H-1″), 5.52, 5.65 (1H each, dd, *J*=18, 1 Hz, H-21a,b), 6.23 (1H, br s, H-22).

Obebioside D (Δ^{16}-Digitoxigenin β-D-Glucosyl(1→4)-β-D-thevetoside, 15) Prisms from MeOH, mp 227—230 °C, $[\alpha]_D^{25}$ −2.9° (*c*=0.96, MeOH). FAB-MS *m/z*: 717.346, Calcd for $C_{36}H_{54}NaO_{13}$: 717.346. ^{1}H-NMR δ: 0.90, 1.47 (3H each, s, H-18,19), 1.77 (3H, d, *J*=6 Hz, H-6′), 2.51 (1H, dd, *J*=17, 3 Hz, H-15a), 2.73 (1H, br d, *J*=17 Hz, H-15b), 3.74 (1H, t, *J*=8 Hz, H-3′), 3.77 (1H, m, H-5′), 3.95 (3H, s, 3′-OMe), 4.28 (1H, br s, H-3), 4.33 (1H, dd, *J*=12, 5 Hz, H-6″a), 4.50 (1H, dd, *J*=12, 3 Hz, H-6″b), 4.73 (1H, d, *J*=8 Hz, H-1′), 4.82, 5.07 (1H each, dd, *J*=16, 1 Hz, H-21a,b), 5.14 (1H, d, *J*=8 Hz, H-1″), 6.16 (1H, br s, H-16), 6.26 (1H, br s, H-22).

Honghelotrioside A (Oleandrigenin β-Gentiobiosyl-β-D-cymaroside, 21) Solid, $[\alpha]_D^{28}$ −12.7° (*c*=0.51, MeOH). *Anal.* Calcd for $C_{44}H_{68}O_{19}\cdot 3H_2O$: C, 55.33; H, 7.81. Found: C, 55.02; H, 7.79. FAB-MS *m/z*: 923 $[M+Na]^+$. ^{1}H-NMR δ: 0.89, 1.07 (3H each, s, H-18,19), 1.57 (3H, d, *J*=6 Hz, H-6′), 1.85 (3H, s, –OAc), 3.37 (1H, d, *J*=9 Hz, H-17), 3.63 (3H, s, 3′-OMe), 3.68 (1H, dd, *J*=8, 2 Hz, H-4′), 4.29 (1H, dd, *J*=11, 6 Hz, H-6″a), 4.36 (1H, dd, *J*=12, 5 Hz, H-6‴a), 4.45 (1H, q, *J*=2 Hz, H-3′), 4.52 (1H, dd, *J*=12, 2 Hz, H-6‴b), 4.83, 5.08 (1H each, d, *J*=8 Hz, H-1″,1‴), 4.89 (1H, br d, *J*=11 Hz, H-6″b), 5.19 (1H, dd, *J*=9, 1 Hz, H-1′), 5.22, 5.41 (1H each, dd, *J*=18, 1 Hz, H-21a,b), 5.68 (1H, td, *J*=9, 2 Hz, H-16), 6.32 (1H, br s, H-22).

Δ^{16}-Digitoxigenin β-Gentiobiosyl-β-D-cymaroside (22) Solid, $[\alpha]_D^{28}$ +60.0° (*c*=0.13, MeOH). FAB-MS *m/z*: 863 ($[M+Na]^+$, $C_{42}H_{64}NaO_{17}$). ^{1}H-NMR δ: 0.96, 1.48 (3H each, s, H-18,19), 1.58 (3H, d, *J*=6 Hz, H-6′), 2.51 (1H, dd, *J*=18, 3 Hz, H-15a), 2.72 (1H, br d, *J*=18 Hz, H-15b), 3.65 (3H, s, 3′-OMe), 3.69 (1H, dd, *J*=9, 2 Hz, H-4′), 4.30, 4.38 (1H each, dd, *J*=11, 6 Hz, H-6″,6‴a), 4.47 (1H, q, *J*=2 Hz, H-3′), 4.53, 4.91 (1H each, br d, *J*=11 Hz, H-6″,6‴b), 4.80, 5.08 (1H each, dd, *J*=16, 1 Hz, H-21a,b), 4.84, 5.09 (1H each, d, *J*=8 Hz, H-1″,1‴), 5.21 (1H, dd, *J*=10, 1 Hz, H-1′), 6.15 (1H, br s, H-16), 6.27 (1H, br s, H-22).

Obetrioside A (Digitoxigenin β-Gentiobiosyl(1→4)-β-D-thevetoside, 23) Solid, $[\alpha]_D^{26}$ −10.00° (*c*=0.10, MeOH). Negative FAB-MS *m/z*: 857 ($[M-1]^-$, $C_{42}H_{66}O_{18}-1$). ^{1}H-NMR δ: 0.84, 1.01 (3H each, s, H-18,19), 1.72 (3H, d, *J*=6 Hz, H-6′), 2.79 (1H, dd, *J*=8, 6 Hz, H-17), 3.96 (3H, s, 3′-OMe), 4.49, 4.80 (1H each, br d, *J*=11 Hz, H-6″,6‴b), 4.72, 5.06, 5.14 (1H each, d, *J*=8 Hz, H-1′,1″,1‴), 5.01, 5.29 (1H each, dd, *J*=18, 1 Hz, H-21a,b), 6.12 (1H, br s, H-22). ^{13}C-NMR: all signals due to the aglycone showed the same chemical shifts as in **25** and those for the sugar moiety as in **24** (Table I).

Obetrioside B (Oleandrigenin β-Gentiobiosyl(1→4)-β-D-thevetoside, 24) Solid, $[\alpha]_D^{26}$ −19.0° (*c*=0.80, MeOH). Negative FAB-MS *m/z*: 915 ($[M-1]^-$, $C_{44}H_{68}O_{20}-1$). ^{1}H-NMR δ: 0.83, 1.07 (3H each, s, H-18,19), 1.72 (3H, d, *J*=6 Hz, H-6′), 1.87 (3H, s, –OAc), 3.37 (1H, d, *J*=9 Hz, H-17), 3.96 (3H, s, 3′-OMe), 4.50, 4.81 (1H each, br d, *J*=11 Hz, H-6″,6‴b), 4.72, 5.05, 5.14 (1H each, d, *J*=8 Hz, H-1′,1″,1‴), 5.22, 5.40 (1H each, dd, *J*=18, 1 Hz, H-21a,b), 5.68 (1H, dt, *J*=2, 9 Hz, H-16), 6.32 (1H br s, H-22).

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