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STRUCTURES OF ELAEODENDROSIDES B, C, F, G, K and L, A SERIES OF CARDIAC GLYCOSIDES ISOLATED FROM *ELAEODENDRON GLAUCUM*

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Key Word Index—*Elaeodendron glaucum*; Celastraceae; seed; cardiac glycoside; doubly linked sugar; elaeodendroside.

Abstract—Six cardiac glycosides having an unusual sugar linkage, elaeodendrosides B, C, F, G, K and L, were isolated from seeds of *Elaeodendron glaucum*. These were characterized on the basis of the physical data and the results obtained by improved procedures for cleavage of their glycoside linkage.

INTRODUCTION

In the preceding papers we reported the isolation and characterization of cardiac steroids named elaeodendrosides A, D, E, H, I, J and elaeodendrogenin from seeds of *Elaeodendron glaucum* PERS. by X-ray crystallography and chemical means [1–5]. The present paper describes the structures of elaeodendrosides B, C, F, G, K and L which have been isolated by the procedure similar to that previously reported [1, 4].

RESULTS AND DISCUSSION

Elaeodendroside B (**1**) and elaeodendroside C (**3**) were isolated as colourless amorphous substances. A molecular formula $C_{29}H_{40}O_8$ was assigned to both compounds by means of high-resolution mass spectrometry and elemental analysis. These were stable for acid treatment and considerably resistant to periodate oxidation and enzymic hydrolysis. Comparison of their ^1H NMR and ^{13}C NMR spectra with those of elaeodendroside A [1], affinoside B [6], humistratin [7] and other related cardiac glycosides [8] strongly indicated that both **1** and **3** could be cardiac glycosides having an unusual double linkage at C-2 and C-3 (Figs. 1 and 2). On treatment with acetic anhydride and pyridine in a sealed tube for 8 days at 37°, the two compounds gave the monoacetates (**2**, **4**). Also, both were transformed into elaeodendrogenin acetate (**12**) in a reasonable yield when refluxed in acetic anhydride and pyridine. Compound **1** or **3** and phenylhydrazine in a 1:2.2 molar ratio were refluxed in ethanol containing sodium acetate to provide desacetylelaeodendrogenin (**10**) and the osazones (**14**). The osazones were optically active, exhibiting $[\alpha]_D^{14.5} + 15.9°$ and $[\alpha]_D^{14.5} - 16.4°$. After refluxed with sodium carbonate in aqueous methanol, both **1** and **3** were converted into the isocardanolide (**15**). In addition, **1** was transformed into 21,3′α-trideuterated elaeodendroside C when treated with CD_3OD–D_2O (10:1) in the presence of sodium carbonate at 60–70° for 1 hr. These results permitted us to assign the structures **1** and **3** to the two glycosides: the epimers involving the 3′-position but not the 1′-position [2, 3, 5]. In the ^1H NMR spectrum of **4**, the H-3′α signal appeared as a broad singlet, indicating the equatorial nature of the 3′-hydrogen. In contrast, the vicinal coupling (J = 11, 4 Hz) of H-3′β in the acetate (**2**) indicated that the 3′-hydrogen is axial in **1**. As for the ^1H NMR and ^{13}C NMR spectra of **3** and its 2′-acetate (**4**) (Tables 1 and 2), the proton and carbon resonances of the sugar moieties are consistent with those of elaeodendroside A, afroside [8], affinoside-A and -B [9] whose structures have been elucidated by chemical and physical means including X-ray crystallography. These data led us to assign the structure **3** to elaeodendroside C.

It has been mentioned above that configurations of the 1′-hydrogen and 3′-methoxyl group of elaeodendroside B are deduced to be β and α, respectively. Inspection of the ^{13}C NMR spectra of the four C-3′ epimeric pairs, gomphoside and 3′-epigomphoside, calactin and calotropin, afroside and 3′-epiafroside [8], affinoside-A and -M [9, 10], revealed the downfield shift (*ca* 2 ppm) of carbons 1′, 3′ and 5′ in the 3′-equatorial epimers. It has been reported that marked downfield shifts of H-1′ and H-3′ (1 ppm) in the ^1H NMR spectra take place upon acetylation of the 2′-hydroxyl group in 3′-epiafroside 3′-acetate, calotropin 3′-acetate and affinoside M. The similar phenomena were observed with the spectra of **1** and **2** (Tables 1 and 2). In the nuclear Overhauser effect (NOE) difference spectrum (300 MHz) of **2**, NOE was observed at H-5′β and H-3′β, but not at H-2β by irradiation of H-1′β. If the configuration of the 2′-hydroxyl group were α, NOE should be recognized between H-2β and H-1′β (see Fig. 3). These results lent a support to the assignment of the structure **1** to elaeodendroside B.

Elaeodendroside F (**5**) and elaeodendroside G (**6**) were isolated as colourless amorphous substances. A molecular formula $C_{31}H_{42}O_{10}$ was assigned to both compounds based upon the data of high-resolution mass spectrometry and elemental analysis. Compounds **5** and **6** were converted to each other when refluxed in pyridine in the

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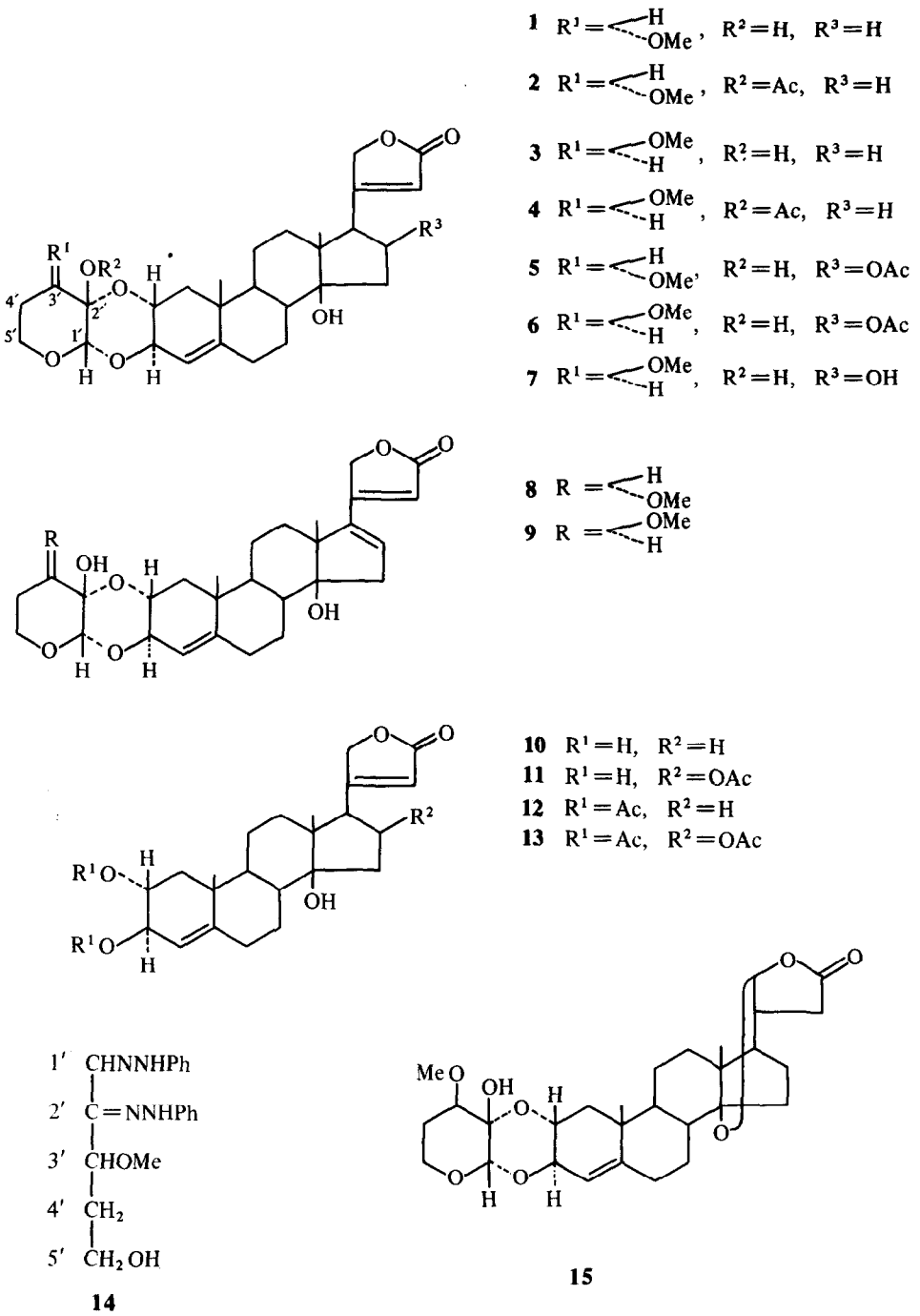
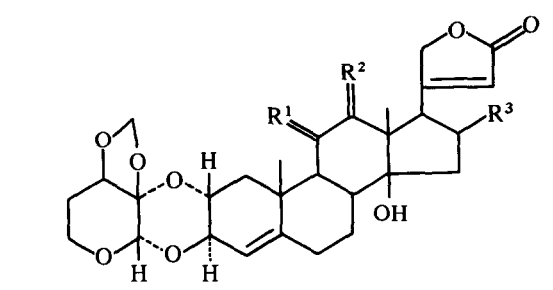


Fig. 1. Structures of elaeodendroside and related compounds.

manner reported for **1** and **3** [5]. Compounds **5** and **6** exhibited ^{1}H NMR signals at δ1.96 (3H, *s*, OAc), 2.6 (1H, *dd*, J = 16, 9 Hz, H-15α), 3.2 (1H, *d*, J = 9 Hz, H-17α) and 5.4 (1H, *t*, J = 9 Hz, H-16α). These data suggested the presence of an acetoxyl group at the 16β-position [11]. Hydrolysis of **6** with potassium hydrogen carbonate under mild conditions afforded desacetylelaeodendroside G (**7**) which in turn, was readily and quantitatively transformed into the cyclic phenylboronate. Treatment of **5** and **6** with phenylhydrazine in the manner described for elaeodendrosides B and C provided 16β-acetoxydesacetylelaeodendrogenin (**11**) and epimeric osazones (**14**). The chemical evidence together with ^{1}H NMR and ^{13}C NMR spectral data revealed that **5** and **6** are epimeric at C-3' whose relationship is similar to that of **1** and **3**. Being adsorbed on alumina in benzene at 60° for 5 hr, both **5** and **6** afforded 16-dehydroelaeodendroside C (**9**) and a small amount of 16-dehydroelaeodendroside B (**8**). The latter of these two compounds was easily converted to the former when refluxed in pyridine. Upon partial hydrogenation



elaeodendroside

A: $R^1 = \langle^{H}_{OH}$, $R^2 = O$, $R^3 = H$

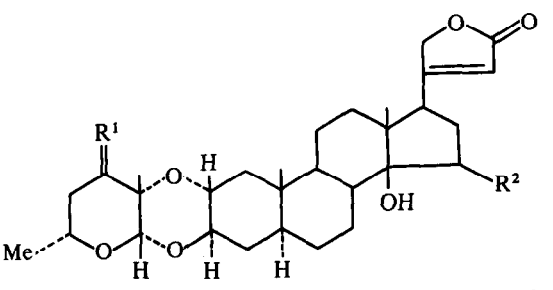
D: $R^1 = R^2 = H_2$, $R^3 = H$

E: $R^1 = R^2 = H_2$, $R^3 = OAc$

H: $R^1 = R^2 = H_2$, $R^3 = \Delta^{16}$

I: $R^1 = \langle^{H}_{OH}$, $R^2 = H_2$, $R^3 = H$

J: $R^1 = O$, $R^2 = \langle^{H}_{OH}$, $R^3 = H$

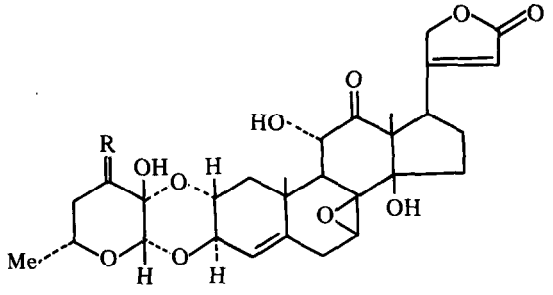


afroside: $R^1 = \langle^{OH}_{H}$, $R^2 = OH$

3′-epiafroside: $R^1 = \langle^{H}_{OH}$, $R^2 = OH$

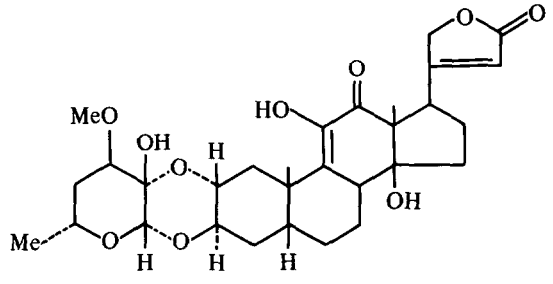
gomphoside: $R^1 = \langle^{OH}_{H}$, $R^2 = H$

3′-epigomphoside: $R^1 = \langle^{H}_{OH}$, $R^2 = H$



affinoside A: $R = \langle^{OMe}_{H}$

affinoside M: $R = \langle^{H}_{OMe}$



affinoside B

Fig. 2. Structures of cardiac glycosides having a doubly linked sugar.

over 5% Pd–C for 30 min, **8** provided 17α-elaeodendroside B together with a small amount of **1**. In similar fashion, catalytic hydrogenation of **9** gave 17α-elaeodendroside C besides a small amount of **3**. These results led us to assign the structures **5** and **6** to elaeodendrosides F and G, respectively.

Compounds **8** and **9** were also obtained from the natural source and named elaeodendroside K and L, respectively. Thus, the structures of elaeodendrosides B, C, F, G, K and L have been unambiguously established on the basis of chemical and physical data.

The cardiotonic activities of these glycosides are being investigated in our laboratories, and the details will be reported elsewhere in the near future.

EXPERIMENTAL

Mps are uncorr. ^{1}H NMR (100 MHz) and ^{13}C NMR (25.15 MHz) spectra were recorded with soln in $CDCl_3$ using TMS as internal standard, unless otherwise stated. TLC was carried out on silica gel HF_{254}. Alumina 90 was used for the elimination reaction.

Extractions of steroidal components. Seeds (5 kg) of *Elaeodendron glaucum* PERS. collected in India in March, 1975, were

Table 1. ^{1}H NMR spectra of cardiac glycosides having a doubly linked sugar (δ values in $CDCl_3$: J in Hz)

Compound	1′β-H	3′-H	5′α-H	5′β-H
Elaeodendroside A [1]	4.67 *s*	← 3.80 *m* →		
Elaeodendroside B (1)	4.55 (5.00)* *s*	3.30 *dd*; 11, 4	4.10 *d*; 9	3.55 *m*
2′-Acetylelaeodendroside B (2)	5.45 *s*	4.40 *dd*; 11, 4	4.05 *d*; 9	3.60 *m*
Elaeodendroside C (3)	4.62 (5.30)* *s*	3.38 *br s*	← 3.80 *m* →	
2′-Acetylelaeodendroside C (4)	4.70 *s*	4.32 *br s*	← 3.80 *m* →	
Afroside [8]	4.78 *s*	3.69 *t*; 3		*ca* 4.10
3′-Epiafroside [8]	4.60 *s*	3.65 *m*		*ca* 3.65 *m*
2′,3′-Diacetyl-3′-epiafroside [8]	5.55 *s*	5.85 *dd*; 6.5, 10.5		3.7–4.2 m
Affinoside A [9]	4.68 *s*	3.28 *br s*		
11,2′-Diacetylaffinoside A [9]	4.78 *s*	4.31 *br s*		
Affinoside B [9]	5.36* *s*	3.61* *br s*		

*In C_5D_5N.

Table 2. ^{13}C NMR spectra of cardiac glycosides having a doubly linked sugar (δ values in C_5H_5N)

Compound	2-C	3-C	1′-C	2′-C	3′-C	5′-C
Elaeodendroside B (1)	67.5 (67.8)*	70.9 (70.6)*	98.0 (96.5)*	93.5 (92.3)*	83.5 (82.4)*	62.5 (62.3)*
Elaeodendroside C (3)	67.9 (68.6)*	70.8 (70.2)*	96.5 (96.1)*	92.4 (90.7)*	81.0 (80.0)*	60.7 (60.1)*
Afroside [8]†	69.4	72.6	94.4	90.5	70.8	66.4
3′-Epiafroside [8]†	68.9	72.7	96.0	91.3	72.3	68.2
Affinoside A [9]	67.3	70.5	96.2	92.0	81.4	66.4
Affinoside B [9]	68.4	69.2	96.0	91.7	81.3	66.4

*In $CDCl_3$.
†In $CDCl_3$–CD_3OD.

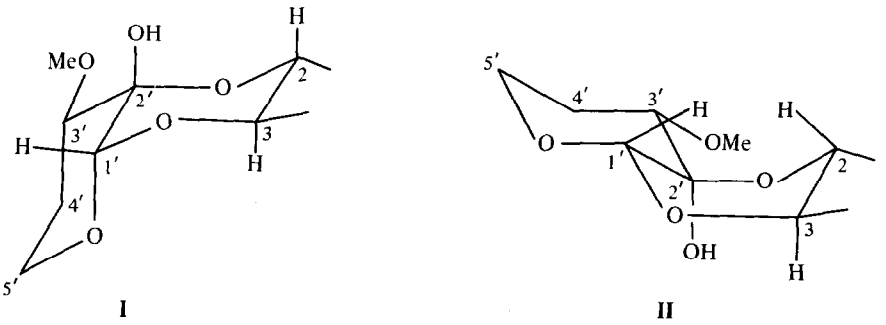


Fig. 3. Possible partial structures of elaeodendroside B.

extracted and purification of the extract as described before [1, 4] gave the following cardiac steroids.

Elaeodendroside B (1). (1 g), mp 252–257° (dec.), colourless amorphous substance (from MeOH–EtOAc). $[\alpha]_D^{26}$ +32.7° ($CHCl_3$; *c* 0.15). Found: C, 67.46; H, 7.68. $C_{29}H_{40}O_8$ requires: C, 67.42; H, 7.80%. CIMS (CH_4, probe) 70 eV *m/z*: 498.2597 [M − H_2O]$^+$, (Calc. for $C_{29}H_{38}O_7$, 498.2616). ^{1}H NMR (300 MHz, $CDCl_3$): δ0.89 (3H, *s*, Me-18), 1.12 (3H, *s*, Me-19), 2.75 (1H, *m*, H-17α), 3.30 (1H, *dd*, *J* = 11, 4 Hz, H-3′β), 3.47 (3H, *s*, OMe), 3.55 (1H, *m*, H-5′β), 4.10 (1H, *d*, *J* = 9 Hz, H-5′α), 4.38 (1H, *m*, H-2β), 4.55 (1H, *s*, H-1′β), 4.57 (1H, *d*, *J* = 9 Hz, H-3α), 4.90 (2H, *dd*, *J* = 18, 2 Hz, H_2-21), 5.20 (1H, *s*, H-4), 5.87 (1H, *br s*, H-22). ^{1}H NMR (C_5H_5N): δ0.85 (3H, *s*, Me-18), 1.00 (3H, *s*, Me-19), 3.60 (3H, *s*, OMe), 4.90 (1H, *d*, *J* = 10 Hz, H-3α), 5.00 (1H, *s*, H-1′β), 5.20 (2H, AB*q*, H_2-21), 5.38 (1H, *br s*, H-4), 6.15 (1H, *br s*, H-22). ^{13}C NMR: δ62.3 (*t*, C-5′), 67.8 (*d*, C-2), 70.6 (*d*, C-3), 82.4 (*d*, C-3′), 92.3 (*s*, C-2′), 96.5 (*d*, C-1′).

Elaeodendroside C (3). (145 mg), mp 233–236°, colourless amorphous substance (from MeOH–Et_2O). $[\alpha]_D^{21}$ +6.1° ($CHCl_3$; *c* 0.20). Found: C, 67.50; H. 7.81. $C_{29}H_{40}O_8$ requires: C, 67.42; H, 7.80%. CIMS, *m/z*: 517.2798 [M+H]$^+$, (Calc. for $C_{29}H_{41}O_8$ 517.2801). ^{1}H NMR: δ0.90 (3H, *s*, Me-18), 1.13 (3H, *s*, Me-19), 2.75 (1H, *m*, H-17α), 3.38 (1H, *br s*, H-3′α), 3.42 (3H, *s*, OMe), 3.80 (2H, *m*, H_2-5′), 4.20 (1H, *m*, H-2β), 4.50 (1H, *d*, *J* = 9 Hz, H-3α), 4.62 (1H, *s*, H-1′β), 4.89 (2H, *dd*, *J* = 18, 2 Hz, H_2-21), 5.22 (1H, *br s*, H-4), 5.88 (1H, *br s*, H-22). ^{1}H NMR (C_5D_5N): δ0.90 (3H, *s*, Me-18), 1.02 (3H, *s*, Me-19), 3.50 (3H, *s*, OMe), 3.70 (1H, *br s*, H-3′α), 3.95 (2H, *m*, H_2-5′), 5.30 (1H, *s*, H-1′β), 5.40 (1H,

br s, H-4), 6.10 (1H, *br s*, H-22). ^{13}C NMR: δ60.1 (*t*, C-5'), 68.6 (*d*, C-2), 70.2 (*d*, C-3), 80.0 (*d*, C-3') 90.7 (*s*, C-2'), 96.1 (*d*, C-1').

Elaeodendroside F (**5**). (150 mg), mp 182.7–185.1°, colourless amorphous substance (from C_6H_6–Et_2O–MeOH). $[\alpha]_D^{21}$ −33.3° ($CHCl_3$; *c* 0.23). Found: C, 64.79; H, 7.31. $C_{31}H_{42}O_{10}$ requires: C, 64.79; H, 7.37%. CIMS, *m/z*: 575.2838 $[M+H]^+$, (Calc. for $C_{31}H_{43}O_{10}$ 575.2856). ^{1}H NMR: δ0.95 (3H, *s*, Me-18), 1.12 (3H, *s*, Me-19), 1.96 (3H, *s*, OAc), 2.61 (1H, *dd*, *J* = 16, 9 Hz, H-15α), 3.16 (1H, *d*, *J* = 9 Hz, H-17α), 3.47 (2H, *m*, H-3'β, -5'β), 3.50 (3H, *s*, OMe), 4.00 (1H, *m*, H-5'α), 4.19 (1H, *m*, H-2β), 4.57 (1H, *d*, *J* = 9 Hz, H-3α), 4.57 (1H, *s*, H-1'β), 4.87 (2H, *br s*, H_2-21), 5.23 (1H, *br s*, H-4), 5.42 (1H, *t*, *J* = 9 Hz, H-16α), 5.98 (1H, *s*, H-22). ^{13}C NMR: δ62.2 (*t*, C-5'), 82.3 (*d*, C-3'), 92.3 (*s*, C-2'), 96.3 (*d*, C-1').

Elaeodendroside G (**6**). (147 mg), mp 173.7–174.4°, colourless amorphous substance (from C_6H_6–Et_2O–MeOH). $[\alpha]_D^{21}$ −29.3° ($CHCl_3$; *c* 0.22). Found: C, 64.68; H, 7.35. $C_{31}H_{42}O_{10}$ requires: C, 64.79; H, 7.37%. CIMS, *m/z*: 575.2940 $[M+H]^+$, (Calc. for $C_{31}H_{43}O_{10}$ 575.2856). ^{1}H NMR: δ0.96 (3H, *s*, Me-18), 1.13 (3H *s*, Me-19), 1.96 (3H, *s*, OAc), 2.60 (1H, *dd*, *J* = 16, 9 Hz, H-15α), 3.17 (1H, *d*, *J* = 9 Hz, H-17α), 3.35 (1H, *br s*, H-3'α), 3.40 (3H, *s*, OMe), 3.80 (2H, *m*, H_2-5'), 4.20 (1H, *m*, H-2β), 4.54 (1H, *d*, *J* = 8.3 Hz, H-3α), 4.66 (1H, *s*, H-1'β), 4.87 (2H, *br s*, H_2-21), 5.43 (1H, *t*, *J* = 9 Hz, H-16α), 5.98 (1H, *s*, H-22). ^{13}C NMR: δ60.1 (*t*, C-5'), 80.0 (*d*, C-3'), 90.8 (*s*, C-2'), 96.1 (*d*, C-1').

Elaeodendroside K (**8**). (25 mg), mp 248–250° (dec.), colourless needles (from MeOH–Et_2O). $[\alpha]_D^{25}$ −10.0° (MeOH–$CHCl_3$, 1:1, *c* 0.10). EIMS (probe) 40 eV, *m/z*: 514.2563 $[M]^+$, (Calc. for $C_{29}H_{38}O_8$ 514.2567). ^{1}H NMR: δ1.15 (3H, *s*, Me-19), 1.30 (3H, *s*, Me-18), 3.50 (2H, *m*, H-3'β, -5'β), 3.50 (3H, *s*, OMe), 4.15 (2H, *m*, H-2β, -5'α), 4.50 (1H, *d*, *J* = 8.3 Hz, H-3α), 4.50 (1H, *s*, H-1'β), 4.95 (2H, *br s*, H_2-21), 5.20 (1H, *br s*, H-4), 5.98 (1H, *br s*, H-22), 6.10 (1H, *br s*, H-16).

Elaeodendroside L (**9**). (10 mg), mp 248–254° (dec.), colourless leaflets (from MeOH). $[\alpha]_D^{25}$ +67.8° ($CHCl_3$; *c* 0.12). EIMS, *m/z*: 514.2553 $[M]^+$, (Calc. for $C_{29}H_{38}O_8$ 514.2565). ^{1}H NMR: δ1.18 (3H, *s*, Me-19), 1.30 (3H, *s*, Me-18), 3.40 (1H, *br s*, H-3'α), 3.50 (3H, *s*, OMe), 3.80 (2H, *m*, H_2-5'), 4.20 (1H, *m*, H-2β), 4.45 (1H, *d*, *J* = 8 Hz, H-3α), 4.62 (1H, *s*, H-1'β), 5.00 (2H, *s*, H_2-21), 5.20 (1H, *br s*, H-4), 5.95 (1H, *br s*, H-22), 6.18 (1H, *br s*, H-16).

Preparation of elaeodendroside B and C acetates (**2**, **4**). Compound **1** (50 mg) dissolved in Ac_2O–pyridine (1:1; 2 ml) was sealed under N_2 gas stream and allowed at 37° for 8 days. The reaction mixture was treated in the usual manner and purified on preparative TLC using C_6H_6–EtOAc (2:1) as the developing solvent. Elution of the adsorbent corresponding to the spot of R_f 0.50 with EtOAc and recrystallization of the dried eluate from MeOH–Et_2O gave elaeodendroside B acetate (**2**) (10 mg) as a colorless amorphous substance, mp 209–211°. ^{1}H NMR (300 MHz, $CDCl_3$): δ2.15 (3H, *s*, OAc), 3.60 (1H, *m*, H-5'β), 4.05 (1H, *d*, *J* = 9 Hz, H-5'α), 4.20 (1H, *m*, H-2β), 4.40 (1H, *dd*, *J* = 11, 4 Hz, H-3'β), 4.55 (1H, *d*, *J* = 10 Hz, H-3α), 5.45 (1H, *s*, H-1'β). ^{13}C NMR: δ61.9 (*t*, C-5'), 69.2 or 69.7 (*d*, C-2 or -3), 76.5 (*d*, C-3'), 93.3 (*d*, C-1'), 101.5 (*s*, C-2'), 170.4 (*s*, OAc). Compound **3** (50 mg) was treated with Ac_2O–pyridine as described above. The reaction mixture was treated in the usual manner and purified on preparative TLC using C_6H_6–EtOAc (2:1) as the developing solvent. Elution of the adsorbent corresponding to the spot of R_f 0.64 with EtOAc and evaporation of the solvent gave elaeodendroside C acetate (**4**) (10 mg) as a colourless oily substance. ^{1}H NMR: δ2.10 (3H, *s*, OAc), 3.80 (2H, *m*, H_2-5'), 3.90 (1H, *m*, H-2β), 4.32 (1H, *br s*, H-3'α), 4.60 (1H, *d*, *J* = 10 Hz, H-3α), 4.70 (1H, *s*, H-1'β). ^{13}C NMR: δ60.2 (*t*, C-5'), 69.5 or 69.6 (*d*, C-2 or -3), 76.2 (*d*, C-3'), 93.8 (*d*, C-1'), 97.2 (*s*, C-2'), 169.4 (*s*, OAc). Compound **2** or **4** (8 mg) in MeOH (2 ml) was treated with satd aq. $KHCO_3$ soln (1 ml) at room temp for 10 hr. Reaction mixtures were extracted with EtOAc, which was washed with H_2O, dried over dry Na_2SO_4 and then evaporated down *in vacuo*. The obtained residue was recrystallized from MeOH–EtOAc or MeOH–Et_2O to give elaeodendroside B (5 ml) or C (2 mg), which was identical with the authentic sample.

Degradation of elaeodendroside B (**1**) *and C* (**3**). (i) Pyridine–Ac_2O method: Compound **1** or **3** (20 mg) dissolved in pyridine–Ac_2O (1:1; 4 ml) was refluxed for 1 hr. After evaporation of the solvent under N_2 gas stream, the residue was subjected to preparative TLC using Me_2CO–$CHCl_3$ (1:4) as the developing solvent. Elution of the adsorbent corresponding to the spot of R_f 0.25 with EtOAc and evaporation of the solvent gave elaeodendrogenin acetate (**12**) (9 mg) as colorless leaflets (from Et_2O), mp 225–230° [4].

(ii) Phenylhydrazine method: Phenylhydrazine·HCl (10 mg; more than 2.2 mole) and NaOAc (15 mg) were added to a soln of glycoside (10 mg) in 50% EtOH (4 ml), and the whole was refluxed for 1.5 hr. The reaction mixture was extracted with EtOAc, which was washed with H_2O and then dried over dry Na_2SO_4. After evaporation of the solvent, the residue was subjected to preparative TLC using C_6H_6–EtOAc (1:1) as the developing solvent. Elution of the adsorbent corresponding to the spot of R_f 0.50 with EtOAc and evaporation of the solvent gave the osazone (**14**) (7 mg). From compound **1**: mp 138–140° (from MeOH–Et_2O). $[\alpha]_D^{14.5}$ +15.9° ($CHCl_3$; *c* 0.18). From compound **3**: mp 134–137° (from MeOH–Et_2O). $[\alpha]_D^{14.5}$ −16.4° ($CHCl_3$; *c* 0.34). ^{1}H NMR: δ1.50–2.20 (2H, *m*, H_2-4'), 3.33 (3H, *s*, OMe), 3.80 (2H, *m*, H_2-5'), 4.18 (1H, *dd*, *J* = 10, 5 Hz, H-3'), 6.80–7.45 (10H, *m*, aromatic H), 7.54 (1H, *s*, H-1'), 7.88 (1H, *s*, NH). Elution of the adsorbent corresponding to the spot of R_f 0.10 with EtOAc and evaporation of the solvent gave desacetylelaeodendrogenin (**10**) (3 mg) as colorless prisms (from MeOH), mp 262–266° [4].

Transformation of elaeodendrosides B (**1**) *and C* (**3**) *to isocardanolide* (**15**). Compound **1** or **3** (10 mg) in MeOH–H_2O (10:1; 2 ml) satd with Na_2CO_3 was refluxed for 1.5 hr. The reaction mixture was extracted with EtOAc, which was washed with 5% HCl, H_2O, dried over dry Na_2SO_4, and evaporated down. The residue obtained was subjected to preparative TLC using C_6H_6–EtOAc (1:1) as the developing solvent. Elution of the adsorbent corresponding to the spot of R_f 0.40 with EtOAc and recrystallization of the dried eluate from CH_2Cl_2–Me_2CO gave isocardanolide **15** (2 mg) as colourless prisms, mp 263–265°. $[\alpha]_D^{22}$ −38.5° ($CHCl_3$–MeOH, 2:3; *c* 0.13). Found: C, 66.46; H, 7.41. $C_{29}H_{40}O_8 \cdot 1/2H_2O$ requires: C, 66.26; H, 7.86%. CIMS, *m/z*: 517.2798 $[M+H]^+$, (Calc. for $C_{29}H_{41}O_8$ 517.2801). ^{1}H NMR: δ1.02 (3H, *s*, Me-18), 1.12 (3H, *s*, Me-19), 2.2–3.0 (3H, *m*, H-20, H_2-22), 3.35 (1H, *br s*, H-3'α), 3.40 (3H, *s*, OMe), 3.80 (2H, *m*, H_2-5'), 4.20 (1H, *m*, H-2β), 4.50 (1H, *d*, *J* = 10 Hz, H-3α), 4.70 (1H, *s*, H-1'β), 5.20 (1H, *br s*, H-4), 5.85 (1H, *d*, *J* = 5 Hz, H-21).

Transformation of elaeodendroside B (**1**) *to 21,3'α-trideuterated elaeodendroside C*. Dry Na_2CO_3 (5 mg) was added to a soln of **1** (10 mg) in CD_3OD–D_2O (10:1; 1.1 ml), and the whole was warmed at 60–70° for 1 hr. The reaction mixture was extracted with EtOAc, which was washed with H_2O, dried over dry Na_2SO_4 and evaporated down *in vacuo*. The residue was subjected to preparative TLC using C_6H_6–EtOAc (1:1) as a developing solvent. Elution of the adsorbent corresponding to the spot of R_f 0.40 and evaporation of the solvent gave 21,3'α-trideuterated elaeodendroside C (5 mg) as a colourless amorphous substance. ^{1}H NMR spectrum of the product showed no peak corresponding to H-3'α and H_2-21.

Hydrolysis of elaeodendroside G (**6**) *and its transformation to cyclic phenylboronate*. Compound **6** (10 mg) in MeOH (1 ml) was added to a soln of $KHCO_3$ (100 mg) in H_2O (2.5 ml) and the

mixture was allowed to stand at room temp for 12 hr. The reaction mixture was extracted with EtOAc, which was washed with H_2O, dried over dry Na_2SO_4, and evaporated down *in vacuo*. The residue, desacetylelaeodendroside G (**7**; oily substance), showed the following spectrum. ^{1}H NMR ($CDCl_3$–CD_3OD): δ0.96 (3H, *s*, Me-18), 1.13 (3H, *s*, Me-19), 2.98 (1H, *d*, J = 7 Hz, H-17α), 3.40 (3H, *s*, OMe), 3.78 (2H, *m*, H_2-5'), 4.20 (1H, *m*, H-2β), 4.50 (2H, *m*, H-3α, -16α), 4.68 (1H, *s*, H-1'β), 5.04 (2H, *br s*, H_2-21), 5.16 (1H, *br s*, H-4), 5.92 (1H, *br s*, H-22). Phenylboric acid (10 mg) was added to a soln of **7** (5 mg) in dry Me_2CO (1 ml), and the mixture was allowed to stand at room temp for 30 min. After removal of the solvent by evaporation, the residue obtained was subjected to preparative TLC using C_6H_6–EtOAc (1:1) as the developing solvent. Elution of the adsorbent corresponding to the spot of R_f 0.40 with EtOAc and evaporation of the solvent gave cyclic phenylboronate (5 mg) as colourless prisms. ^{1}H NMR: δ0.98 (3H, *s*, Me-18), 1.20 (3H, *s*, Me-19), 2.86 (1H, *d*, J = 4 Hz, H-17α), 3.35 (1H, *s*, H-3'α), 3.42 (3H, *s*, OMe), 3.78 (2H, *br s*, CH_2-5'), 4.22 (1H, *m*, H-2β), 4.55 (1H, *m*, H-3α), 4.60 (1H, *m*, H-16α), 4.66 (1H, *s*, H-1'β), 4.90 (2H, *br s*, H_2-21), 5.22 (1H, *br s*, H-4), 6.00 (1H, *br s*, H-22), 7.3–8.3 (5H, *m*, aromatic H).

Degradation of elaeodendrosides F (**5**) *and G* (**6**). (i) Pyridine–Ac_2O method: Compound **5** or **6** (10 mg) dissolved in pyridine–Ac_2O was refluxed for 2 hr as described above. After usual work-up, the residue obtained was subjected to preparative TLC using C_6H_6–EtOAc (1:1) as the developing solvent. Elution of the adsorbent corresponding to the spot of R_f 0.50 with EtOAc and recrystallization of the dried eluate from Et_2O gave 16β-acetoxyelaeodendrogenin acetate (**13**) (3 mg) as colourless needles, mp 220–222°. $[\alpha]_D^{18.0}$ – 86.0° ($CHCl_3$; *c* 0.03). Found: C, 64.74; H, 7.13. $C_{29}H_{38}O_9 \cdot 1/2H_2O$ requires: C, 64.55; H, 7.29%. ^{1}H NMR: δ0.96 (3H, *s*, Me-18), 1.16 (3H, *s*, Me-19), 1.94 (3H, *s*, OAc-16β), 1.99 and 2.01 (each 3H, each *s*, OAc-2α or -3β), 3.16 (1H, *d*, J = 9 Hz, H-17α), 4.85 (2H, *br s*, H_2-21), 5.13 (2H, *m*, H-4, -2β), 5.40 (2H, *m*, H-3α, -16α), 5.96 (1H, *br s*, H-22).

(ii) Phenylhydrazine method: Compound **5** or **6** (20 mg) in EtOH (2 ml) was treated with phenylhydrazine·HCl as described above. After usual work-up, the residue obtained was subjected to preparative TLC using C_6H_6–EtOAc (2:1 and then 1:1) as a developing solvent. Elution of the adsorbent corresponding to the spot of R_f 0.50 with EtOAc and evaporation of the solvent gave the osazone (**14**) (7 mg). From compound **5**: mp 138–140° (from MeOH–Et_2O). $[\alpha]_D^{18.5}$ + 20.0° ($CHCl_3$; *c* 0.18). From compound **6**: mp 136–139° (from MeOH–Et_2O). $[\alpha]_D^{16}$ – 24.5° ($CHCl_3$; *c* 0.12). These were identical with those obtained from **1** and **3**, respectively. Elution of the adsorbent corresponding to the spot of R_f 0.15 with EtOAc and evaporation of the solvent gave 16β-acetoxydesacetylelaeodendrogenin (**11**) (5 mg) as a colourless amorphous substance. ^{1}H NMR: δ0.97 (3H, *s*, Me-18), 1.10 (3H, *s*, Me-19), 1.96 (3H, *s*, OAc-16β), 3.15 (1H, *d*, J = 9 Hz, H-17α), 3.64 (1H, *m*, H-2β), 3.98 (1H, *d*, J = 7 Hz, H-3α), 4.84 (2H, *br s*, H_2-21), 5.16 (1H, *br s*, H-4), 5.38 (1H, *t*, J = 9 Hz, H-16α), 5.96 (1H, *br s*, H-22). Treatment of **11** with Ac_2O and pyridine in the usual manner gave **13**, which was identical with the authentic sample.

Epimerization of elaeodendrosides F (**5**) *and G* (**6**). Compound **5** or **6** (10 mg) was refluxed in pyridine (1 ml) for 19 hr. The solvent was evaporated down *in vacuo* and the residue was subjected to preparative TLC using C_6H_6–EtOAc (1:2) as a developing solvent. Elution of the adsorbent corresponding to the spot of R_f 0.50 (from **5**) or R_f 0.29 (from **6**) and evaporation of the solvent gave **6** (2 mg: from **5**) or **5** (1 mg: from **6**) as colorless amorphous substances, which was identical with authentic samples. Elution of the adsorbent corresponding to the spot of R_f 0.15 and evaporation of the solvent gave **11** (1 mg) as a colorless oily substance. Compound **11** was transformed into the acetate (**13**) in the usual manner and identified with the authentic sample.

Transformation of elaeodendrosides F (**5**) *and G* (**6**) *to elaeodendrosides K* (**8**) *and L* (**9**). Compound **5** or **6** (10 mg) suspended in C_6H_6 (1 ml) was treated with Al_2O_3 (1 g) at 60° for 10 hr. Elution of the adsorbent with MeOH–EtOAc (1:1) and evaporation of the solvent gave the residue (10 mg), which was subjected to preparative TLC using C_6H_6–EtOAc (4:1) as the developing solvent. Elution of the adsorbent corresponding to the spot of R_f 0.50 with EtOAc and evaporation of the solvent gave **9** (5 mg) as a colorless amorphous substance, which was identical with the sample obtained from the natural source. Elution of the adsorbent corresponding to the spot of R_f 0.30 with EtOAc and evaporation of the solvent gave **8** (2 mg) as a colourless amorphous substance, which was identical with the sample obtained from the natural source.

Transformation of elaeodendrosides K (**8**) *and L* (**9**) *to elaeodendrosides B* (**1**) *and C* (**3**). Compound **8** or **9** (10 mg) dissolved in EtOH (2 ml) was stirred with 5% Pd–C (10 mg) under H_2 gas stream for 30 min. After usual work-up the residue obtained was subjected to preparative TLC using C_6H_6–EtOAc (1:1) as a developing solvent. The adsorbent corresponding to the spot of R_f 0.20 (from **8**) or R_f 0.30 (from **9**) was eluted with EtOAc and evaporation of the solvent gave **1** or **3** (1 mg) as a colorless amorphous substance, which was identical with the sample from the natural source.

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