Iridoid and Phenylethyl Glycosides from *Globularia sintenisii*

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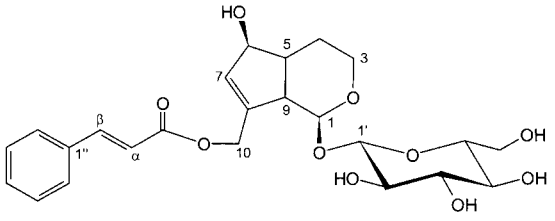
A new iridoid glycoside, sintenoside (**1**) and two new phenylethyl glycosides, globusintenoside (=2-(3,4-dihydroxyphenyl)ethyl-*O*-6-*O*-feruloyl-*β*-D-glucopyranosyl-(1→4)-*α*-L-rhamnopyranosyl-(1→3)-4-*O*-caffeoyl-*β*-D-glucopyranoside; **2**) and 3‴-*O*-methylcrenatoside (=1,2-*O*-[2-(3,4-dihydroxyphenyl)ethan-1,2-diyl]-3-*O*-*α*-L-4-*O*-feruloyl-rhamnopyranosyl-*β*-D-glucopyranose; **3**) were isolated from the underground parts of *Globularia sintenisii*, along with three known iridoid glycosides, lytanthosalin, globularin, catalpol, and six known phenylethyl glycosides, verbascoside, isoverbascoside, leucoscepthoside A, plantainoside C, martynoside, and isocrenatoside. The structure elucidation of the isolated compounds was performed by spectroscopic methods (MS and 1D and 2D NMR).

1. Introduction. – In the flora of Turkey, the genus *Globularia* L. (Globulariaceae) is represented by nine species [1][2], some of which are traditionally used as a diuretic, laxative, carminative, and tonic and for the treatment of hemorrhoids [3][4]. Our previous studies have resulted in the isolation of phenylethyl, iridoid, and flavonoid glycosides as well as of sugar esters from five *Globularia* species (*G. trichosantha*, *G. davisiana*, *G. orientalis*, *G. dumulosa*, and *G. cordifolia*) [5–10]. In the course of our ongoing phytochemical studies on Turkish *Globularia* species, we have investigated *G. sintenisii*. In this paper, we report the isolation and structure elucidation of a new iridoid glycoside, sintenoside (**1**), and of two new phenylethyl glycosides, globusintenoside (**2**) and 3‴-*O*-methylcrenatoside (**3**), obtained from the underground parts of *Globularia sintenisii* (*Fig.*)

2. Results and Discussion. – The crude MeOH extract of the underground parts of *G. sintenisii* were fractionated by column chromatography (CC; *Polyamide*). Iridoid and phenylethyl glycosides were obtained from these fractions by utilizing various types of liquid chromatography (MPLC (C_{18}) and CC (silica gel)).

Compound **1** was obtained as an amorphous powder. The molecular formula was determined as $C_{24}H_{30}O_{10}$ by positive-ion ESI-MS (*m/z* 501 ($[M+Na]^+$), 979 ($[2M+Na]^+$)). The UV spectrum exhibited maxima at 217 and 275 nm. Its IR spectrum showed absorptions at 3421, 1704, 1636, and 1450 cm^{-1} indicating OH and ester C=O functionalities and aromatic C=C bonds. Further spectroscopic data of **1** allowed to establish its structure as 10-*O*-[(*E*)-cinnamoyl]-3,4-dihydroaucubin, which we name sintenoside[1]).

[1]) Trivial numbering; for systematic names, see *Exper. Part.*



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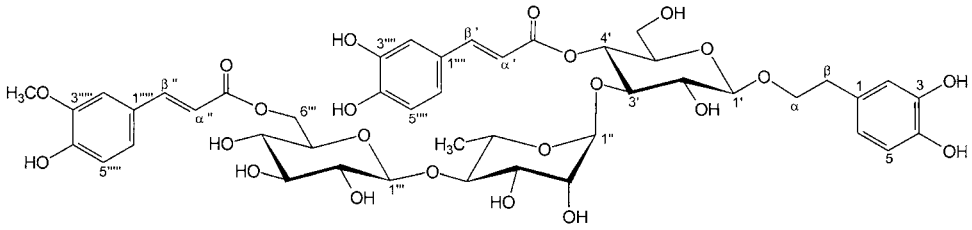

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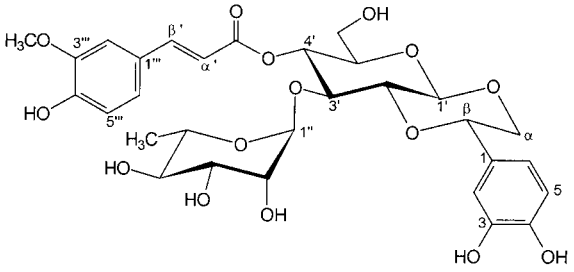

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Figure. *Structures of compounds* **1**–**3**[1])

The ^{1}H-NMR spectrum (*Table 1*) of **1** displayed signals due to an acylated iridoid glycoside. The anomeric-proton resonance at δ 4.64 ($d, J = 7.9$ Hz) and the signals in the region δ 3.25–3.88 together with the corresponding C-resonances indicated the presence of a β-D-glucopyranosyl unit. In addition, two olefinic protons observed as an AX system at δ 6.62 and 7.77 ($J_{AX} = 16.2$ Hz) and five aromatic protons at δ 7.67 (2 H) and 7.44 (3 H) were consistent with the presence of an (*E*)-cinnamoyl moiety. The ^{13}C-NMR spectrum of **1** exhibited 24 signals; six of them were attributed to a β-D-glucopyranosyl (Glc) unit, while nine of them were ascribed to an (*E*)-cinnamoyl moiety. All the remaining C-resonances indicated that **1** has an iridoid skeleton (cyclopentapyran ring system) with nine C-atoms. The complete assignments of all δ(H) and δ(C) were based on DQF-COSY, HSQC, and HMBC experiments. Thus, the OCH_2 signals (δ 4.02 and 3.60) and the CH_2 resonances (δ 1.84 and 1.69) ascribed to CH_2(3) and CH_2(4)[1]), respectively, indicated the lack of a C=C bond between C(3) and C(4) in the pyran ring, like in davisioside [7]. The assigned NMR data of **1** were similar to those of davisioside, except for the presence of signals due to the (*E*)-cinnamoyl moiety in the spectra of **1**, instead of those of a benzoyl moiety as is the case of davisioside. The downfield shifts for the CH_2(10) signals

(δ 4.99 and 4.86) and the significant long-range correlations between CH_2(10) and the carbonyl C-atom (δ 168.3) of the cinnamic acid indicated the site of acylation. The HMBC correlations (*Table 1*) between H–C(1) and C(1′) and *vice versa* revealed that the β-D-glucopyranosyl unit was attached at the usual position, OH–C(1).

Table 1. *^{1}H- and ^{13}C-NMR Data*[a]) (MeOD) *and HMBC Correlations for* **1**[1]). δ in ppm, J in Hz.

	δ (H)[b])	δ (C)[c])	HMBC (H → C)
Aglycone: H–C(1)	4.95 (d, J = 5.7)	99.4	C(1′), C(3)
CH_2(3)	4.02 (m), 3.60 (m)	61.7	C(1), C(5)
CH_2(4)	1.84 (m), 1.69 (m)	25.3	
H–C(5)	2.45 (m)	46.1	C(1), C(3), C(4), C(6)
H–C(6)	4.58 (br. d, J = 5.3)	79.3	
H–C(7)	5.86 (br. s)	132.1	C(5), C(9)
C(8)	–	143.8	
H–C(9)	2.86 (t, J = 6.6)	48.6	C(1), C(7), C(8)
CH_2(10)	4.99, 4.86 (2d, J = 14.5)	63.5	C(7), C(8), C=O
Glc: H–C(1′)	4.64 (d, J = 7.9)	99.6	C(1)
H–C(2′)	3.25 (dd, J = 7.9, 8.7)	75.0	C(1′)
H–C(3′)	3.39 (t, J = 8.7)	78.1	C(4′)
H–C(4′)	3.33 (t, J = 8.7)	71.6	C(3′), C(5′)
H–C(5′)	3.30 (m)	78.2	
CH_2(6′)	3.88 (dd, J = 11.9, 1.6),	62.9	
	3.68 (dd, J = 11.9, 5.3)		C(5′)
Cinnamoyl: C(1″)	–	135.7	
H–C(2″)	7.67 (m)	129.3	C(4″)
H–C(3″)	7.44 (m)	130.6	C(1″)
H–C(4″)	7.44 (m)	131.6	
H–C(5″)	7.44 (m)	130.6	C(1″)
H–C(6″)	7.67 (m)	129.3	C(4″)
H–C(α)	6.62 (d, J = 16.2)	118.6	C(1″)
H–C(β)	7.77 (d, J = 16.2)	146.7	C(2″), C(6″), C=O
C=O	–	168.3	

[a]) All δ(H) and δ(C) assignments are based on 2D NMR (DQF-COSY, HSQC, HMBC). [b]) Recorded at 600 MHz. [c]) Recorded at 150 MHz.

Compound **2** was obtained as a pale yellow amorphous powder with a molecular formula of $C_{45}H_{54}O_{23}$, as determined by data of the negative- and positive-ion ESI-MS, showing $[M-H]^-$ at m/z 961 and $[M+Na]^+$ at m/z 985. The NMR spectra clearly established that **2** is a phenylethyl triglycoside esterified with a caffeic acid (= 3-(3,4-dihydroxyphenyl)prop-2-enoic acid) and a ferulic acid (= 3-(4-hydroxy-3-methoxyphenyl)prop-2-enoic acid). Based on further spectroscopic data, the structure of **2** was identified as 2-(3,4-dihydroxyphenyl)ethyl *O*-6-*O*-feruloyl-β-D-glucopyranosyl-(1 → 4)-*O*-α-L-rhamnopyranosyl-(1 → 3)-4-*O*-caffeoyl-β-D-glucopyranoside, for which the trivial name globusintenoide[1]) is proposed.

The ^{1}H-NMR spectrum (*Table 2*) of **2** exhibited the characteristic signals belonging to a 2-(3,4-dihydroxyphenyl)ethoxy moiety: protons of the aromatic ring as an *ABX* system at δ 6.72 (d, J = 1.3 Hz), 6.71 (d, J = 8.0 Hz), and 6.60 (dd, J = 1.3, 8.0 Hz) as well as $CH_2(\beta)$ at δ 2.83 (t, J = 7.1 Hz) and the two nonequivalent of $CH_2(\alpha)$ at δ 4.07 and 3.73 (each 1 H, m). Additional resonances appeared as 2 *ABX* systems (δ 7.08 (d, J = 1.3 Hz, H–C(2‴)), 6.82 (d, J = 8.0 Hz, H–C(5‴)), and 6.98 (dd, J = 1.3 and 8.0 Hz, H–C(6‴)); δ 7.18 (d, J = 1.3 Hz, H–C(2⁗)), 6.83 (d, J = 8.0 Hz, H–C(5⁗)), and 7.05 (dd, J = 1.3 and 8.0 Hz, H–C(6⁗))

and as two *AX* systems (δ 6.25 and 7.61 (d, J_{AX} = 16.0 Hz, H–C(α') and H–C(β') resp.); δ 6.34 and 7.61 (d, J_{AX} = 16.0 Hz, H–C(α'') and H–C(β''), resp.), which were indicative of the presence of a (*E*)-caffeoyl and a (*E*)-feruloyl unit in **2**. Moreover, three anomeric-proton resonances appeared at δ 5.27 (d, J = 1.5 Hz, H–C(1″) of α-L-rhamnose (Rha)), 4.45 (d, J = 8.3 Hz, H–C(1‴) of β-D-glucose), and 4.38 (H–C(1′) of β-D-glucose), indicating its triglycosidic structure. The complete assignments of all δ(H) and δ(C) were based on DQF-COSY, TOCSY, HSQC, and HMBC experiments. The ^{13}C-NMR data confirmed the triglycosidic sugar chain in **2**, exhibiting three anomeric C-resonances at δ 105.6, 103.6, and 101.7, which show correlations with the anomeric protons of the two Glc and the Rha unit, respectively. The δ(C) arising from one Glc and the Rha moieties indicated that this Glc unit is glycosylated at C(3′) (δ 80.0) and the Rha unit at C(4″) (δ 84.2). The acyloxy moieties were located at C(4′) and C(6‴) of the Glc units, on the basis of significant deshielding of the H–C(4′) (δ 4.95) and CH_2(6‴) signals (δ 4.49 and 4.24). Finally, the HMBC experiment (*Table 2*) permitted the determination of all of the relevant interfragmental connectivities. Thus, cross-peaks were observed between H–C(1′) (δ 4.38) of Glc and C(α) (δ 72.6) of the phenylethyl moiety, between H–C(1″) (δ 5.27) of Rha and C(3′) (δ 80.0) of Glc, between H–C(1‴) (δ 4.45) of the terminal Glc and C(4″) (δ 84.2) of Rha, between H–C(4′) of Glc and the carbonyl C-atom (δ 168.8) of the caffeoyl moiety, and between CH_2(6‴) of the terminal Glc and the carbonyl C-atom (δ 168.8) of the feruloyl moiety. Based on these observations, compound **2** was found to be ferulic acid ester of rossicaside A [11].

Compound **3** was obtained as a pale yellow amorphous powder, and its molecular formula was established as $C_{30}H_{36}O_{15}$ by negative-ion ESI-MS (m/z 635 [$M-H$]$^-$). The UV and IR spectra were characteristic for a phenylethyl glycoside. Based on the spectral data and comparison with those of crenatoside [12], the structure of compound **3** was established as 3‴-*O*-methylcrenatoside[1]), *i.e.*, as 1,2-*O*-[2-(3,4-dihydroxyphenyl)-ethane-1,2-diyl]-3-*O*-α-L-4-*O*-feruloyl-rhamnopyranosyl-β-D-glucopyranose.

The ^{1}H-NMR spectrum (*Table 3*) displayed signals of two *ABX*-type aromatic protons at δ 6.73–7.24, one pair of *trans*-olefinic protons as an *AX* system at δ 6.40 and 7.72 (J_{AX} = 15.8 Hz), two anomeric protons, indicative of the presence of one β- and one α-linked sugar (δ 4.59 d, J = 7.8 Hz; δ 5.22 d, J = 1.5 Hz, resp.), one secondary Me group at δ 1.17 (d, J = 6.5 Hz) as well as a MeO signal at δ 3.93. Moreover, the ^{1}H-NMR spectrum showed signals of *ABX*-type alphatic protons at δ 4.02 (dd, J = 2.6, 12.3 Hz), 3.67 (dd, J = 10.0, 12.3 Hz), and 4.64 (dd, J = 2.6 and 10.0 Hz). The ^{1}H- and ^{13}C-NMR data of **3** based on 2D NMR were closely similar to those of crenatoside [12], except for the resonances at δ 3.93 and 56.1 arising from a MeO group. The MeO group was found to be located at C(3‴) of the acyl moiety due to the downfield shift (0.1 ppm) of the *trans*-olefinic protons and the long-range correlations between the protons of MeO and C(3‴) (δ 149.4) of the acyl unit observed in the HMBC spectrum (*Table 3*). Thus, **3** contains feruloyl moiety instead of the caffeoyl moiety of crenatoside.

Besides these new compounds, three known iridoid glycosides, lytanthosalin [13], globularin [14], and catalpol [14], and six known phenylethyl glycosides, verbascoside [15], isoverbascoside [16], leucoscepthoside A [16], plantainoside C [17], martynoside [18], and isocrenatoside [19], were isolated and identified by comparison of their spectroscopic data with published values.

Sintenoside (**1**) is another representative of the rare iridoid skeleton lacking the C=C bond between C(3) and C(4). In our previous studies, we have also isolated these kinds of ester iridoids, *i.e.*, davisioside [7], 5-hydroxydavisioside [10], and 10-*O*-benzoylglobularigenin [9], from several *Globularia* species. Thus, these compounds can be considered chemotaxonomic markers for the genus *Globularia*. Globusintenoside (**2**) is the first example of a phenylethyl glycoside bearing two aromatic acyl units. The 3‴-*O*-methylcrenatoside (**3**) and isocrenatoside have an ether linkage between a glucose and a phenylethyl moiety in addition to a glycosidic linkage. These compounds are also rare compounds, and 3‴-*O*-methylcrenatoside (**3**) is the third example of this group. The other examples, crenatoside [12] and isocrenatoside [19], have only been

Table 2. *^{1}H- and ^{13}C-NMR Data*[a]) (MeOD) *and HMBC Correlations for* **2**[1]). δ in ppm, J in Hz.

	δ(H)[b])	δ(C)[c])	HMBC (H → C)
Aglycone: C(1)	–	131.3	
H–C(2)	6.72 (*d*, *J* = 1.3)	116.8	C(4), C(6)
C(3)	–	146.0	
C(4)	–	144.5	
H–C(5)	6.71 (*d*, *J* = 8.0)	116.2	C(1), C(3)
H–C(6)	6.60 (*dd*, *J* = 1.3, 8.0)	121.0	C(2), C(4)
$CH_2(\alpha)$	4.07 (*m*), 3.73 (*m*)	72.6	C(1)
$CH_2(\beta)$	2.83 (*t*, *J* = 7.1)	36.2	
Glc: H–C(1′)	4.38 (*d*, *J* = 7.8)	103.6	C(α)
H–C(2′)	3.42 (*dd*, *J* = 7.8, 9.0)	76.2	
H–C(3′)	3.86 (*t*, *J* = 9.0)	80.0	
H–C(4′)	4.95 (*t*, *J* = 9.0)	70.2	C=O
H–C(5′)	3.56 (*m*)	75.7	
CH_2(6′)	3.65 (*dd*, *J* = 2.5, 11.5), 3.55 (*dd*, 5.5, 11.5)	62.0	
Rha: H–C(1″)	5.27 (*d*, *J* = 1.5)	101.7	C(3′), C(2″), C(5″)
H–C(2″)	3.95 (*dd*, *J* = 1.5, 2.5)	71.9	
H–C(3″)	3.75 (*dd*, *J* = 2.5, 9.0)	72.0	
H–C(4″)	3.49 (*t*, *J* = 9.0)	84.2	
H–C(5″)	3.72 (*m*)	68.6	
Me(6″)	1.22 (*d*, *J* = 6.5)	18.6	C(4″), C(5″)
Glc(→ Rha): H–C(1‴)	4.45 (*d*, *J* = 8.3)	105.6	C(4″)
H–C(2‴)	3.05 (*dd*, *J* = 8.3, 8.9)	75.5	
H–C(3‴)	3.34 (*t*, *J* = 8.9)	77.8	
H–C(4‴)	3.19 (*t*, 8.9)	71.6	
H–C(5‴)	3.49 (*m*)	75.3	
CH_2(6‴)	4.49 (*dd*, *J* = 1.9, 11.5), 4.24 (*dd*, *J* = 5.6, 11.5)	64.7	C=O
Caffeoyl: C(1⁗)		127.4	
H–C(2⁗)	7.08 (*d*, *J* = 1.3)	115.1	C(β′), C(3⁗), C(4⁗), C(6⁗)
C(3⁗)	–	148.2	
C(4⁗)	–	149.7	
H–C(5⁗)	6.82 (*d*, *J* = 8.0)	116.3	C(1⁗), C(3⁗)
H–C(6⁗)	6.98 (*dd*, *J* = 1.3, 8.0)	123.0	C(β′), C(2⁗), C(4⁗)
H–C(α′)	6.25 (*d*, *J* = 16.0)	114.4	C(1⁗)
H–C(β′)	7.61 (*d*, *J* = 16.0)	146.9	C=O, C(2⁗), C(6⁗)
C=O	–	168.8	
Feruloyl: C(1⁗′)	–	127.6	
H–C(2⁗′)	7.18 (*d*, *J* = 1.3)	111.4	C(β″), C(4⁗′), C(6⁗′)
C(3⁗′)	–	150.5	
C(4⁗′)	–	149.3	
H–C(5⁗′)	6.83 (*d*, *J* = 8.0)	116.2	C(1⁗′), C(3⁗′)
H–C(6⁗′)	7.05 (*dd*, *J* = 1.3, 8.0)	123.8	C(β″), C(2⁗′), C(4⁗′)
H–C(α″)	6.34 (*d*, *J* = 16.0)	115.1	C(1⁗′)
H–C(β″)	7.61 (*d*, *J* = 16.0)	146.9	C=O, C(2⁗′), C(6⁗′)
C=O	–	168.8	
MeO	3.92 (*s*)	56.2	C(3⁗′)

[a]) All δ(H) and δ(C) assignments are based on 2D NMR (DQF-COSY, HSQC, HMBC). [b]) Recorded at 600 MHz. [c]) Recorded at 150 MHz.

Table 3. *^{1}H- and ^{13}C-NMR Data*[a]) (MeOD) *and HMBC Correlations for* **3**[1]). δ in ppm, J in Hz.

	δ(H)[b])	δ(C)[c])	HMBC (H → C)
Aglycone: C(1)	–	129.8	
H–C(2)	6.86 (*d*, *J* = 1.2)	114.0	C(4), C(6)
C(3)	–	146.4	
C(4)	–	146.4	
H–C(5)	6.76 (*d*, *J* = 8.3)	115.8	C(1), C(3)
H–C(6)	6.73 (*dd*, *J* = 1.2, 8.3)	118.7	C(2), C(4)
$CH_{27}(\alpha)$	4.02 (*dd*, *J* = 2.6, 12.3), 3.67 (*dd*, *J* = 10.0, 12.3)	72.6	C(1)
H–C(β)	4.64 (*dd*, *J* = 2.6, 10.0)	78.1	
Glc: H–C(1′)	4.59 (*d*, *J* = 7.8)	98.9	C(2′)
H–C(2′)	3.50 (*dd*, *J* = 7.8, 9.2)	81.6	C(1′), C(3′)
H–C(3′)	4.18 (*dd*, *J* = 9.2, 9.6)	76.9	C(1″), C(2′), C(4′)
H–C(4′)	5.13 (*t*, *J* = 9.6)	69.8	C=O, C(3′)
H–C(5′)	3.81 (*m*)	77.5	
CH_2(6′)	3.71 (*dd*, *J* = 2.0, 12.2), 3.62 (*dd*, *J* = 5.2, 12.2)	61.8	
Rha: H–C(1″)	5.22 (*d*, *J* = 1.5)	102.0	C(3′), C(2″)
H–C(2″)	3.81 (*dd*, *J* = 1.5, 2.3)	71.7	
H–C(3″)	3.56 (*dd*, *J* = 2.3, 8.9)	71.7	
H–C(4″)	3.31 (*t*, *J* = 8.9)	73.3	
H–C(5″)	3.66 (*m*)	70.1	
Me(6″)	1.17 (*d*, *J* = 6.5)	17.9	C(4″), C(5″)
Feruloyl: C(1‴)	–	127.8	
H–C(2‴)	7.24 (*d*, *J* = 1.2)	111.4	C(β′), C(3‴), C(4‴), C(6‴)
C(3‴)	–	149.4	
C(4‴)	–	151.0	
H–C(5‴)	6.85 (*d*, *J* = 8.5)	116.2	C(1‴), C(3‴)
H–C(6‴)	7.12 (*dd*, *J* = 1.2, 8.5)	124.1	C(β′), C(2‴), C(4‴)
H–C(α′)	6.40 (*d*, *J* = 15.8)	114.6	C(1‴)
H–C(β′)	7.72 (*d*, *J* = 15.8)	147.9	C=O, C(2‴), C(6‴)
C=O	–	168.0	
MeO	3.93 (*s*)	56.1	C(3‴)

[a]) All δ(H) and δ(C) assignments are based on 2D NMR (DQF-COSY, HSQC, HMBC). [b]) Recorded at 600 MHz. [c]) Recorded at 150 MHz.

reported from the genus *Orobanche* besides *Globularia* [5][6] until. Martynoside and plantainoside C are also reported for the first time from a *Globularia* species.

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Experimental Part

General. TLC: precoated silica gel *60 F_{254}* (*Merck*) plates; eluents $CHCl_3$/MeOH/H_2O 80:20:1, 70:30:3, and 61:32:7, and AcOEt/MeOH/H_2O 20:2:1; visualization by spraying with 1% vanillin in conc. H_2SO_4 soln. followed by heating at 105° for 5 min. Medium-pressure liquid chromatography (MPLC): *Lewa-M5* pump, *LKB-17000-Minirac* fraction collector, *Rheodyne* injector, *Büchi* columns (2.6 × 46 cm and 3 × 24 cm); *LiChroprep C_{18}* (*Merck*). Column chromatography (CC): silica gel *60* (0.063–0.200 mm; *Merck*, Darmstadt) and *Polyamide* (*Fluka*). Optical rotations: *Autopol-IV* polarimeter. UV Spectra: λ_{max} in nm. IR Spectra (KBr): *Perkin-Elmer 2000* FT-IR spectrometer; in cm^{-1}. NMR Spectra: *Bruker AMX-600* instruments (600 (^{1}H) and 150 MHz (^{13}C)) with XWIN NMR software package; δ in ppm, J in Hz. ESI-MS: *Finnigan TSQ-7000* instrument; positive- and negative-ion mode; in m/z.

Plant Material. Globularia sintenisii HAUSSKN. & WETTST. was collected from Mardin, Mazıdağı in Southeast Anatolia, Turkey, in June 2002, and identified by Dr. *Ali A. Dönmez* Department of Biology, Faculty of Science, Hacettepe University, 06532 Ankara, Turkey. A voucher specimen has been deposited in the Herbarium of the same department (AAD 10945).

Extraction and Isolation. The powdered underground parts of *Globularia sintenisii* (250 g) were extracted with MeOH (3×1.5 l, 5 h) and then filtered. The combined filtrates were evaporated: 18 g (7.2%) of crude extract. An aliquot of the extract (17 g) was subjected to CC (*Polyamide* (80 g), H_2O (200 ml), then $15 \rightarrow 100\%$ MeOH/H_2O in steps of 15% of MeOH (each 200 ml)): *Frs. A–H*. *Fr. B* (1 g) was subjected to MPLC (*LiChroprep C*$_{18}$, 3×24 cm column, $0 \rightarrow 60\%$ MeOH/H_2O in steps of 5% of MeOH (each 100 ml)): *catalpol* (6 mg) and *Fr. B*$_2$–*B*$_4$. *Fr. B*$_3$ (149 mg) was subjected to CC a (silica gel (15 g), AcOEt/MeOH/H_2O 40 : 2 : 1 (200 ml)): *globularin* (105 mg). *Fr. B*$_4$ (55 mg) was likewise subjected to CC (silica gel (8 g), same eluent (200 ml): *lytanthosalin* (21 mg) and *sintenoside* (**1**; 8 mg). *Fr. D* (3.100 g) was subjected to MPLC (*C*$_{18}$, 2.6×46 cm column, $15 \rightarrow 50\%$ MeOH/H_2O in steps of 5% of MeOH (each 200 ml)): *verbascoside* (540 mg) and *Fr. D*$_2$–*D*$_8$. *Fr. D*$_3$ (132 mg) was further subjected to CC (silica gel (15 g), $CHCl_3$/MeOH/H_2O 85 : 15 : 1 and 80 : 20 : 1 (both 100 ml)): *leucosceptoside A* (18 mg) and *isoverbascoside* (25 mg). Purification of *Fr. D*$_4$ (200 mg) by CC (silica gel (20 g), CH_2Cl_2/MeOH/H_2O 90 : 10 : 1 and 40 : 10 : 1 (both 100 ml)) furnished *3‴-O-methylcrenatoside* (**3**; 7 mg). *Fr. D*$_5$ (175 mg) was subjected to CC (silica gel (18 g), $CHCl_3$/MeOH/H_2O 90 : 10 : 1, 40 : 10 : 1, and 70 : 30 : 3 (each 100 ml)): pure *martynoside* (4 mg) and *plantainoside C* (24 mg). *Fr. F* (1.360 g) was subjected to MPLC (*C*$_{18}$, 3×24 cm column, $20 \rightarrow 50\%$ MeOH/H_2O in steps of 5% of MeOH (each 100 ml)): *verbascoside* (8 mg), *isoverbascoside* (25 mg), and *Fr. F*$_3$–*F*$_5$. *Fr. F*$_3$ (76 mg) was subjected to CC (silica gel (8 g), $CHCl_3$/MeOH/H_2O 40 : 10 : 1 (200 ml)): *isocrenatoside* (13 mg). Repeated CC (silica gel (15 g), $CHCl_3$/MeOH/H_2O 70 : 30 : 3 (200 ml), 61 : 32 : 7 (50 ml)) of *Fr. F*$_4$ (140 mg) afforded *globusintenoside* (**2**, 21 mg).

Sintenoside (*(2*E*)-3-Phenylprop-2-enoic Acid [(1*S*,4*aR*,5*S*,7a*S*)-1-(β-*D*-Glucopyranosyloxy)-1,3,4,4a,5,7a-hexahydro-5-hydroxycyclopenta[*c*]pyran-7-yl]methyl Ester* **1**): Amorphous powder. $[\alpha]_D^{20} = -73.9$ ($c = 0.1$, MeOH). UV (MeOH): 217, 275. IR (KBr): 3421, 1704, 1636, 1450. ^{1}H- and ^{13}C-NMR: *Table 1*. ESI-MS: 501 ($[M + Na]^+$, $C_{24}H_{30}NaO_{10}^+$), 979 ($[2M + Na]^+$).

Globusintenoside (*2-(3,4-Dihydroxyphenyl)ethyl* O-*6*-O-*[(2*E*)-3-(4-Hydroxy-3-methoxyphenyl)-1-oxoprop-2-enyl]-β-*D*-glucopyranosyl-(1 → 4)*-O-*6-deoxy-α-*L*-mannopyranosyl-(1 → 3)-β-*D*-glucopyranoside 4-[(2*E*)-3-(3,4-Dihydroxyphenyl)prop-2-enoate]* **2**): Amorphous powder: $[\alpha]_D^{20} = -63.9$ ($c = 0.1$, MeOH). UV (MeOH): 218, 235 (sh), 248 (sh), 288 (sh), 328. IR (KBr): 3404, 1697, 1632, 1602, 1517, 1454. ^{1}H- and ^{13}C-NMR: *Table 2*. ESI-MS: 961 ($[M - H]^-$, $C_{45}H_{53}O_{23}^+$); 985 ($[M + Na]^+$).

3‴-O-Methylcrenatoside (*= 3-O-(6-Deoxy-α-L-mannopyranosyl)-1,2-*O*-[(2*S*)-2-(3,4-dihydroxyphenyl)-ethane-1,2-diyl]-β-D-glucopyranose 4-[(2*E*)-3-(4-Hydroxy-3-methoxyphenyl)prop-2-enoate]* **3**): Amorphous powder. $[\alpha]_D^{20} = -42$ ($c = 0.1$, MeOH). UV (MeOH): 219, 233 (sh), 287 (sh), 328. IR (KBr): 3418, 1718, 1635, 1600, 1558, 1517, 1449. ^{1}H- and ^{13}C-NMR: *Table 3*. ESI-MS: 635 ($[M - H]^-$, $C_{30}H_{35}O_{15}^+$).

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