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FLAVONOL GLYCOSIDES FROM *SEDUM ALBUM*

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Key Word Index—*Sedum album*; Crassulaceae: flavonols; isorhamnetin 3-rhamnoside-7-glucoside, 3-rhamnoside-7-sophoroside and 7-sophoroside.

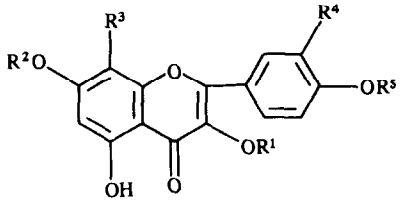
Abstract—Three new flavonol glycosides, isorhamnetin 3-rhamnoside-7-glucoside, isorhamnetin 3-rhamnoside-7-sophoroside and isorhamnetin 7-sophoroside, were isolated from the areial parts of *Sedum album*. The known compounds, quercetin, isorhamnetin and their 3-rhamnosides, quercetin 3-methyl ether, quercetin 4′-glucoside, isorhamnetin 7-glucoside, herbacetin and gossypetin 8-glucuronides were also identified. The structures of compounds were determined by means of chemical and spectroscopic methods.

INTRODUCTION

Sedum album L. is a perennial, common in the western and central parts of Europe [1, 2]. Small populations of this plant are found in Poland in the submontane regions [3]. To date, sugars, alkaloids, phenolic acids, hydroquinone, coumarins and proanthocyanins have been found in the aerial parts of the plant [4–10] and the flavonols, isorhamnetin and its 3-rhamnoside have been identified [11]. In the present study the isolation and structural determination of 12 flavonoids (**1–12**), including three new compounds (**7, 11, 12**) are described.

RESULTS AND DISCUSSION

In the aerial parts of *Sedum album* 16 flavonoids were detected, 12 of which have been isolated and identified. The presence of the previously described isorhamnetin (**4**) and isorhamnetin 3-rhamnoside (**1**) [11] was confirmed. The remaining flavonoids were isolated from the taxon for the first time. Quercetin 3-*O*-α-rhamnoside (**2**), herbacetin 8-*O*-β-glucuronide (**3**), quercetin 3-methyl ether (**5**), quercetin (**6**), isorhamnetin 7-*O*-β-glucoside (**8**), quercetin 4′-*O*-β-glucoside (**9**), and gossypetin 8-*O*-β-glucuronide (**10**) were identified on the basis of chemical, UV and ^{1}H NMR spectral analysis. The presence of 8-*O*-glycosidation in compounds **3** and **10** was confirmed by ^{13}C NMR analysis. In both compounds a chemical shift of C-9 occurs at 148.5 and of C-5 at 156.9, whereas for 8-hydroxyflavonols these resonances appear at *ca* 144 and 151 ppm, respectively [12–14]. Herbacetin 8-*O*-β-glucuronide (mp 212–214°) has been detected previously in *Rhodiola algida* [15, 16] and in *Melochia corchorifolia* (280° dec.) [17], where its structure was determined by UV and ^{1}H NMR analysis. Gossypetin 8-*O*-β-glucuronide (220° dec.) has been isolated before from *Hibiscus vitifolius* [18] and has been described as a product of acid hydrolysis of gossypetin 8-*O*-glucuronide-3-sulphate (UV, ^{1}H and ^{13}C NMR) [13]. However it should be noted that the melting points of compounds **3** (190–193°) and **10** (199–202°) are different from those described previously for herbacetin and gossypetin 8-*O*-β-glucuronides, respectively.



1 R^1 = Rha, R^2 = R^3 = R^5 = H, R^4 = OMe
2 R^1 = Rha, R^2 = R^3 = R^5 = H, R^4 = OH
3 R^1 = R^2 = R^4 = R^5 = H, R^3 = OGlur
4 R^1 = R^2 = R^3 = R^5 = H, R^4 = OMe
5 R^1 = Me, R^2 = R^3 = R^5 = H, R^4 = OH
6 R^1 = R^2 = R^3 = R^5 = H, R^4 = OH
7 R^1 = Rha, R^2 = Glc, R^3 = R^5 = H, R^4 = OMe
8 R^1 = R^3 = R^5 = H, R^2 = Glc, R^4 = OMe
9 R^1 = R^2 = R^3 = H, R^4 = OH, R^5 = Glc
10 R^1 = R^2 = R^5 = H, R^3 = OGlur, R^4 = OH
11 R^1 = Rha, R^2 = Soph, R^3 = R^5 = H, R^4 = OMe
12 R^1 = R^3 = R^5 = H, R^2 = Soph, R^4 = OMe

Three flavonoids (**7, 11, 12**) have been isolated from nature for the first time. On acid hydrolysis they all gave isorhamnetin (mp, UV and ^{1}H NMR) and sugars, which were identified as glucose in **12** and as glucose and rhamnose in **7** and **11** (COPC, TLC). FDMS yielded quasimolecular ions $[M+H]^+$ at *m/z* 625, 787 and 641, respectively which correspond to the following molecular formulae: $C_{28}H_{32}O_{16}$ for **7**, $C_{34}H_{42}O_{21}$ for **11**, and $C_{28}H_{32}O_{17}$ for **12**. These data as well as the products of partial hydrolysis provide information about the character of the diglycosides **7** and **12** and the triglycoside **11** (rhamnose to glucose ratio 1:2). The position of glycosidation, for **7** and **11** at C-3 and C-7 and for **12** at C-7, as well as the configuration of the glycosidic bonds and cyclic forms of sugars were determined by UV and NMR analysis. In the ^{1}H NMR spectrum of the TMS ether of **7** (Table 1), the presence of two anomeric proton signals at 4.96 (doublet of $J=2$ Hz) and 4.93 (doublet of $J=8$ Hz)

Table 1. ^{1}H NMR data for **7**, **11** and **12** (δ ppm)

	7	11	12
Aglycone			
H-6	6.16 *d*(2)	6.23 *d*(2)	6.26 *d*(2)
H-8	6.50 *d*(2)	6.56 *d*(2)	6.63 *d*(2)
H-5′	6.76 *d*(8)	6.80 *d*(8)	6.80 *d*(8)
H-2′	7.16–7.40 *m*	7.13–7.43 *m*	7.70 *d*(8)
H-6′			7.55 *dd*(2, 8)
OMe	3.90 *s*	3.86 *s*	3.90 *s*
Sugars			
3-Rha H-1	4.96 *d*(2)	5.00 *d*(2)	—
Me	0.80 *d*(6)	0.80 *d*(6)	—
7-Glc H-1	4.93 *d*(8)	5.20 *d*(7)	5.26 *d*(7)
2^{Glc}-Glc H-1	—	4.43 *d*(8)	4.43 *d*(8)

The remaining sugar protons were found in the regions, 3-Rha H-2 4.26 tr(3) and 2.90–3.96 *m*. Coupling constants in Hz are given in parentheses.

ppm indicated an α-rhamnose at the 3-hydroxyl, and β-glucose at the 7-hydroxyl [19, 20], which allowed the identification of **7** as isorhamnetin 3-*O*-α-L-rhamnopyranoside-7-*O*-β-D-glucopyranoside. ^{1}H NMR of the TMS ether of **11** indicated that the signal of the anomeric rhamnose proton at the 3-hydroxyl is accompanied by signals of two anomeric glucose protons at δ 5.20 and 4.43 (doublets of $J = 7 \sim 8$ Hz), the first of which is shifted downfield by 0.27 ppm as compared with that of compound **7** at the corresponding position [21]. In the ^{13}C NMR spectrum (Table 2) the signal for C-2 of the inner glucose was shifted downfield by 9.7, and C-1 upfield by 1.3 ppm [22]. Thus, **11** has the structure isorhamnetin 3-*O*-α-L-rhamnopyranoside-7-*O*-β-D-glucopyranosyl (1→2)-β-D-glucopyranoside. The interglycosidic linkage in compound **12** was determined in a similar way using (^{1}H and ^{13}C NMR spectroscopy) which suggested that it is isorhamnetin 7-*O*-β-D-glucopyranosyl (1→2)-β-D-glucopyranoside. An isorhamnetin 7-diglucoside with an undefined interglycosidic linkage (mp 202–205°) has been isolated from *Argemone mexicana* [23].

EXPERIMENTAL

Plant material. S. album was cultivated in the Garden of Medicinal Plants in Łódź, Poland from seeds provided by the Botanical Garden in Wageningen. Aerial parts of the plant were collected at the time of flowering in July 1985. A voucher specimen is deposited in the Herbarium of the Department of Pharmacognosy Medical Academy of Łódź, Poland.

General. Mps uncorr. PC-Whatman No. 1 paper, solvent systems: (1) *n*-BuOH–HOAc–H_2O (4:1:5), (2) 15% HOAc. TLC: CD-Alufolien Kieselgel 60 (Merck) with EtOH–25% NH_4OH (4:1). FDMS: Varian MAT 711, emitter current 20–25 mA. ^{1}H NMR: 360 60 MHz (TMS ethers of compounds in CCl_4, acetate in $CDCl_3$) and ^{13}C NMR: 300 MHz (underivatized glycosides in DMSO-d_6), both with TMS as int. standard.

Flavonoids were visualized in UV light. UV spectra and TMS ethers were obtained according to [19]. Acid hydrolysis was conducted in: 1% H_2SO_4 for compounds **1**, **2**, 5% H_2SO_4 **9**, 10% H_2SO_4, **7**, **8**, **11**, **12** and 5% HCl **3**, **10**; partial hydrolysis of **7**, **11** with 1% H_2SO_4, **12**, 2.5% H_2SO_4. Enzymatic hydrolysis of **3**, **10** was conducted with β-glucuronidase. Acetylation was by standard procedures: glycosides — $Ac_2O + C_2H_5N$, aglycones — Ac_2O + NaOAc.

Extraction and isolation. Dried aerial parts (stems, leaves and flowers) (1.5 kg), were extracted succesively with petrol, $CHCl_3$, MeOH and 70% MeOH. 177 g of MeOH extract were dissolved in 1 l H_2O and subsequently extracted with Et_2O and Et_2O–EtOAc (1:1) (E I, 16.5 g), EtOAc (E II, 12.5 g), EtOAc–MeOH (9:1) and *n*-BuOH (E III, 41 g). E I, E II and E III extracts were sepd independently on MN-Polyamide SC6

Table 2. ^{13}C NMR data for **7**, **11** and **12** (δ ppm)

	Aglycone				Sugars		
C	7	11	12	C	7	11	12
2	155.9	155.9	147.3	3-Rha 1	101.6	101.5	—
3	134.3	134.3	136.0	2	70.3	70.3	—
4	177.8	177.8	175.9	3	70.6	70.6	—
5	160.7	160.7	160.2	4	71.0	70.9	—
6	99.3	99.4	98.9	5	69.9	69.9	—
7	162.8	162.7	162.5	6	17.4	17.4	—
8	94.7	95.2	95.0	7-Glc 1	99.9	98.6	98.7
9	157.6	157.6	155.9	2	73.0	82.7	82.7
10	105.7	105.7	104.7	3	76.3	75.6	75.6
1′	120.5	120.5	121.7	4	69.6	69.2	69.2
2′	112.7	112.6	111.7	5	77.2	76.9	76.9
3′	149.6	149.6	148.9	6	60.6	60.5	60.5
4′	147.2	147.2	147.2	2^{Glc}-Glc 1	—	104.6	104.7
5′	115.3	115.3	115.5	2	—	74.4	74.6
6′	122.6	122.6	121.9	3	—	76.1	76.1
OMe	55.6	55.6	55.7	4	—	69.6	69.6
				5	—	76.9	76.9
				6	—	60.6	60.7

Sugar carbons for **1**: 101.7, 70.4, 70.6, 71.1, 69.9, 17.4.

columns (eluent H_2O–MeOH). After the sepn of E I the following compounds were obtained: **1** (0.6 g) from the 40% aq. MeOH fraction, **2** (0.1 g) from 50–60% aq. MeOH, **3** (80 mg) from 70% aq. MeOH. The fraction eluted with 80–90% aq. MeOH was subjected to repeated CC on polyamide (eluent C_6H_6–MeOH), to afford **4** (40 mg), **5** (60 mg) and **6** (92 mg). The E II extract gave **7** (0.3 g) from the 20–40% aq. MeOH fraction, **8** (80 mg) from 50% aq. MeOH, **9** (64 mg) from 60–70% aq. MeOH, **10** (0.2 g) from 80–90% aq. MeOH and the E III extract gave **11** (0.4 g) from 10–30% aq. MeOH and **12** (80 mg), from 40% aq. MeOH.

Herbacetin 8-*O*-β-D-*glucuronide* (**3**). Yellow needles, mp 190–193° (aq. MeOH) [15, 16] 212 214°, [17] 280° dec. PC R_fs: (1) 0.47 (2) 0.12. FDMS *m/z* 479 (13%, $[M+H]^+$), 478 (100%, $[M]^+$), 303 (16%, $[A+H]^+$). UV and ^1H NMR spectra identical with [15, 16]. ^{13}C NMR data (ppm) aglycone: 147.7 (C-2), 135.7 (C-3), 175.8 (C-4), 156.9 (C-5), 98.8 (C-6), 157.3 (C-7), 126.0 (C-8), 148.5 (C-9), 102.4 (C-10), 121.0 (C-1'), 130.9 (C-2'), 115.4 (C-3'), 159.6 (C-4'), 115.2 (C-5'), 130.4 (C-6'); glucuronic acid: 105.9 (C-1), 71.6 (C-2), 73.8 (C-3), 75.5 (C-4), 76.2 (C-5), 171.3 (C-6).

Isorhamentin 3-*O*-α-L-*rhamnoside*-7-*O*-β-D-*glucoside* (**7**). Light-yellow needles, mp 180–182° (MeOH); nonaacetate, mp 178–179° (EtOH). PC R_fs: (1) 0.42, (2) 0.70. FDMS *m/z* 625 (25%, $[M+H]^+$), 479 (40%, $[M+H]^+$-rha), 478 (100%, $[M]^{\cdot+}$-rha). UV λ_{max}^{MeOH} nm: 254, 267sh, 347; NaOMe, 264, 410; $AlCl_3$, 268, 300sh, 364, 400; $AlCl_3$–HCl, 269, 300sh, 356, 398; NaOAc, 253, 267sh, 297sh, 354, 410sh; NaOAc–H_3BO_3, 253, 268sh, 350. Acid hydrolysis products: isorhamnetin, mp 308–310°; tetracetate, mp 210–212°; D-glucose [R_fs: PC (1) 0.17, TLC 0.43] L-rhamnose R_fs: PC (1) 0.37, TLC 0.63] and isorhamnetin 7-*O*-β-D-glucoside, mp 252–255°.

Gossypetin 8-O-β-D-*glucuronide* (**10**). Yellow needles, mp 199–202° (aq. MeOH) [18] 220° dec. PC R_fs: (1) 0.30, (2) 0.10. FDMS *m/z* 495 (3%, $[M+H]^+$), 494 (13%, $M^{\cdot+}$), 319 (36%, $[A+H]^+$), 318 (100%, A). ^1H NMR of the TMS ether (ppm): 3.33–3.90 (*m*, 4 sugar protons), 4.86 (*d*, $J=7$ Hz, anomeric proton), 6.13 (*s*, H-6), 6.76 (*d*, $J=9$ Hz, H-5'), 7.53–7.90 (*m*, H-2' and 6'). UV and ^{13}C NMR spectra identical with ref. [13].

Isorhamentin 3-O-α-L-*rhamnoside*-7-O-β-D-*sophoroside* (**11**). Light-yellow needles, mp 193–195° (aq. MeOH). PC R_fs: (1) 0.24, (2) 0.78. FDMS *m/z* 787 (4%, $[M+H]^+$), 786 (10%, $M^{\cdot+}$), 641 (45%, $[M+H-rha]^+$), 640 (100% $[M-rha]^{\cdot+}$). UV λ_{max}^{MeOH} nm: 254, 267sh, 349; NaOMe, 265, 297sh, 400; $AlCl_3$, 271, 300sh, 364, 404; $AlCl_3$–HCl, 269, 300sh, 356, 400; NaOAc, 255, 265sh, 354, 406sh; NaOAc–H_3BO_3, 254, 266sh, 349.

Acid hydrolysis products: isorhamnetin, D-glucose, L-rhamnose and isorhamnetin 7-*O*-β-D-sophoroside (mp, ^1H NMR spectrum identical with **12**).

Isorhamnetin 7-O-β-D-*sophoroside* (**12**). Yellow needles, mp 260–262° (aq. MeOH). PC R_fs: (1) 0.23, (2) 0.19, FDMS *m/z* 641 (100%, $[M+H]^+$), 640 (96%, $[M]^{\cdot+}$), 478 (94%, $[M-glc]^{\cdot+}$). UV λ_{max}^{MeOH} nm: 254, 271sh, 300sh, 375, 430sh; NaOMe, 250sh, 268, 320sh, 440; $AlCl_3$, 264, 302sh, 367, 430; $AlCl_3$–HCl, 265, 300sh, 366, 429; NaOAc, 255, 270sh, 300sh, 383, 425sh; NaOAc–H_3BO_3, 254, 270sh, 300sh, 375.

Acid hydrolysis products: isorhamnetin, D-glucose, D-sophorose (R_fs: PC (1) 0.05, TLC 0.21 and isorhamnetin 7-*O*-β-D-glucoside.

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