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SEPTEMFIDOSIDE: A NEW BIS-IRIDOID DIGLUCOSIDE FROM *GENTIANA SEPTEMFIDA*

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ABSTRACT.—From the MeOH extract of the aerial parts of *Gentiana septemfida* a new bisiridoid diglucoside, septemfidoside [**9**], was isolated along with eight known glucosides, gelidoside [**1**], sweroside [**2**], gentiopicroside [**3**], swertiamarin [**4**], eustomoside [**5**], eustomorusside [**6**], eustoside [**7**], and loganic acid [**8**]. Their structures were established by spectral studies.

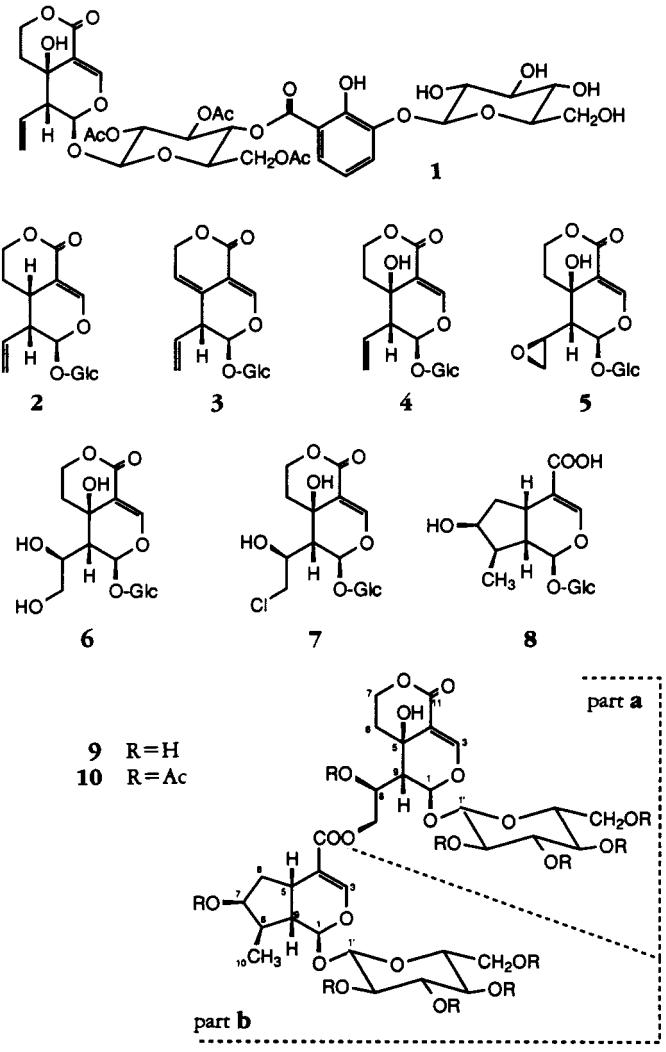
Gentiana species (Gentianaceae) have been used in traditional folk medicine for a long time. *Gentiana lutea, Gentiana asclepiadea, Gentiana olivieri,* and *Gentiana cruciata* have been used as antipyretics, stomachics, and stimulants of appetite in Anatolia. Recently five iridoid and secoiridoid glucosides have been reported from *G. olivieri* Griseb. (Turkish crude drug name Afat) (1), seven secoiridoid glucosides from *Gentiana gelida* Bieb. (2,3), and five from *G. cruciata* L. (4). Among the isolated compounds from *G. gelida* three were the acylsecoiridoids trifloroside, gelidoside, and gentomoside. Of these only trifloroside has been detected in *G. olivieri*. The common secoiridoids for the investigated plants were sweroside, gentiopicroside, and swertiamarin. The carbocyclic iridoid glucoside loganic acid has only been isolated from *G. olivieri*. Ikeshiro *et al.* (5) have also reported gelidoside from *Gentiana scabra* var. *burgeri* (Japanese crude drug name Rindo) and named it rindoside.

As a part of this series, we have now investigated the constituents of *Gentiana septemfida* Pallas. We describe the structure elucidation of a new bisiridoid diglucoside, septemfidoside [**9**]. This is the first occurrence of a bisiridoid glycoside reported in *Gentiana* species.

RESULTS AND DISCUSSION

Gelidoside [**1**] (2,3), sweroside [**2**] (6,7), gentiopicroside [**3**] (7), swertiamarin [**4**] (7,8), eustomoside [**5**] (8), eustomorusside [**6**] (8), eustoside [**7**] (8), and loganic acid [**8**] (9) were identified by comparison with authentic samples (tlc). Spectral data of compounds **1–8** (uv, ir and ^{1}H-nmr) were identical to those published.

Compound **9** gave an H_2SO_4/vanillin coloration identical to that of loganic acid [**8**]. It showed uv maxima at 237.5 nm and ir bands at 3384 (OH), 1700 (C=O), and 1617 cm^{-1} (C=C-O). The one-dimensional ^{1}H- (Table 1) and ^{13}C-nmr spectra (Experimental) of **9** indicated the presence of one iridoid, one secoiridoid, and two glucose units. The chemical shift values of the ^{13}C-nmr signals of **9** were in good agreement with those of loganic acid (9) and eustomorusside (3). Furthermore, in the ^{1}H-nmr spectrum, the chemical shifts and the coupling constants of these two sets of signals (Table 1) confirmed this suggestion. The low-field ^{1}H chemical shifts of the ABX system signals attributed to protons on C-10 of the eustomorusside moiety (δ 3.99 and 4.31, each 1H, dd, J = 11.8 and 6.9 Hz and 11.8 and 2.8



Hz, respectively) showed that this group was esterified to the carboxyl group of the loganic acid unit. This conclusion was also supported by comparison of the ^{13}C-nmr signals attributed to C-10 part **a** (66.38 ppm) and C-8 part **a** (68.14 ppm) with those of C-10 (64.7 ppm) and C-8 (70.8 ppm) signals of eustomorusside (3). Other evidence was obtained by the positive fabms of **9**. Ions at *m/z* 767 $[M+H]^+$ and 789 $[M+Na]^+$ confirmed mol wt 766 compatible with the molecular formula $C_{32}H_{46}O_{21}$.

Mild acetylation of **9** yielded septemfidoside decaacetate [**10**]. The complete interpretation of the ^{1}H-nmr spectrum of **10** (Table 1) was based on a 2D ^{1}H,^{1}H-homonuclear COSY experiment. Furthermore, the positive fabms of **10** was in accordance with the proposed structure (quasi molecular ions at *m/z* 1187 $[M+H]^+$ and 1211 $[M+Na]^+$).

Septemfidoside [**9**] is closely related to the bisiridoids cantleyoside, isolated from *Cantleya corniculata* (10), sylvestrosides I–IV from *Dipsacus sylvestris* (11) and laciniatosides V from *Dipsacus laciniatus* (12). The ester linkage between an iridoid and a secoiridoid moiety is the common property of all these bis-iridoid compounds, and secoiridoids are the acidic units of all dimers. How-

TABLE 1. ^{1}H-nmr Spectral Data of **9** (CD_3OD) and **10** ($CDCl_3$) (400 MHz).

Proton	Compound			
	9		**10**[a]	
	δ (ppm)	*J* (Hz)	δ (ppm)	*J* (Hz)
Eustomorusside moiety (part **a**)				
H-1a	6.04 s		5.81 br s	
H-3a	7.59 s		7.50 s	
H_2-6a	1.99 br d	14.8	1.90–2.10[b]	
	2.24 br dd	14.8, 5.3	1.90–2.10[b]	
H_2-7a	4.38 dd	10.8, 3.9	4.37 br dd	11.1, 3.6
	4.79 br d	10.8	4.90 br dd	11.1, 4
H-8a	3.86–3.90[b]		5.12[b]	
H-9a	2.53 d	5.9	2.69 br d	5.5
H_2-10a	3.99 dd	11.8, 6.9	4.01 dd	12.6, 7.5
	4.31 dd	11.8, 2.8	4.43 dd	12.6, 2.1
H-1′a	4.64 d	7.9	4.83 d	8.1
H-2′a	3.16–3.4[b]		5.00 dd	8.1, 9.7
H-3′a	3.16–3.4[b]		5.30 t	9.6
H-4′a	3.16–3.4[b]		5.09 t	9.8
H-5′a	3.16–3.4[b]		3.78 m	
H_2-6′a	3.63–3.70[b]		4.18 dd	12.4, 2.2
	3.86–3.90[b]		4.30 dd	12.4, 5.3
5-OH			3.83 s	
Loganic acid moiety (part **b**)				
H-1b	5.28 d	4.4	5.16 d	3.4
H-3b	7.46 d	0.9	7.29 br s	
H-5b	3.12 m		2.96 m	
H_2-6b	1.65 ddd	13.5, 7.5, 5	1.69 ddd (dt)	14.9, 5.7
	2.25 ddd	13.5, 8, 1.6	2.23 ddd	14.9, 6.7, 1.4
H-7b	4.04 m		5.11[b]	
H-8b	1.87 m		1.95[b]	
H-9b	2.04 ddd (dt)	4.4, 9.2	2.18[b]	
H-10b	1.09 d	6.9	1.03 d	6.8
H-1′b	4.65 d	7.9	4.85 d	8.1
H-2′b	3.16–3.4[b]		4.97 dd	8.1, 9.5
H-3′b	3.16–3.4[b]		5.24 t	9.5
H-4′b	3.16–3.4[b]		5.10 t	9.7
H-5′b	3.16–3.4[b]		3.75 m	
H_2-6′b	3.63–3.70[b]		4.16 dd	12.3, 2.3
	3.86–3.90[b]		4.30 dd	12.3, 5

[a]Compound **10** has additional signals at δ 1.93, 2.01, 2.02, 2.03, 2.046, 2.049, 2.06, 2.09 (×2), and 2.011 (each 3H, s) belonging to ten aliphatic acetoxy groups.

[b]Signal pattern unclear due to overlapping.

ever, septemfidoside [**9**] differs from the other in having a carbocyclic iridoid moiety as the acidic part of the ester group.

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—Medium pressure liquid chromatography (mplc) Sepralyte C18, 40 μm (Analytichem); tlc Si gel 60 F_{254} (Merck) plates; cc Si gel 60 (0.063–0.2 mm, Merck) and polyamide (Woelm); iridoids were detected by spraying with 1% vanillin/H_2SO_4, followed by heating at 100° for 5 min.

Uv spectra (λ max) Shimadzu 160 A Spectrophotometer; spectroscopic-grade MeOH. Ir spectra (cm^{-1}) Perkin-Elmer 1600 Spectrograph (FT mode). Optical rotations Jobin-Yvon Polarimeter. ^{1}H- and ^{13}C-nmr spectra [δ (ppm), *J* (Hz)] at 300.13 and 400 MHz (^{1}H) and 75.47

and 100 MHz (^{13}C) in Ft mode using Bruker WM 300 (1D) and AM 400 (1D and 2D) instruments with TMS as internal standard. Positive fabms Finnigan MAT 90 mass spectrometer in glycerol or NOBA.

ISOLATION.—Aerial parts of *G. septemfida* were collected in July 1989 in the vicinities of Göle-KARS (Turkey). Voucher specimens are deposited in the Herbarium of Hacettepe University, Faculty of Pharmacy (HUEF 89-025). Dried and powdered aerial parts of the plants (290 *g*) were extracted with MeOH (1 liter × 3). After concentration of the combined extracts in vacuo, H_2O (500 ml) was added and the insoluble material was filtered off. The H_2O layer was then extracted successively with petroleum ether, $CHCl_3$ (0.5 liter × 4) and *n*-BuOH (0.5 liter × 4). The $CHCl_3$ and *n*-BuOH layers were concentrated in vacuo to give the residues 1.80 g and 22.5 g, respectively. The *n*-BuOH extract was chromatographed on a Polyamide (80 g) column with H_2O as eluent, and fractions A–E were collected. Fraction A was chromatographed on a Si gel (200 g) column. Elution with $CHCl_3$-MeOH-H_2O (80:20:2, 70:30:3, 60:40:4) gave four major fractions (A1–A4). Fraction A3 was applied to mplc. Eluting with 30–40% MeOH, septemfidoside [**9**] (25 mg) and eustomorusside [**6**] (146 mg) were obtained. Septemfidoside [**9**] was purified by a Si gel (25 g) cc eluting with $CHCl_3$-MeOH-H_2O (60:40:4). Eustoside [**7**] (27 mg) and eustomoside [**5**] (16 mg) were obtained from fraction A2 and purified by mplc with 5–30% MeOH. Sweroside [**2**] (30 mg), gentiopicroside [**3**] (45 mg), and swertiamarin [**4**] (20 mg) were isolated from fraction A1 and purified by mplc using 10–30% MeOH as solvent system. Loganic acid [**8**] (47 mg) was obtained from fraction A4 by mplc with 20–30% MeOH and purified by mplc using 5% MeOH as solvent system.

The $CHCl_3$ extract was first chromatographed on a Si gel (100 g) column with $CHCl_3$-MeOH (9:1), and a major fraction was obtained. Purification of this fraction by mplc with 60% MeOH yielded gelidoside [**1**] (69 mg).

Septemfidoside [**9**].—$[\alpha]^{20}D$ −105° (MeOH, c = 1.7 mg/ml); uv 237.5 nm (log ε 4.19); ir (KBr) 3384 cm^{-1} (O-H), 1700 cm^{-1} (C=O, conjugated ester), 1617 cm^{-1} (C=C-O); ^1H nmr (400 MHz, CD_3OD) see Table 1; ^{13}C nmr (75.47 MHz, CD_3OD) eustomorusside moiety (aglycone) δ 96.5 d (**1a**), 154.62 d (**3a**), 109.95 s (**4a**), 64.44 s (**5a**), 33.06 t (**6a**), 65.9 t (**7a**), 68.14 d (**8a**), 51.1 d (**9a**), 66.38 t (**10a**), 167.75 s (**11a**); loganic acid moiety (aglycone) δ 97.62 d (**1b**), 152.74 d (**3b**), 113.87 s (**4b**), 32.14 d (**5b**), 42.7 t (**6b**), 75.12 d (**7b**), 42.12 d (**8b**), 46.53 d (**9b**), 13.39 q (**10b**), 168.77 s (**11b**); glucose moieties δ 100.06 d, 100.06 d (**1'a,b**), 74.77 d, 74.46 d (**2'a,b**), 78.04 d, 77.66 d (**3'a,b**), 71.62 d, 71.34 d (**4'a,b**), 78.4 d, 78.36 d (**5'a,b**), 62.77 t, 62.59 t (**6'a,b**); fabms (glycerol, positive ion mode) (rel. int. %) *m/z* $[M+K]^+$ 805 (32.26), $[M+Na]^+$ 789 (42), $[M+H]^+$ 767 (100).

SEPTEMFIDOSIDE DECAACETATE [**10**].—Compound **9** (20 mg) in pyridine-Ac_2O (1:1) (2 ml) was kept at room temperature overnight. The mixture was poured into ice-H_2O and the precipitate filtered off. The precipitate was then washed with ice-H_2O and lyophilized: ir (KBr) 1752 cm^{-1} (C=O, ester), 1629 cm^{-1} (C=C-O); ^1H-nmr see Table 1; fabms (NOBA, positive ion mode) *m/z* $[M+Na]^+$ 1211, $[M+H]^+$ 1187.

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