Constituents of Fevillea cordifolia: New Norcucurbitacin and Cucurbitacin Glycosides

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J. Nat. Prod., **1993**, 56 (9), 1506-1519• DOI: 10.1021/np50099a009 • Publication Date (Web): 01 July 2004

Journal of Natural Products
Vol. 56, No. 9, pp. 1506-1519, September 1993

CONSTITUENTS OF *FEVILLEA CORDIFOLIA*: NEW NORCUCURBITACIN AND CUCURBITACIN GLYCOSIDES[1]

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ABSTRACT.—The seeds of *Fevillea cordifolia* have yielded 11 new fevicordin-type 29-norcucurbitacins **3–13**, and two new cucurbitacin glycosides **14** and **15**, which were isolated along with previous reported fevicordin A [**2**] and its glucoside [**1**]. Structure determinations are based on spectroscopic studies and on chemical interconversions.

Fevillea cordifolia L. (Cucurbitaceae) grows in South and Central America and on Caribbean islands. The seeds are used in folk medicine against various diseases (1–3). The fatty material of the seeds has been used commercially (4).

Recently we described the isolation of fevicordin A glucoside [**1**] and its aglycone **2** from the seeds of the Costa Rican *F. cordifolia* (1). Compound **1** constitutes about 15% of the MeOH extract of the endosperm, and it represents the first member of the previously unknown norcucurbitanes. Meanwhile we gave a preliminary report on a number of structurally related minor constituents of *F. cordifolia* (5), and we have also analyzed the fatty material of the endosperm (6). This report describes the structure work on **1** in detail and the isolation and structure determination of the further fevicordin-type compounds **3–13** and the new cucurbitacin glycosides **14** and **15**, which are minor components of the seeds.

RESULTS

A series of chromatographic separations of the MeOH extract from defatted endosperm of seeds of *F. cordifolia* afforded a series of new compounds **3–12**, **14**, and **15**, and the main constituent **1** (1).

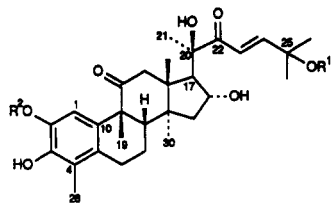
Extensive nmr studies with **1**, including homo- and heteronuclear COSY measurements, resulted in the assignment of all ^{1}H- and ^{13}C-nmr signals (Tables 1 and 2). The most important long-range ^{1}H/^{13}C couplings of **1** are depicted in Figure 1.

The position of the acetyl group at C-25 followed from comparison of the ^{13}C-nmr spectra of **1** and cucurbitacin E (8).

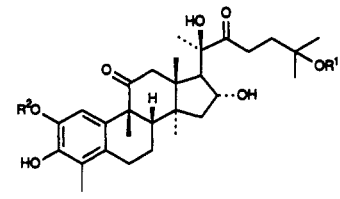
A selective INEPT experiment (9) was performed to discriminate between the similar resonances of C-2 and C-3. Irradiation at the frequency of the protons of the Me group at C-4 corroborated the assignment of C-3. Subsequent irradiation at the anomeric proton allowed us to establish the position of the glycosidic linkage unambiguously at C-2. The nature of the sugar followed from the shifts of the ^{1}H-nmr signals on acetylation and their typical coupling constants. The coupling constant of the anomeric proton revealed the β-glucosidic configuration. Acid hydrolysis of **1** gave glucose, which was proven to belong to the D series by gc analysis on cyclodextrin (10). Compound **1** on treatment with cellulase yielded glucose and fevicordin A [**2**], whereas cleavage with β-glucosidase occurred only very slowly. Compound **2** was also found among the components of the CH_2Cl_2 extract from the seeds.

Compound **2** was easily dehydrogenated by DDQ, or even by air, to yield the yellow-

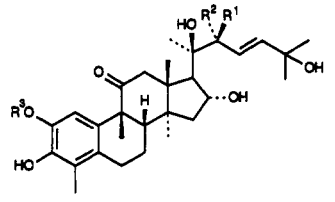
[1]Part 59 in the series "Constituents of Tropical Medicinal Plants." For part 58, see H. Achenbach and M. Löwel, *Planta Med.*, **59**, 388 (1993).



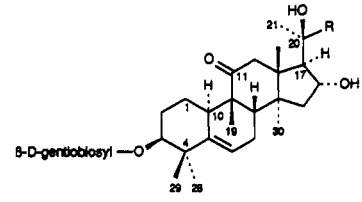
1 R^1=Ac, R^2=β-D-glucopyranosyl
2 R^1=Ac, R^2=H
4 R^1=H, R^2=β-D-glucopyranosyl
7 R^1=Ac, R^2=β-D-gentiobiosyl
9 R^1=H, R^2=β-D-gentiobiosyl

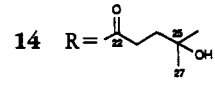


3 R^1=Ac, R^2=β-D-glucopyranosyl
13 R^1=Ac, R^2=H
5 R^1=H, R^2=β-D-glucopyranosyl
8 R^1=Ac, R^2=β-D-gentiobiosyl
10 R^1=H, R^2=β-D-gentiobiosyl

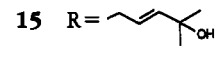


6 R^1=R^2=H, R^3=β-D-glucopyranosyl
11 R^1=R^2=H, R^3=β-D-gentiobiosyl
12 R^1=OH, R^2=H, R^3=β-D-gentiobiosyl





14 R=



15 R=

colored 6,7-dehydro-*o*-quinone **17**. The catechol system could be reconstituted by treatment of **17** with ascorbic acid, and ascorbic acid can also be used as an antioxidant to protect **2**.

The relative configuration of **1** resulted from nOe studies on fevicordin A 2,3-dimethyl ether [**16**] (Figure 2).

Fevicordin B glucoside [**3**] was detected as a minor component accompanying **1**; it was enriched in the mother liquors from repeated recrystallizations of **1** and was purified by hplc. The spectra revealed **3** as the 23,24-dihydro derivative of **1**, and this was proven by hydrogenation of **1** (Scheme 1).

The structures of fevicordin C glucoside [**4**] and fevicordin D glucoside [**5**] as desacetyl derivatives of **1** and **3** were also determined from their spectra and were corroborated by alkaline cleavage of **1** to yield **4**, and **3** to yield **5**.

The nmr spectra of fevicordin E glucoside [**6**] exhibited all resonances of glucose and the basic tetracyclic ring system of the fevicordins, but the spectra significantly differed in the signals of the side chain at C-17. An HMBC spectrum (11) revealed the structure, and chemical relationship with **5** was confirmed via the key compound **18** according to Scheme 1.

Compounds **7–12**, **14**, and **15** were isolated from a more polar fraction. The ^{1}H- and ^{13}C-nmr signals revealed **7–12** as fevicordin gentiobiosides. The structure details of the aglycones again were determined from the nmr spectra and showed **7–11** to be the gentiobiosides of fevicordins A–E. Consequently, **7** was treated with β-glucosidase to yield **1** and D-glucose besides small amounts of **2**.

However, the aglycone of gentiobioside **12** proved to be different from the others in the side chain at C-17: Long-range correlations observed by HMBC (Figure 3) established a 1,4-dihydroxy-4-methyl-2-pentenyl moiety formed by C-22 to C-27.

TABLE 1. ^{1}H-nmr Data of the Fevicordin Glycosides **1** and **3–12** (in CD_3OD, ppm, J in Hz).

Proton	Compound				
	1	**3**	**4**	**5**	**6**
H-1	6.66 s	6.65 s	6.66 s	6.67 s	6.66 s
H_a-6	2.84 ddd J=18.0,9.0,9.0	2.81 ddd J=18.0,9.0,9.0	2.84 ddd J=18.0,9.0,9.0	2.84 ddd J=18.0,9.0,9.0	2.85 ddd J=18.0,9.0,9.0
H_b-6	2.64 brdd J=18.0,9.0	2.66 brdd J=18.0,9.0	2.64 brdd J=18.0,9.0	2.64 brdd J=18.0,9.0	2.66 brdd J=18.0,9.0
H_a-7	2.26 dddd J=15.0,9.0, 9.0,7.0	2.24 dddd J=15.0,9.0, 9.0,7.0	2.25 dddd J=15.0,9.0, 9.0,7.0	2.25 dddd J=15.0,9.0, 9.0,7.0	2.27 dddd J=15.0,9.0, 9.0,7.0
H_b-7	[a]	[a]	[a]	[a]	1.98 brdd J=15.0,9.0
H-8	2.12 brd J=7.0	2.12 brd J=7.0	2.12 brd J=7.0	2.12 brd J=7.0	2.13 brd J=7.0
H_a-12	2.88 d J=14.5	2.90 d J=14.5	2.90 d J=14.5	2.91 d J=14.5	2.76 d J=14.5
H_b-12	2.62 d J=14.5	2.61 d J=14.5	2.64 d J=14.5	2.65 d J=14.5	2.56 d J=14.5
H_a-15	[a]	[a]	[a]	[a]	1.99 dd J=13.5,7.5
H_b-15	1.49 brd J=13.5	1.48 brd J=13.5	1.48 brd J=13.5	1.48 brd J=13.5	1.58 brd J=13.5
H-16	4.53 brdd J=7.5,7.0	4.42 brdd J=7.5,7.0	4.45 brdd J=7.5,7.0	4.41 brdd J=7.5,7.0	4.58 brdd J=7.5,7.0
H-17	2.49 d J=7.0	2.47 d J=7.0	2.53 d J=7.0	2.51 d J=7.0	2.16 d J=7.0
Me-18	0.91 s (3H)	0.92 s (3H)	0.94 s (3H)	0.95 s (3H)	0.95 s (3H)
Me-19	1.30 s (3H)	1.29 s (3H)	1.30 s (3H)	1.30 s (3H)	1.30 s (3H)
Me-21	1.36 s (3H)	1.34 s (3H)	1.35 s (3H)	1.36 s (3H)	1.22 s (3H)
H_a-22	—	—	—	—	2.39 dd J=15.0,6.5
H_b-22	—	—	—	—	2.29 dd J=15.0,6.5
H_a-23	6.80 d J=15.5	2.79 ddd J=18.0,10.0,6.0	6.78 d J=15.5	2.84 ddd J=18.0,10.0,6.0	5.70 ddd J=15.5,6.5,6.5
H_b-23		2.69 ddd J=18.0,10.0,6.0		2.70 ddd J=18.0,10.0,6.0	
H_a-24	6.98 d J=15.5	[a]	6.94 d J=15.5	1.74 ddd J=14.0,10.0,6.0	5.63 d J=15.5
H_b-24		[a]		1.68 ddd J=14.0,10.0,6.0	
Me-26	1.53 s (3H)	1.41 s (3H)	1.28 s (3H)	1.17 s (3H)	1.23 s (3H)
Me-27	1.53 s (3H)	1.41 s (3H)	1.28 s (3H)	1.17 s (3H)	1.23 s (3H)
Me-28	2.08 s (3H)	2.08 s (3H)	2.08 s (3H)	2.08 s (3H)	2.08 s (3H)
Me-30	0.99 s (3H)	0.99 s (3H)	1.00 s (3H)	1.00 s (3H)	1.00 s (3H)
Me-CO_2	1.98 s (3H)	1.90 s (3H)	—	—	—
H-1′	4.56 d J=7.5	4.56 d J=7.5	4.54 d J=7.5	4.58 d J=7.5	4.54 d J=7.5
H-2′ H-3′ H-4′	3.5–3.4	3.5–3.4	3.5–3.4	3.5–3.4	3.5–3.4
H-5′	3.32 ddd J=9.0,4.0,2.5	3.32 ddd J=9.0,4.0,2.5	3.32 ddd J=9.0,4.0,2.5	3.34 ddd J=9.0,4.0,2.5	3.33 ddd J=9.0,4.0,2.5
H_a-6′	3.96 dd J=12.0,2.5	3.95 dd J=12.0,2.5	3.96 dd J=12.0,2.5	3.97 dd J=12.0,2.5	3.95 dd J=12.0,2.5
H_b-6′	3.83 dd J=12.0,4.0	3.82 dd J=12.0,4.0	3.82 dd J=12.0,4.0	3.84 dd J=12.0,4.0	3.82 dd J=12.0,4.0
H-1″	—	—	—	—	—
H-2″	—	—	—	—	—
H-3″	—	—	—	—	—
H-4″	—	—	—	—	—
H-5″	—	—	—	—	—
H_a-6″	—	—	—	—	—
H_b-6″	—	—	—	—	—

[a]Overlapped signal at about 1.95 ppm.

TABLE 1. ^{1}H-nmr Data of the Fevicordin Glycosides **1** and **3–12** (in CD_3OD, ppm, J in Hz).

Compound					
7	**8**	**9**	**10**	**11**	**12**
6.65 s	6.65 s	6.66 s	6.66 s	6.62 s	6.62 s
2.84 ddd	2.84 ddd	2.85 ddd	2.84 ddd	2.86 ddd	2.87 ddd
J=18.0,9.0,9.0	J=18.0,9.0,9.0	J=18.0,9.0,9.0	J=18.0,9.0,9.0	J=18.0,9.0,9.0	J=18.0,9.0,9.0
2.64 brdd	2.65 brdd	2.66 brdd	2.64 brdd	2.66 brdd	2.66 brdd
J=18.0,9.0	J=18.0,9.0	J=18.0,9.0	J=18.0,9.0	J=18.0,9.0	J=18.0,9.0
2.26 dddd	2.25 dddd	2.26 dddd	2.25 dddd	2.25 dddd	2.27 dddd
J=15.0,9.0,	J=15.0,9.0,	J=15.0,9.0,	J=15.0,9.0,	J=15.0,9.0,	J=15.0,9.0,
9.0,7.0	9.0,7.0	9.0,7.0	9.0,7.0	9.0,7.0	9.0,7.0
*	*	*	*	1.97 brdd	1.97 brdd
				J=15.0,9.0	J=15.0,9.0
2.11 brd	2.13 brd	2.14 brd	2.13 brd	2.12 brd	2.15 brd
J=7.0	J=7.0	J=7.0	J=7.0	J=7.0	J=7.0
2.88 d	2.92 d	2.92 d	2.92 d	2.78 d	2.79 d
J=14.5	J=14.5	J=14.5	J=14.5	J=14.5	J=14.5
2.63 d	2.64 d	2.67 d	2.66 d	2.57 d	2.60 d
J=14.5	J=14.5	J=14.5	J=14.5	J=14.5	J=14.5
*	*	*	*	1.99 dd	1.99 dd
				J=13.5,7.5	J=13.5,7.5
1.50 brd	1.48 brd	1.49 brd	1.48 brd	1.58 brd	1.59 brd
J=13.5	J=13.5	J=13.5	J=13.5	J=13.5	J=13.5
4.53 brdd	4.44 brdd	4.47 brdd	4.42 brdd	4.58 brdd	4.62 brdd
J=7.5,7.0	J=7.5,7.0	J=7.5,7.0	J=7.5,7.0	J=7.5,7.0	J=7.5,7.0
2.49 d	2.48 d	2.53 d	2.51 d	2.18 d	2.34 d
J=7.0	J=7.0	J=7.0	J=7.0	J=7.0	J=7.0
0.90 s (3H)	0.93 s (3H)	0.95 s (3H)	0.95 s (3H)	0.93 s (3H)	0.98 s (3H)
1.30 s (3H)	1.31 s (3H)	1.31 s (3H)	1.30 s (3H)	1.30 s (3H)	1.30 s (3H).
1.38 s (3H)	1.35 s (3H)	1.38 s (3H)	1.36 s (3H)	1.24 s (3H)	1.21 s (3H)
—	—	—	—	2.39 dd	3.96 brd
				J=15.0,6.5	J=5.0
—	—	—	—	2.30 dd	—
				J=15.0,6.5	
	2.80 ddd		2.84 ddd		
6.79 d	J=18.0,10.0,6.0	6.81 d	J=18.0,10.0,6.0	5.69 ddd	5.75 dd
J=15.5	2.68 ddd	J=15.5	2.71 ddd	J=15.5,6.5,6.5	J=15.5,5.0
	J=18.0,10.0,6.0		J=18.0,10.0,6.0		
	*		1.72 ddd		
6.97 d		6.95 d	J=14.0,10.0,6.0	5.63 d	5.82 dd
J=15.5	*	J=15.5	1.67 ddd	J=15.5	J=15.5,0.5
			J=14.0,10.0,6.0		
1.53 s (3H)	1.42 s (3H)	1.30 s (3H)	1.16 s (3H)	1.24 s (3H)	1.25 s (3H)
1.53 s (3H)	1.42 s (3H)	1.30 s (3H)	1.16 s (3H)	1.24 s (3H)	1.25 s (3H)
2.08 s (3H)	2.08 s (3H)	2.09 s (3H)	2.08 s (3H)	2.07 s (3H)	2.09 s (3H)
0.99 s (3H)	0.99 s (3H)	1.01 s (3H)	0.99 s (3H)	1.00 s (3H)	1.00 s (3H)
1.98 s (3H)	1.92 s (3H)	—	—	—	—
4.58 d	4.55 d	4.55 d	4.56 d	4.53 d	4.53 d
J=7.5	J=7.5	J=7.5	J=7.5	J=7.5	J=7.5
3.6–3.3	3.6–3.3	3.6–3.3	3.6–3.3	3.6–3.3	3.6–3.3
4.30 dd	4.30 dd	4.29 dd	4.30 dd	4.29 dd	4.28 dd
J=11.0,1.5	J=11.0,1.5	J=11.0,1.5	J=11.0,1.5	J=11.0,1.5	J=11.0,1.5
3.86 dd	3.84 dd	3.85 dd	3.86 dd	3.84 dd	3.84 dd
J=11.0,4.0	J=11.0,4.0	J=11.0,4.0	J=11.0,4.0	J=11.0,4.0	J=12.0,4.0
4.39 d	4.37 d	4.37 d	4.38 d	4.37 d	4.36 d
J=7.5	J=7.5	J=7.5	J=7.5	J=7.5	J=7.5
3.6–3.3	3.6–3.3	3.6–3.3	3.6–3.3	3.6–3.3	3.6–3.3
3.89 dd	3.88 dd	3.88 dd	3.89 dd	3.87 dd	3.87 dd
J=12.0,2.0	J=12.0,2.0	J=12.0,2.0	J=12.0,2.0	J=12.0,2.0	J=12.0,2.0
3.70 dd	3.68 dd	3.69 dd	3.69 dd	3.68 dd	3.68 dd
J=12.0,4.5	J=12.0,4.5	J=12.0,4.5	J=12.0,4.5	J=12.0,4.5	J=12.0,4.5

TABLE 2. ^{13}C-nmr Shifts of Compounds **1–13**, **16**, and **18** (in CD_3OD, int. ref. δ=49.0).

Carbon	Compound														
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**16**[a]	**18**
C-1	113.28	110.66	113.40	113.27	113.30	113.30	113.22	113.47	113.50	113.39	113.59	113.45	110.45	108.18	113.38
C-2	144.70	143.01[b]	144.60	144.60	144.61	144.66	144.68	144.96	144.84	144.75	145.29	145.60	142.96[b]	151.77	144.71
C-3	144.83	143.96[b]	144.83	144.78	144.80	144.84	144.75	145.33	145.02	144.90	146.48	147.31	143.83[b]	146.95	144.88
C-4	124.84	124.63	124.83	124.83	124.83	124.85	124.89	125.08	125.01	124.96	125.34	125.57	124.48	131.56	124.93
C-5	131.27	130.35	131.29	131.25	131.26	131.32	131.37	131.50	131.55	131.48	131.46	131.28	130.03	128.66	131.33
C-6	24.81	24.72	24.78	24.80	24.79	24.90	24.75	24.81	24.80	24.78	24.95	24.95	24.64	24.78	24.82
C-7	20.28	20.31	20.22	20.25	20.23	20.29	20.16	20.24	20.25	20.19	20.32	20.31[b]	20.20	20.22	20.30
C-8	44.11	44.03	44.01	44.00	43.97	44.09	43.98	44.10	44.12	43.99	44.20	44.09	44.26	44.11	44.26
C-9	52.12	52.09	52.08	52.05	52.05	51.97	52.07	52.22	52.21	52.13	52.11	52.09	52.19	52.43	52.02
C-10	129.95	126.95	129.90	129.87	129.86	129.93	129.97	129.88	130.12	130.04	129.15	128.45	126.99	134.77	130.01
C-11	217.18	217.11	217.06	217.08	217.23	217.46	217.31	217.27	217.24	217.25	217.62	217.76	217.08	217.18	217.36
C-12	51.81	51.85	51.91	51.84	51.92	51.97	51.69	51.96	51.90	51.93	51.97	52.02	51.99	52.02	52.04
C-13	51.30	51.36	51.20	51.32	51.23	51.19	51.24	51.35	51.47	51.32	51.28	52.02	51.37	51.26	51.15
C-14	49.67	49.55	49.77	49.70	49.77	49.75	49.57	49.85	49.77	49.78	49.80	49.81	49.97	49.71	49.82
C-15	46.34	46.38	46.39	46.36	46.37	46.72	46.21	46.42	46.43	46.37	46.69	45.45	46.48	46.29	46.61
C-16	71.83	71.69	71.46	71.69	71.42	71.26	71.77	71.53	71.77	71.44	71.27	72.29	71.61	71.86	73.08
C-17	60.44	60.07	59.69	59.57	59.43	60.32	60.31	59.78	59.85	59.51	60.49	56.53	59.79	60.46	60.59
C-18	20.66	20.58	20.39	20.61	20.38	20.34	20.61	20.40	20.62	20.38	20.32	20.14[b]	20.37	20.68	20.29
C-19	29.21	29.24	29.22	29.20[b]	29.15[b]	29.31	29.26	29.20	29.22[b]	29.14[b]	29.25	29.11	29.15	29.26	29.29
C-20	80.26	80.07	80.86	79.92	80.82	75.65	80.21	80.92	80.00	80.84	75.72	77.09	80.91	80.26	76.01
C-21	25.49	25.31	25.46	25.24	25.36	26.45	25.46	25.54	25.43	25.47	26.53	24.04	25.52	25.45	26.24
C-22	205.38	205.32	216.64	205.00	216.99	47.52	205.34	216.86	205.17	216.98	47.49	81.75	216.59	205.32	45.22
C-23	122.63	122.36	32.76	121.15	33.08	123.85	122.50	32.81	121.31	33.13	123.87	126.24	32.80	122.63	23.08
C-24	151.57	151.51	35.77	155.41	38.04	142.70	151.60	35.70	155.37	38.06	142.79	141.53	35.90	151.62	38.61
C-25	81.04	80.88	83.04	71.49	70.80[c]	73.03	80.99	83.10	71.53	70.81[c]	73.15	71.23	83.10	81.04	71.09
C-26	26.60[b]	26.64[c]	26.20[b]	29.20[b]	29.27[b]	29.97	26.62[b]	26.23[b]	29.19[b]	29.26[b]	30.00	29.96[c]	26.21[c]	26.51[b]	29.83
C-27	26.74[b]	26.79[c]	26.29[b]	29.30[b]	29.35[b]	29.97	26.71[b]	26.32[b]	29.19[b]	29.37[b]	30.00	30.06[c]	26.34[c]	26.76[b]	29.83
C-28	11.50	11.59	11.53	11.56	11.55	11.51	11.61	11.60	11.54	11.60	11.70	11.80	11.55	11.80	11.54
C-30	20.07	19.88	20.09	20.07	20.11	19.89	20.02	20.10	20.04	20.09	19.93	19.93	20.11	20.02	19.92
$MeCO_2$	171.87	171.71	172.39	—	—	—	171.87	172.45	—	—	—	—	172.36	171.83	—
$MeCO_2$	21.86	21.84	22.32	—	—	—	21.89	22.32	—	—	—	—	22.29	21.83	—

TABLE 2. Continued.

Carbon	Compound														
	1	2	3	4	5	6	7	8	9	10	11	12	13	16[a]	18
C-1′	105.12	—	105.10	105.02	105.04	105.12	105.22	105.51	105.52	105.38	105.60	105.60	—	—	105.21
C-2′	74.79	—	74.76	74.72	74.74	74.78	74.57	74.75	74.73	74.66	74.78	74.81	—	—	74.83
C-3′	77.71	—	77.66	77.61	77.63	77.68	76.79	77.00	77.04	76.91	76.99	76.99	—	—	77.72
C-4′	70.87	—	70.89	70.82	70.84[c]	70.86	71.37	71.53	71.53	71.44[c]	71.57	71.54	—	—	70.89
C-5′	78.11	—	78.07	78.04	78.05	78.11	77.27	77.45	77.45	77.34	77.53	77.55	—	—	78.08
C-6′	62.07	—	62.11	62.04	62.04	62.05	69.32	69.48	69.48	69.40	69.54	69.52	—	—	62.14
C-1″	—	—	—	—	—	—	104.44	104.63	104.63	104.54	104.64	104.65	—	—	—
C-2″	—	—	—	—	—	—	74.97	75.12	75.10	75.04	75.12	75.12	—	—	—
C-3″	—	—	—	—	—	—	77.71	77.88	77.89	77.79	77.89	77.89	—	—	—
C-4″	—	—	—	—	—	—	70.87	71.07	71.07	70.96[c]	71.15	71.10	—	—	—
C-5″	—	—	—	—	—	—	77.79	77.89	77.99	77.88	77.97	77.99	—	—	—
C-6″	—	—	—	—	—	—	62.63	62.76	62.77	62.68	62.78	62.75	—	—	—
MeO-2	—	—	—	—	—	—	—	—	—	—	—	—	—	56.05	—
MeO-3	—	—	—	—	—	—	—	—	—	—	—	—	—	60.72	—

[a]All assignments by C-H COSY.

[b,c]Signals within a vertical column may be interchanged.

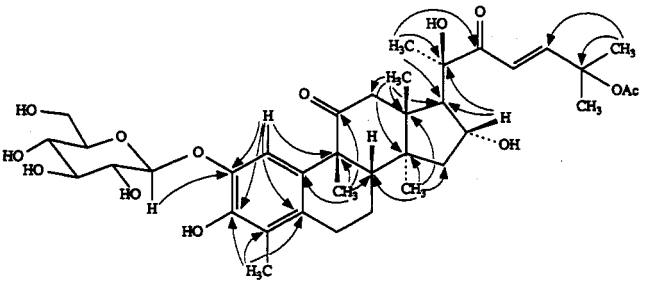


FIGURE 1. Important $^{1}H/^{13}C$ couplings observed in the COLOC spectrum (7) of **1**.

The structure was corroborated by $NaBH_4$ reduction of **7**, which yielded **12** as the major product. The relative configuration at C-22 depicted for **12** followed from comparison of the ^{13}C-nmr data with those recently published for kinoin A, a cucurbitacin with an identical side chain and with established configuration (12). In that report, evidence was given that the stereochemistry of the hydroxy group at C-22 characteristically influences the nmr resonances of C-21 to C-25.

Cucurbitacin U gentiobioside [**14**] and cucurbitacin V gentiobioside [**15**] also showed the ^{1}H- and ^{13}C-nmr resonances typical of the gentiobiosyl moiety. However, the aglycones did not contain any aromatic structural element (Table 3). Furthermore, the ^{13}C-nmr spectrum indicated the presence of 30 carbon atoms in the aglycone, among which 8 signals were attributable to Me groups, whereas the skeleton of the fevicordin-type norcucurbitanes was characterized by only 29 carbon atoms, including 7 Me groups and an aromatic ring A. Nmr studies, including COSY, HMQC (13), HMBC, and nOe measurements determined the structures **14** and **15**.

The CH_2Cl_2 extract of the seeds, when chromatographed in absence of air and light, afforded fevicordin A [**2**] and fevicordin B [**13**], the structures of which were deduced from their spectroscopic properties and by comparison with the enzymatic cleavage products of **1** and **3**, respectively.

DISCUSSION

The fevicordins **1–13** represent new natural products which belong to the hitherto unknown class of 29-norcucurbitacins. Cucurbitacin U gentiobioside [**14**] and V gentiobioside [**15**] are also new compounds. The co-occurrence of both fevicordins and cucurbitacins in *F. cordifolia* corroborates the latter as biogenetic precursors of the fevicordins. The biogenetic relationship is supported by the close structural similarity (stereochemistry, substitution pattern) of the isolated fevicordins and cucurbitacins. Oxidation at C-28 (or C-29) of the cucurbitacins to the corresponding acids followed by

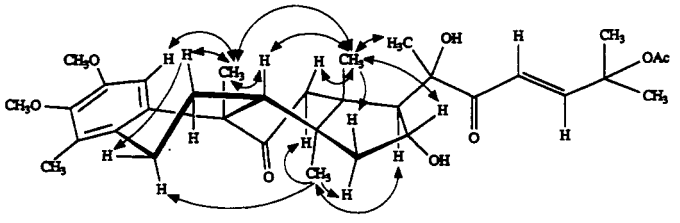
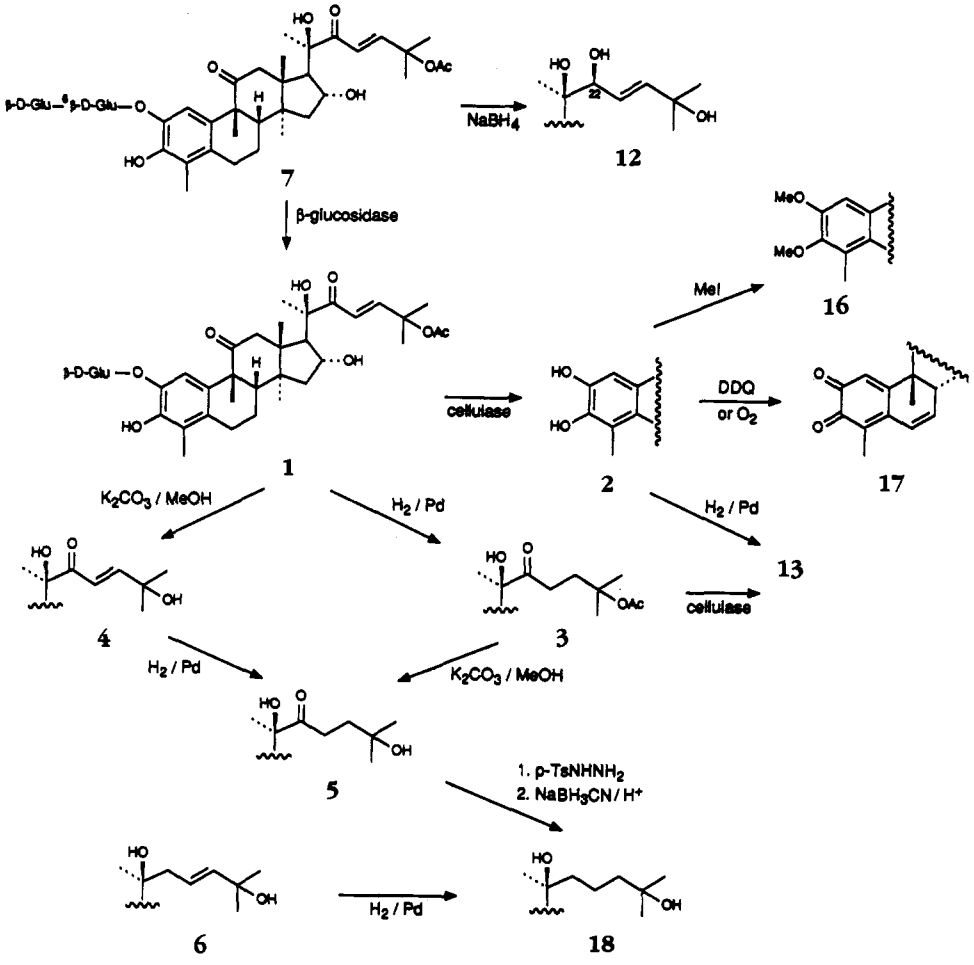


FIGURE 2. Major nOe's observed in fevicordin A dimethyl ether [**16**].



SCHEME 1. Chemical interconversions in the fevicordin series.

decarboxylation and an aromatization of ring A via oxidation and dehydration might readily convert the cucurbitacins into their 29-nor-1,2,3,4,5,10-dehydro derivatives (=fevicordins).

Subsequent to our communications on the fevicordins (1,5), two 29-norcucurbitacin glucosides have recently been obtained from the roots of a *Wilbrandia* species (Cucurbitaceae) (14). The reported compounds contain an additional 6,7-double bond and can be regarded as 6,7-dehydrofevicordin A glucoside and 6,7-dehydrofevicordin D glucoside, respectively.

Johnson and co-workers (15,16) investigated the seeds of *F. cordifolia* collected in Jamaica and isolated the cordifolins, cucurbitacins with an 20,25-epoxy ring within the side chain at C-17. We were unable to detect these substances in our extracts. However, it should be noted that structurally and stereochemically cordifolin A and cordifolin C represent the 20,25-anhydro derivatives of cucurbitacin U [aglycone of **14**] and cucurbitacin V [aglycone of **15**], respectively. Johnson also announced the isolation of two norcucurbitacines, and one of them might be identical with fevicordin F gentiobioside [**12**] or its 22-epimer (L.B.N. Johnson, personal communication, December 29, 1992).

In the carrageenan-induced rat paw edema test, fevicordin A [**2**] and its glucoside **1** exhibited a cortisone-like anti-inflammatory activity even when administered in low doses (Table 4).

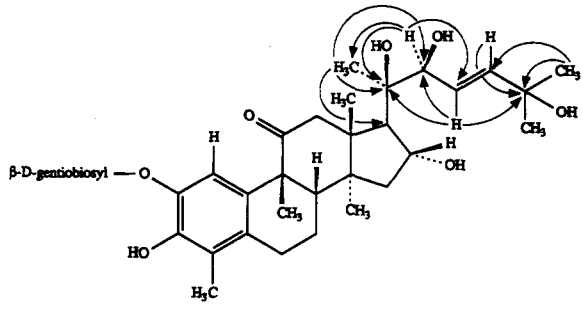


FIGURE 3. Long-range couplings observed in the HMBC of **12**.

For fevicordin A the anti-inflammatory effect observed was proportional to the dose applied; in the animal test system the toxic dose for fevicordin A glucoside was found to be close to an effective therapeutic dose.

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—The mp's were determined on a Kofler hot-stage apparatus and are uncorrected. Optical rotations and uv measurements were made for MeOH solutions; ir data refer to KBr discs. Nmr spectra, if not otherwise stated, refer to CD_3OD solutions at 360 MHz (^1H nmr) and 90.5 MHz (^{13}C nmr); chemical shifts were referenced to TMS for ^1H nmr and to the deuterated solvent ($\delta=49.0$ ppm for CD_3OD and $\delta=128.0$ ppm for C_6D_6) for ^{13}C nmr. For ^1J C-H correlations the sequence according to Bax and Morris (17) was used, and for long-range correlation the COLOC sequence (7) was used. Inverse heteronuclear correlations were done with the sequences of Bax and Subramanian for HMQC (13) and Bax and Summers for HMBC (11). NOe's were measured by the difference method. Ms was measured on a Finnigan MAT TSQ 70 instrument, equipped with DEP for dci measurements (reagent gas NH_3) and a fab gun; fab spectra were run with Xe (8 kV) from glycerol matrix. Unless they are key ions, only masses with $m/z>200$ and intensities >30% are given. For tlc nano plates ® SIL-20/UV_{254} (Macherey-Nagel) were used;

TABLE 3. ^{13}C-nmr Signals of **14** and **15** (in CD_3OD).

Carbon	Compound		Carbon	Compound	
	14	**15**		**14**	**15**
C-1	22.4	22.5	C-22	217.2	47.6
C-2	28.9	29.0	C-23	33.1	124.0
C-3	87.5	87.6	C-24	38.1	142.7
C-4	42.6	42.6	C-25	70.8	71.3
C-5	142.0	142.0	C-26	29.2[b]	30.0
C-6	119.5	119.7	C-27	29.4[b]	30.0
C-7	24.8	24.8	C-28	25.9	25.9
C-8	44.5	44.6	C-29	28.6	28.6
C-9	50.3	50.3	C-30	19.7	19.6
C-10	36.6	36.8	C-1′	106.3	106.4
C-11	216.8	217.2	C-2′	75.1	75.2
C-12	49.8	49.8	C-3′	77.1	77.2
C-13	51.9	51.8	C-4′	71.6[c]	71.7[c]
C-14	49.2	49.2	C-5′	77.9	78.0
C-15	46.7	46.9	C-6′	69.9	69.9
C-16	71.6[a]	73.2	C-1″	104.8	104.9
C-17	59.2	60.1	C-2″	75.5	75.6
C-18	20.4	20.4	C-3″	77.9	78.0
C-19	20.4	20.4	C-4″	71.5[a]	71.6[c]
C-20	80.8	75.8	C-5″	78.1	78.2
C-21	25.5	26.7	C-6″	62.7	62.8

[a–c]Values may be interchanged.

TABLE 4. Anti-inflammatory Activities Measured by the Carrageenan-Induced Rat Paw Edema Test After Peroral Application.

Substance	Mol wt	Dose (mg/kg)	Inhibition (%)
Fevicordin A	542	10	96
Fevicordin A	542	5	52
Fevicordin A	542	1	8.5
Fevicordin A glucoside	704	10	56
Acetylsalicyclic acid	180	100	44
Indomethacin	357	2	47
Betamethasone	392	0.125	63

detection was by uv and anisaldehyde reagent according to Stahl (18); R_f values are given for solvent systems cyclohexane-EtOAc (3:2) (S-1) and $CHCl_3$-MeOH (7:3) (S-2). For cc Si gel 60 (Macherey-Nagel) or Sephadex LH-20 (Pharmacia) were used. Preparative hplc was carried out on a 7 μ Lichrosorb® RP 18 column with H_2O/MeOH mixtures, flow-rate 12.5 ml/min, length 25 cm, ϕ 2 cm; detection by uv absorbance at 210 nm.

PLANT MATERIAL.—*F. cordifolia* seeds were collected between 1982 and 1984 near Ujarraz/Rio Ceibo, Province Puntarenas, Costa Rica and identified by Rafael A. Ocampo, Herbarium of the National Museum, San José, Costa Rica. Voucher specimens are kept under No. 27793 at the National Museum, San José and under No. 8213 at the Institute of Pharmacy and Food Chemistry, Erlangen.

EXTRACTION AND ISOLATION.—The endosperm (800 g from 1.2 kg dried seeds) was ground (after freezing in liquid N_2) and extracted successively in a Soxhlet apparatus with petroleum ether (50–70°), CH_2Cl_2, and MeOH to yield 450 g extract A (petroleum ether), 4 g extract B (CH_2Cl_2), and 100 g extract C (MeOH). Repeated cc of extract B on SiO_2 with cyclohexane/EtOAc mixtures (exclusion of O_2 and light) afforded **2** and **13**. Extract C was separated first by flash chromatography and then repeatedly by cc on SiO_2 with $CHCl_3$/MeOH mixtures. Purification of the raw compounds was achieved by hplc and subsequent cc on Sephadex LH-20 (Pharmacia) with H_2O-Me_2CO (49:1), yielding compounds **1**, **3–12**, **14**, and **15**.

Fevicordin A [*25-acetoxy-2,3,16α,20-tetrahydroxy-29-norcucurbita-1,3,5(10),23E-tetraene-11,22-dione*] [**2**].—Colorless amorphous powder, sensitive against O_2 (60 mg): tlc R_f 0.37 (S-1), brown with anisaldehyde; $[\alpha]^{21}D$ +15° (*c*=0.5); ir ν max cm^{-1} 3420, 1720, 1680, 1620; uv λ max nm (log ε) 226 (4.11), 287 (3.37); ^1H nmr (C_6D_6) δ ppm 1.08 (3H, s), 1.10 (3H, s), 1.26 (3H, s), 1.30 (3H, s), 1.32 (1H, d, *J*=13.5 Hz), 1.33 (3H, s), 1.40 (3H, s), 1.58 (3H, s), 1.60 (1H, dd, J_1=13.5, J_2=7.5 Hz), 1.69 (1H, dd, J_1=12.5, J_2=8.0 Hz), 1.91 (2H), 2.16 (3H, s), 2.28 (1H, s, OH), 2.34 (1H, m), 2.46 (1H, d *J*=7.0 Hz), 2.51 (1H, m), 2.74 (1H, d, *J*=12.5 Hz), 2.80 (1H, d, *J*=12.5 Hz), 4.25 (1H, br dd, J_1~J_2~7.5 Hz), 4.48 (1H, s, OH), 5.80 (1H, br s, OH), 6.50 (1H, d, *J*=15.5 Hz), 6.73 (1H, s), 7.20 (1H, d, *J*=15.5 Hz); ^{13}C nmr see Table 2; eims *m/z* (%) $[M-60]^+$ 482.2664 (8) (calcd for $C_{29}H_{38}O_6$, 482.2668), 386.2085 (13) (calcd for $C_{23}H_{30}O_5$, 386.2093), 217 (16), 190 (34), 189 (33), 96.0577 (29) (calcd for C_6H_8O, 96.0575), 43 (100); dcims *m/z* (%) $[M+NH_4]^+$ 560 (100).

Fevicordin B [*25-acetoxy-2,3,16α,20-tetrahydroxy-29-norcucurbita-1,3,5(10)-triene-11,22-dione*] [**13**].—Colorless amorphous powder, sensitive against O_2 (14 mg): tlc R_f 0.43 (S-1), light brown with anisaldehyde; $[\alpha]^{21}D$ +7° (*c*=0.4); ir ν max cm^{-1} 3400, 1700, 1620; uv λ max nm (log ε) 228 (3.86), 286 (3.37); ^1H nmr (C_6D_6) δ ppm 0.95 (3H, s), 1.10 (3H, s), 1.17 (3H, s), 1.28 (1H, d, *J*=13.5 Hz), 1.35 (3H, s), 1.40 (3H, s), 1.43 (3H, s), 1.58 (3H), 1.68 (3H, s), 1.69 (1H), 1.92 (2H), 2.15 (3H, s), 2.22 (1H, m), 2.32 (2H), 2.54 (1H, ddd, J_1=12.5, J_2~J_3~8.5 Hz), 2.67 (1H, d, *J*=12.5 Hz), 2.77 (1H, d, *J*=12.5 Hz), 2.79 (1H), 3.98 (1H, br dd, J_1~J_2~7.0 Hz), 4.52 (1H, s, OH), 5.73 (1H, s, OH), 6.70 (1H, s); ^{13}C nmr see Table 2; eims *m/z* (%) $[M-60]^+$ 484 (16), 386 (14), 217 (33), 190 (67), 189 (64), 113 (33), 43 (100).

Fevicordin A glucoside [*25-acetoxy-2-(β-D-glucopyranosyloxy)-3,16α,20-trihydroxy-29-norcucurbita-1,3,5(10),23E-tetraene-11,22-dione*] [**1**].—Colorless needles (3 g): mp 148° (from EtOAc); tlc R_f 0.71 (S-2), brown with anisaldehyde; $[\alpha]^{21}D$ −24° (*c*=0.5); ir ν max cm^{-1} 3420, 1720, 1685, 1630; uv λ max nm (log ε) 224 (4.15), 285 (3.35); ^1H nmr see Table 1; results of selective INEPT experiments see Table 5; ^{13}C nmr see Table 2; fabms *m/z* (%) $[M-1]^-$ 703 (10), 645 (10), 499 (75), 483 (100), 481 (87), 385 (92), 327 (83).

Fevicordin B glucoside [*25-acetoxy-2-(β-D-glucopyranosyloxy)-3,16α,20-trihydroxy-29-norcucurbita-1,3,5(10)-triene-11,22-dione*] [**3**].—Colorless needles (100 mg): mp 143–144° (from EtOAc); tlc R_f 0.70 (S-2), light brown with anisaldehyde; $[\alpha]^{21}D$ −27° (*c*=0.5); ir ν max cm^{-1} 3440, 1700, 1620; uv λ max nm

TABLE 5. Results of Selective INEPT Experiments.

Decoupler setting (δ)	Selective INEPT Signals Observed (δ)
6.66 (H-1)	144.8 (C-3)
	144.7 (C-2)
	131.3 (C-5)
	52.1 (C-9)
4.56 (H-1′)	144.7 (C-2)
2.08 (Me-28)	144.8 (C-3)
	131.3 (C-5)
	124.8 (C-4)

(log ε) 228 (3.86), 286 (3.35); ^{1}H nmr see Table 1; ^{13}C nmr see Table 2; fabms *m/z* (%) $[M-1]^-$ 705 (5), 645 (4), 483 (100), 468 (45), 385 (20), 327 (29).

Fevicordin C glucoside [*2-(β-D-glucopyranosyloxy)-3,16α,20,25-tetrahydroxy-29-norcucurbita-1,3,5(10),23E-tetraene-11,22-dione*] [**4**].—Colorless needles (110 mg): mp 172–174° (from EtOAc); tlc R_f 0.65 (S-2), brown with anisaldehyde; $[\alpha]^{21}D$ −33° (*c*=0.5); ir ν max cm^{-1} 3380, 1690, 1680, 1622; uv λ max nm (log ε) 224 (4.15), 285 (3.35); ^{1}H nmr see Table 1; ^{13}C nmr see Table 2; fabms *m/z* (%) $[M-1]^-$ 661 (16), 499 (100), 483 (47), 481 (51), 385 (80), 327 (81).

Fevicordin D glucoside [*2-(β-D-glucopyranosyloxy)-3,16α,20,25-tetrahydroxy-29-norcucurbita-1,3,5(10)-triene-11,22-dione*] [**5**].—Colorless needles (40 mg): mp 157–158° (from EtOAc); tlc R_f 0.63 (S-2), light brown with anisaldehyde; $[\alpha]^{21}D$ −29° (*c*=0.5); ir ν max cm^{-1} 3400, 1680, 1610; uv λ max nm (log ε) 228 (3.85), 285 (3.35); ^{1}H nmr see Table 1; ^{13}C nmr see Table 2; fabms *m/z* (%) $[M-1]^-$ 663 (20), 501 (97), 483 (100), 385 (36), 327 (52).

Fevicordin E glucoside [*2-(β-D-glucopyranosyloxy)-3,16α,20,25-tetrahydroxy-29-norcucurbita-1,3,5(10),23E-tetraen-11-one*] [**6**].—Colorless needles (40 mg): mp 159–161° (from EtOAc); tlc R_f 0.61 (S-2), blue with anisaldehyde; $[\alpha]^{21}D$ −4° (*c*=0.3); ir ν max cm^{-1} 3400, 1730, 1610; uv λ max nm (log ε) 224 (3.85), 284 (3.35); ^{1}H nmr see Table 1; ^{13}C nmr see Table 2; fabms *m/z* (%) $[M-1]^-$ 647 (16), 485 (100), 385 (52), 327 (23).

Fevicordin A gentiobioside [*25-acetoxy-2-(6-O-β-D-glucopyranosyl-β-D-glucopyranosyloxy)-3,16α,20-trihydroxy-29-norcucurbita-1,3,5(10),23E-tetraene-11,22-dione*] [**7**].—Colorless crystals (150 mg): mp 165° (from EtOAc); tlc R_f 0.41 (S-2), brown with anisaldehyde; $[\alpha]^{21}D$ −38° (*c*=0.5); ir ν max cm^{-1} 3400, 1720, 1680, 1630; uv λ max nm (log ε) 223 (4.14), 282 (3.34); ^{1}H nmr see Table 1; ^{13}C nmr see Table 2; fabms *m/z* (%) $[M-1]^+$ 865 (8), 541 (45), 483 (84), 481 (100), 385 (68), 327 (52).

Fevicordin B gentiobioside [*25-acetoxy-2-(6-O-β-D-glucopyranosyl-β-D-glucopyranosyloxy)-3,16α,20-trihydroxy-29-norcucurbita-1,3,5(10)-triene-11,22-dione*] [**8**].—Colorless crystals (45 mg): mp 165–167° (from $CHCl_3$ saturated with H_2O); tlc R_f 0.40 (S-2), light brown with anisaldehyde; $[\alpha]^{21}D$ −36° (*c*=0.4); ir ν max cm^{-1} 3400, 1700, 1620; uv λ max nm (log ε) 225 (3.86), 283 (3.35); ^{1}H nmr see Table 1; ^{13}C nmr see Table 2; fabms *m/z* (%) $[M-1]^-$ 867 (2), 543 (34), 484 (70), 483 (100), 468 (54), 385 (18), 327 (21).

Fevicordin C gentiobioside [*2-(6-O-β-D-glucopyranosyl-β-D-glucopyranosyloxy)-3,16α,20,25-tetrahydroxy-29-norcucurbita-1,3,5(10),23E-tetraene-11,22-dione*] [**9**].—Colorless amorphous powder (60 mg): tlc R_f 0.29 (S-2), brown with anisaldehyde; $[\alpha]^{21}D$ −47° (*c*=0.6); ir ν max cm^{-1} 3400, 1680, 1630; uv λ max nm (log ε) 225 (4.24), 284 (3.43); ^{1}H nmr see Table 1; ^{13}C nmr see Table 2; fabms *m/z* (%) $[M-1]^-$ 823 (7), 499 (100), 483 (37), 481 (39), 385 (30), 327 (40).

Fevicordin D gentiobioside [*2-(6-O-β-D-glucopyranosyl-β-D-glucopyranosyloxy)-3,16α,20,25-tetrahydroxy-29-norcucurbita-1,3,5(10)-triene-11,22-dione*] [**10**].—Colorless amorphous powder (82 mg): tlc R_f 0.28 (S-2), light brown with anisaldehyde; $[\alpha]^{21}D$ −43° (*c*=0.5); ir ν max cm^{-1} 3400, 1685, 1630; uv λ max nm (log ε) 225 (4.04), 284 (3.38); ^{1}H nmr see Table 1; ^{13}C nmr see Table 2; fabms *m/z* (%) $[M-1]^-$ 825 (3), 501 (60), 483 (100), 385 (30), 327 (62).

Fevicordin E gentiobioside [*2-(6-O-β-D-glucopyranosyl-β-D-glucopyranosyloxy)-3,16α,20,25-tetrahydroxy-29-norcucurbita-1,3,5(10),23E-tetraen-11-one*] [**11**].—Colorless amorphous powder (26 mg): tlc R_f 0.25 (S-2), blue with anisaldehyde; $[\alpha]^{21}D$ −20° (*c*=0.6); ir ν max cm^{-1} 3400, 1680, 1620; uv λ max nm (log ε) 225 (4.00), 283 (3.31); ^{1}H nmr see Table 1; ^{13}C nmr see Table 2; fabms *m/z* (%) $[M-1]^-$ 809 (3), 483 (50), 481 (50), 385 (52), 327 (90), 215 (100).

Fevicordin F gentiobioside [*(22S*)-2-(6-O-β-D-glucopyranosyl-β-D-glucopyranosyloxy)-3,16α,20,22,25-*

pentahydroxy-29-norcucurbita-1,3,5(10),23E-tetraen-11-one] [**12**].—Colorless amorphous powder (5 mg): tlc R_f 0.18 (S-2), brownish-grey with anisaldehyde; $[\alpha]^{21}D$ −26° (*c*=0.4); ir ν max cm^{-1} 3400, 1680; uv λ max nm (log ε) 224 (3.92), 280 (3.25); ^1H nmr see Table 1; ^{13}C nmr see Table 2; fabms *m/z* (%) $[M-1]^-$ 825 (6), 483 (100), 385 (50), 327 (65).

Cucurbitacin U gentiobioside [3β-(6-O-β-D-*glucopyranosyl*-β-D-*glucopyranosyloxy*)-16α,20,25-*trihydroxy*-(10α)-cucurbit-5-ene-11,22-dione] [**14**].—Colorless crystals (210 mg): mp 143–144° [from $CHCl_3$-MeOH (4:1)]; tlc R_f 0.31 (S-2), yellow with anisaldehyde; $[\alpha]^{21}D$ +16° (*c*=0.5); ir ν max cm^{-1} 3400, 1690; ^1H nmr δ ppm 0.89 (3H, s), 1.04 (3H, s), 1.05 (3H, s), 1.20 (6H, s), 1.25 (3H, s), 1.32 (3H, s), 1.37 (3H, s), 1.35–2.00 (10H, H_a-1, H_b-1, H_a-2, H_b-2, H_a-7, H-8, H_a-15, H_b-15, H_a-24, H_b-24), 2.30–2.47 (2H, H_b-7, H-10), 2.52 (1H, d, *J*=15.0 Hz, H_a-12), 2.58 (1H, d, *J*=7.0 Hz, H-17), 2.75 (1H, ddd, J_1=15.0, J_2=10.0, J_3=5.0 Hz, H_a-23), 2.86 (1H, ddd, J_1=15.0, J_2=10.0, J_3=5.0 Hz, H_b-23), 2.99 (1H, d, *J*=15.0 Hz, H_b-12), 3.25–3.45 (8H, H-2′, H-2″, H-3′, H-3″, H-4′, H-4″, H-5′, H-5″), 3.67 (1H, dd, J_1=12.0, J_2=4.0 Hz, H_a-6″), 3.80 (1H, dd, J_1=12.0, J_2=4.0 Hz, H_a-6′), 3.88 (1H, dd, J_1=12.0, J_2=2.5 Hz, H_b-6″), 4.07 (1H, dd, J_1=12.0, J_2=2.5 Hz, H_b-6′), 4.28 (1H, d, *J*=7.5 Hz, H-1′), 4.40 (1H, d, *J*=7.5 Hz, H-1″), 4.41 (1H, br dd, J_1~J_2~8.0 Hz, H-16), 5.62 (1H, m, H-6); ^{13}C nmr see Table 3; fabms *m/z* (%) $[M-1]^-$ 827 (90), 809 (98), 647 (42), 501 (51), 483 (64), 327 (56), 311 (66), 221 (100). Elemental analysis: found C 60.59, H 8.09; calcd for $C_{42}H_{68}O_{16}$ C 60.85, H 8.27.

Cucurbitacin V gentiobioside [3β-(6-O-β-D-*glucopyranosyl*-β-D-*glucopyranosyloxy*)-16α,20,25-*trihydroxy*-(10α)-*cucurbita*-5,23E-*dien*-11-*one*] [**15**].—Colorless amorphous powder (21 mg): tlc R_f 0.25 (S-2), violet with anisaldehyde; $[\alpha]^{21}D$ +30° (*c*=0.5); ir ν max cm^{-1} 3400, 1685, 1630; ^1H nmr δ ppm 0.88 (3H, s, Me-18), 1.04 (6H, s, Me-30, Me-28), 1.23 (3H, s, Me-29), 1.26 (6H, s, Me-26, Me-27), 1.28 (3H, s, Me-19), 1.31 (3H, s, Me-21), 1.47 (1H, d, *J*=15.0 Hz, H_a-15), 1.50–2.00 (6H, H_a-1, H_b-1, H_a-2, H_b-2, H_a-7, H_b-15), 2.15–2.47 (5H, H_b-7, H-8, H-10, H_a-12, H_a-22), 2.23 (1H, d, *J*=7.0 Hz, H-17), 2.30 (1H, dd, J_1=14.0, J_2=7.0 Hz, H_b-22), 3.19 (1H, d, *J*=15.0 Hz, H_b-12), 3.25–3.45 (8H, H-2′, H-2″, H-3′, H-3″, H-4′, H-4″, H-5′, H-5″), 3.45 (1H, br s, H-3), 3.66 (1H, dd, J_1=12.0, J_2=4.0 Hz, H_a-6″), 3.78 (1H, dd, J_1=12.0, J_2=4.0 Hz, H_a-6′), 3.87 (1H, dd, J_1=12.0, J_2=2.5 Hz, H_b-6″), 4.06 (1H, dd, J_1=12.0, J_2=2.5 Hz, H_b-6′), 4.30 (1H, d, *J*=7.5 Hz, H-1′), 4.40 (1H, d, *J*=7.5 Hz, H-1″), 4.58 (1H, br dd, J_1~J_2~7.5 Hz, H-16), 5.63 (1H, H-6), 5.65 (1H, d, *J*=16.0 Hz, H-24), 5.75 (1H, ddd, J_1=16.0, J_2~J_3~7.0 Hz, H-23); ^{13}C nmr see Table 3; fabms *m/z* (%) $[M-1]^-$ 811 (100), 693 (70), 549 (50), 531 (60), 267 (69).

ENZYMATIC CLEAVAGE OF **1**.—Compound **1** (50 mg) dissolved in 5 ml H_2O was treated with 100 mg cellulase (Roth) at 32° for 24 h under N_2. The mixture was extracted three times with 10 ml toluene. Evaporation of the combined toluene extracts afforded 20 mg crude **2**, which was purified by cc on Si gel with C_6H_{12}-EtOAc (1:1) (exclusion of O_2). This gave 8 mg amorphous powder. All physico-chemical data were identical with those reported for fevicordin A [**2**].

ENZYMATIC CLEAVAGE OF **3**.—Compound **3** (25 mg) was treated as described for **1** to give 4 mg amorphous powder. All physico-chemical data were identical with those reported for fevicordin B [**13**].

ENZYMATIC CLEAVAGE OF **7**.—Compound **7** (50 mg) was treated (as described for **1** with cellulase) with 100 mg β-glucosidase (Fluka). Workup after evaporation by cc afforded, besides small amounts of **2**, 10 mg amorphous powder with physico-chemical data identical with those of fevicordin A glucoside [**1**].

DETERMINATION OF THE ABSOLUTE CONFIGURATION OF THE GLUCOSE MOIETY IN **1**.—Compound **1** (10 mg) was treated with 2 M MeOH/HCl (2 ml) for 16 h. The residue was trifluoroacetylated and analyzed for D- and L-pertrifluoroacetylmethyl glucosides by gc using a cyclodextrin column (10).

Hexaacetylfevicordin A glucoside [3,16α,25-*triacetoxy*-2-(2,3,4,6-*tetra*-O-*acetyl*-β-D-*glucopyranosyloxy*)-20-*hydroxy*-29-*norcucurbita*-1,3,5(10),23E-*tetraene*-11,22-*dione*].—Compound **1** (10 mg) dissolved in 1 ml Ac_2O-C_5H_5N (1:1) was stirred for 16 h at room temperature. After evaporation of the solvent the product was purified by cc [toluene-MeOH (19:1)] to give 9 mg hexaacetylfevicordin A glucoside. Colorless cubes: mp 193–195° (from MeOH); tlc R_f 0.26 [toluene-MeOH (19:1), brown with anisaldehyde; $[\alpha]^{21}D$ −42° (*c*=0.5, $CHCl_3$); ir ν max cm^{-1} 3440, 1740, 1690, 1625; uv λ max nm (log ε) 224 (4.16), 280 (3.17); ^1H nmr (C_6D_6) δ ppm 0.87 (3H, s), 1.06 (3H, s), 1.27 (3H, s), 1.34 (3H, s), 1.35 (3H, s), 1.39 (3H, s) (Me-18, Me-19, Me-21, Me-26, Me-27, Me-30), 1.60 (3H, s, $MeCO_2$), 1.69 (3H, s, $MeCO_2$), 1.72 (3H, s, $MeCO_2$), 1.86 (3H, s, $MeCO_2$), 1.87 (3H, s, $MeCO_2$), 1.91 (3H, s, $MeCO_2$), 1.94 (3H, s, Me-28), 2.00–1.35 (4H, H_b-7, H-8, H_a-15, H_b-15), 2.17 (3H, s, $MeCO_2$), 2.22 (1H, dd, J_1=18.0, J_2=9.0 Hz, H_b-6), 2.60–2.35 (3H, H_a-6, H_a-7, H_b-12), 2.66 (1H, d, *J*=7.5 Hz, H-17), 2.74 (1H, d, *J*=14.5 Hz, H_a-12), 3.73 (1H, ddd, J_1=9.5, J_2=4.5, J_3=2.0 Hz, H-5′), 4.32 (1H, dd, J_1=12.5, J_2=4.5 Hz, H_b-6′), 4.40 (1H, s, OH), 4.48 (1H, dd, J_1=12.5, J_2=2.0 Hz, H_a-6′), 5.22 (1H, d, *J*=8.0 Hz, H-1′), 5.30 (1H, dd, J_1~J_2~9.5 Hz, H-4′), 5.47 (1H, dd, J_1~J_2~9.5 Hz, H-3′), 5.48 (1H, br dd, J_1~J_2~7.5 Hz, H-16), 5.60 (1H, dd, J_1=9.5, J_2=8.0 Hz, H-2′), 6.54 (1H, d, *J*=15.5 Hz, H-23), 7.03 (1H, s, H-1), 7.25 (1H, d, *J*=15.5, Hz, H-24); ^{13}C nmr

(CD_3OD) δ ppm 215.8 (C-11), 204.1 (C-22), 172.5, 172.2, 171.5, 171.4, 171.1, 171.0, 170.2 (7×*Me*CO_2), 152.8 (C-24), 147.6 (C-2), 138.1 (C-3), 137.1 (C-10), 131.6 (C-5), 130.6 (C-4), 121.7 (C-23), 110.9 (C-1), 99.6 (C-1′), 80.8, 79.6 (C-20, C-25), 75.2, 73.9, 73.1, 72.0, 69.5 (C-2′, C-3′, C-4′, C-5′, C-16), 63.0 (C-6′), 56.0 (C-17), 52.2 (C-9), 52.0 (C-12), 50.7 (C-13), 49.6 (C-14), 43.9 (C-15), 43.3 (C-8), 29.6 (C-19), 27.1, 26.8 (C-26, C-27), 24.7 (C-6), 24.4 (C-21), 21.9, 21.2, 20.9, 20.8, 20.6, 20.5 (6×*Me*CO_2), 20.5 (C-18), 20.4 (*Me*CO_2), 20.0 (C-7), 19.8 (C-30), 12.3 (C-28); dcims *m/z* (%) $[M+NH_4]^+$ 974 (100), 914 (2), 331 (25).

2,3-Di-O-methylfevicordin A [25-acetoxy-2,3-dimethoxy-16α,20-dihydroxy-29-norcucurbita-1,3,5(10),23E-tetraene-11,22-dione] [**16**].—Compound **2** (10 mg) dissolved in 2.5 ml dry Me_2CO was treated at room temperature with 0.5 ml MeI in the presence of 10 mg K_2CO_3 for 18 h under N_2. After filtration and evaporation the crude product was purified by cc [toluene-EtOAc (17:3)], affording 5 mg **16** as a colorless amorphous powder: tlc R_f 0.27 [toluene-EtOAc (3:1)], brown with anisaldehyde; $[\alpha]^{21}D$ −2.8° (*c*=0.1); ir ($CHCl_3$) ν max cm^{-1} 1730, 1690, 1590; uv λ max nm (log ε) 224 (4.14), 285 (3.44); ^1H nmr ($CDCl_3$) δ ppm 1.01 (3H, s, Me-18), 1.04 (3H, s, Me-30), 1.39 (3H, s, Me-19), 1.42 (3H, s, Me-21), 1.52 (3H, s, Me-26), 1.54 (3H, s, Me-27), 1.54 (1H, d, *J*=14.0 Hz, H_b-15), 1.85–2.0 (2H, H_a-15, H_b-7), 1.96 (3H, s, Me-CO_2), 2.10 (3H, s, Me-28), 2.12 (1H, d, *J*=7.0 Hz, H-8), 2.22 (1H, m, H_a-7), 2.42 (1H, d, *J*=7.0 Hz, H-1), 2.60 (1H, br dd, J_1=18.0, J_2=9.0 Hz, H_b-6), 2.71 (1H, d, *J*=14.5 Hz, H_b-12), 2.77 (1H, ddd, J_1=18.0, J_2=J_3=9.0 Hz, H_a-6), 2.88 (1H, d, *J*=14.5 Hz, H_a-12), 3.75 (3H, s, OMe), 3.78 (3H, s, OMe), 4.29 (1H, br dd, J_1=7.5, J_2=7.0 Hz, H-16), 6.38 (1H, d, *J*=15.5 Hz, H-23), 6.40 (1H, s, H-1), 7.00 (1H, d, *J*=15.5 Hz, H-24); ^{13}C nmr see Table 2; eims *m/z* (%) $[M]^+$ 570 (7), 510 (1), 414 (39), 245 (9), 218 (28), 217 (23), 203 (9), 111 (19), 96 (100), 43 (37).

Oxidation of **2** *to 25-acetoxy-16α,20-dihydroxy-29-norcucurbita-1(10),4,6,23E-tetraene-2,3,11,22-tetraone* [**17**].—To **2** (50 mg) in 5 ml Et_2O a solution of 80 mg DDQ in 10 ml Et_2O was added. After stirring at 0° for 12 h the solvent was evaporated and the product purified by cc on Si gel [C_6H_{12}-EtOAc (1:1)] to yield **17** (20 mg) as a yellow amorphous powder: tlc R_f 0.25 [C_6H_{12}-EtOAc (1:1)]; $[\alpha]^{21}D$ −433° (*c*=0.05, MeOH); ir ν max cm^{-1} 1720, 1685, 1650, 1620; uv/vis λ max nm (log ε) 238 (4.15), 340 (3.47), 450 (3.14); ^1H nmr (C_6D_6) λ ppm 0.89 (3H, s), 0.94 (3H, s), 1.16 (3H, s), 1.23 (3H, s), 1.32 (3H, s), 1.35 (3H, s), 1.56 (3H, s, *Me*CO_2), 1.74 (3H, s, Me-28), 2.15 (1H, d, *J*=8.0 Hz, H-8), 2.31 (1H, d, *J*=7.0 Hz, H-17), 2.38 (1H, d, *J*=15.0 Hz, H-12), 2.57 (1H, d, *J*=15.0 Hz, H-12), 4.19 (1H, br dd, J_1~J_2~7.5 Hz, H-16), 4.43 (1H, s, OH), 5.55 (1H, dd J_1=11.0, J_2=8.0 Hz, H-7), 6.09 (1H, s, H-1), 6.19 (1H, d, *J*=11.0 Hz, H-6), 6.52 (1H, d, *J*=16.0 Hz, H-23), 7.19 (1H, d, *J*=16.0 Hz, H-24); ^{13}C nmr (C_6D_6) δ ppm 208.3, 202.3, 180.4, 179.9, 169.8, 155.0, 151.6, 138.4, 136.3, 132.1, 125.1, 123.0, 121.3, 79.2, 78.5, 71.6, 58.8, 52.0, 50.7, 50.5, 49.9, 49.2, 44.2, 27.2, 26.2 (2x), 24.1, 21.5, 20.2, 19.3, 10.7; dcims *m/z* (%) $[M+2+NH_4]^+$ 558 (39), 498 (11), 174 (100).

Hydrogenation of **1**.—Compound **1** (10 mg) dissolved in 2 ml MeOH was hydrogenated over Pd/C (10%) (room temperature, 1 atm, 2 h). Filtration and evaporation afforded 10 mg colorless amorphous powder, the physico-chemical data of which were identical with those reported for **3**.

Hydrogenation of **4**.—Hydrogenation of **4** (8 mg) afforded 8 mg of a colorless amorphous powder, the physico-chemical data of which were identical with those of **5**.

Hydrogenation of **6**.—Hydrogenation of **6** (10 mg) gave 10 mg colorless amorphous powder, the physico-chemical data of which were in agreement with those of **18**.

Desacetylation of **1**.—Compound **1** (25 mg) dissolved in 2 ml MeOH was treated with 50 mg K_2CO_3 for 48 h at room temperature. Filtration and evaporation of the solvent gave a crude product, which was purified by cc [$CHCl_3$-MeOH (9:1)] to yield 10 mg of an amorphous powder identical in physico-chemical data with **4**.

Desacetylation of **3**.—The desacetylation of **3** (15 mg) was achieved as described for **1** to give 4 mg of compound **5**.

Desoxygenation of **5** *to 2-(β-D-glucopyranosyloxy)-3,16α,20,25-tetrahydroxy-29-norcucurbita-1,3,5(10)-trien-11-one* [**18**].—Compound **5** (66 mg) was added to a solution of 20 mg *p*-toluenesulfonyl hydrazide (*p*-TsNHNH_2) in 2 ml EtOH according to Miller *et al.* (19). After refluxing for 3 h, the solvent was evaporated. The residue was redissolved in 3 ml MeOH-THF (2:1) and treated dropwise with 150 mg $NaBH_3CN$ in 4 ml dry THF and 2 ml methanolic HCl (0.1 M) over a period of ca. 8 h at 0°. After neutralization with $NaHCO_3$, the solvent was evaporated. Workup by cc [5 g Al_2O_3, $CHCl_3$-MeOH (7:3)] and subsequent purification by hplc afforded 18 mg of compound **18** as a colorless amorphous powder: tlc R_f 0.30 (S-2), red-brown with anisaldehyde; $[\alpha]^{21}D$ −24° (*c*=0.2); ir ν max cm^{-1} 3400, 1678, 1618; uv λ max nm (log ε) 226 (4.04), 282 (3.40); ^1H nmr δ ppm 0.95 (3H, s, Me-18), 1.00 (3H, s, Me-30), 1.16 (6H, s Me-26 and Me-27), 1.20 (3H, s, Me-21), 1.31 (3H, s, Me-19), 1.20–2.00 (9H, H_b-7, H_a-15, H_b-15, H_a-22, H_b-22, H_a-23,

H_b-23, H_a-24, H_b-24), 2.07 (3H, s, Me-28), 2.11 (1H, br d, J=7.0 Hz, H-8), 2.15 (1H, d, J=7.0 Hz, H-17), 2.24 (1H, dddd, J_1=15.0, J_2~J_3~9.0, J_4=7.0 Hz, H_a-7), 2.63 (1H, br dd, J_1=18.0, J_2=9.0 Hz, H_b-6), 2.66 (1H, d, J=14.5 Hz, H_b-12), 2.82 (1H, ddd, J_1=18.0, J_2~J_3~9.0 Hz, H_a-6), 2.94 (1H, d, J=14.5 Hz, H_a-12), 3.35 (1H, ddd, J_1=9.0, J_2=4.0, J_3=2.5 Hz, H-5′), 3.40–3.50 (3H, H-2′, H-3′, H-4′), 3.85 (1H, dd, J_1=12.0, J_2=4.0 Hz, H_b-6′), 3.99 (1H, dd, J_1=12.0, J_2=2.5 Hz, H_a-6′), 4.55 (1H, br dd, J_1~J_2~7.5 Hz, H-16), 4.58 (1H, d, J=7.5 Hz, H-1′), 6.66 (1H, s, H-1); ^{13}C nmr see Table 2; fabms *m/z* (%) $[M-1]^-$ 649 (12), 487 (100), 485 (80), 385 (43), 327 (27).

NOTE ADDED IN PROOF.—Fevicordin B glucoside (**3**) might be identical with cayaponoside A from *Cayaponia tayuya*, fevicordin D glucoside (**5**) with cayaponoside C and fevicordin F with the aglucone of cayaponoside D (E. Himeno, T. Nagao, J. Honda, H. Okabe, N. Irino, and T. Nakasumi, *Chem. Pharm. Bull.* **40**, 2884 (1992)).

ACKNOWLEDGMENTS

We are thankful to Dr. S.S. Chatterjee, SCHWABE Arzneimittel, Karlsruhe, for the pharmacological tests. Thanks are also due to Rafael A. Ocampo, Coordinator del Proyecto Conservación en Talamanca, Centro Agronomico Tropical de Investigación y Enseñanza, Turrialba, Costa Rica, for the botanical identification and the collection of plant material. We further thank the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie for financial support.

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Received 22 January 1993