Flavonoids from Stachys annua Growing in Azerbaijan

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FLAVONOIDS FROM *Stachys annua* GROWING IN AZERBAIJAN

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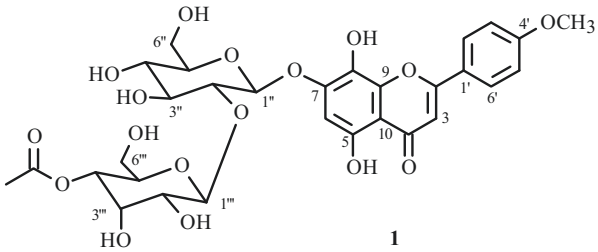
*The new acylated flavonoid bioside 4′-*O*-methylisoscutellarein-7-*O*-[4‴-O-acetyl]allopyranosyl-(1→2)-glucopyranoside (**1**) was isolated from the aerial parts of* Stachys annua *L. (Lamiaceae). Subterranean organs yielded for the first time 4′-*O*-methylisoscutellarein (**2**) and 4′-*O*-methylisoscutellarein-7-*O*-[6″-*O*-acetyl]allopyranosyl-(1→2)-glucopyranoside (**3**). Chemical structures of the isolated compounds were elucidated using NMR spectroscopy.*

Keywords: *Stachys annua*, Lamiaceae, new acylated bioside, annuoside.

In continuation of the search for potential new sources of biologically active compounds [1], we studied the aerial and subterranean organs of *Stachys annua* L. from the flora of Azerbaijan.

Previously, several *Stachys* species including *S. annua* from Ukraine, Azerbaijan, and European countries were incompletely studied [2]. Earlier, we isolated from the aerial parts of *S. annua* β-sitosterol, ursolic acid, and 4′-*O*-methylisoscutellarein-7-*O*-[6‴-*O*-acetyl]allopyranosyl-(1→2)-glucopyranoside [3].

Herein, data are presented for the new acylated bioside 4′-*O*-methylisoscutellarein-7-*O*-[4‴-*O*-acetyl]allopyranosyl-(1→2)-glucopyranoside (annuoside, **1**) from the aerial part and 4′-*O*-methylisoscutellarein (**2**) and 4′-*O*-methylisoscutellarein- 7-*O*-(6‴-*O*-acetyl)allopyranosyl-(1→2)-glucopyranoside (**3**) from the subterranean organs of *S. annua*.



1

Acid hydrolysis of **1** produced the aglycon, acetic acid, D-glucose, and D-allose.

PMR spectra showed resonances for aromatic-ring protons at δ 8.2–6.0 ppm. Correlations were observed in the COSY spectrum between H-1″–H-2″–H-3″–H-4″–H-5″ and H-1‴–H-2‴–H-3‴–H-4‴–H-5‴ and corresponded to ring protons of the two sugars.

Resonances for anomeric protons could be seen in the HMBC spectrum. A correlation between H-1″ (δ 5.17 ppm) and C-7 (δ 151.0) confirmed that the first sugar was bonded to C-7. Two correlations between H-2″ (δ 3.63) and C-1‴ (δ 101.4) in addition to H-1‴ (δ 4.97) and C-2″ (δ 81.7) confirmed that the second sugar was bonded to the first at C-2″. The HMBC spectrum established that the OCH_3 group (δ 3.87) was situated on C-4′ (δ 162.3); the CH_3 (δ 1.99), to –COO (δ 169.4); the methyl ester $–COOCH_3$, to C-4‴ (δ 4.53).

The aglycon had the formula $C_{16}H_{12}O_6$, mp 272–274°C (EtOH), and R_f 0.81. The physicochemical and chemical properties and chromatographic and spectroscopic data for the aglycon of annuoside identified it as 4′-*O*-methylisoscutellarein.

EXPERIMENTAL

General Comments. Chromatography used Filtrak FN5 paper and solvent system *n*-BuOH–HOAc–H_2O (4:1:5, 1). UV spectra were recorded on an Agilent Technologies Cary 60 UV-Vis instrument; NMR spectra, on a Bruker AM-600 spectrometer; melting points, on a CMP 20 apparatus.

Isolation of Glavonoids from the Aerial Part of *S. Annua*. Raw material was collected in June 2015 in the vicinity of Shamakhi, Republic of Azerbaijan. Air-dried and ground aerial plant parts (1.0 kg) were extracted (3×) with EtOH (80%) at room temperature. The extracts were combined and evaporated in vacuo to a watery residue that was worked up sequentially with hexane, $CHCl_3$, and EtOAc.

Recrystallization from aqueous EtOH of the EtOAc extract afforded 4′-*O*-methylisoscutellarein-7-*O*-(6‴-*O*-acetyl)allopyranosyl-(1→2)-glucopyranoside [3] and compound **1**, which was called annuoside [3].

Annuoside (1), $C_{30}H_{34}O_{17}$, greenish-yellow crystals; soluble in aqueous EtOH, DMF, and Py; poorly soluble in EtOH and H_2O; insoluble in $CHCl_3$ and EtOAc; mp 176–178°C (H_2O), R_f 0.59. ^{1}H NMR spectrum (600 MHz, DMSO-d_6, δ, ppm, J/Hz): 8.11 (2H, d, J = 8.8, H-2′, 6′), 7.14 (2H, d, J = 8.8, H-3′, 5′), 6.92 (1H, s, H-3), 6.64 (1H, s, H-6), 5.17 (1H, d, J = 7.7, H-1″), 4.97 (1H, d, J = 7.7, H-1‴), 4.53 (1H, dd, J = 10.2, 2.5, H-4‴), 4.09 (1H, br.t, J = 2.8, H-3‴), 3.87 (3H, s, OCH_3), 3.86 (1H, m, H-5‴), 3.73 (1H, m, H-6″), 3.63 (1H, dd, J = 9.0, 7.7, H-2″), 3.51 (1H, m, H-3″), 3.48 (1H, m, H-6″), 3.46 (1H, m, H-5″), 3.27 (1H, m, H-6‴), 3.25 (1H, m, H-4″), 3.22 (1H, m, H-2‴), 3.23 (1H, m, H-6‴), 1.99 (s, OAc). ^{13}C NMR spectrum (150 MHz, DMSO-d_6, δ, ppm): 163.5 (C-2), 103.4 (C-3), 182.2 (C-4), 152.3 (C-5), 98.1 (C-6), 151.0 (C-7), 126.8 (C-8), 144.1 (C-9), 104.8 (C-10), 122.8 (C-1′), 128.3 (C-2′, 6′), 114.4 (C-3′, 5′), 162.3 (C-4′), 55.4 (OCH_3), 98.9 (C-1″), 81.7 (C-2″), 75.4 (C-3″), 69.0 (C-4″), 76.7 (C-5″), 60.3 (C-6″), 101.4 (C-1‴), 70.9 (C-2‴), 67.6 (C-3‴), 69.0 (C-4‴), 71.6 (C-5‴), 59.6 (C-6‴), 20.8, 169.4 (OAc) [3].

Isolation of Flavonoids from Subterranean Organs of *S. Annua* L. Ground and air-dried subterranean organs (0.8 kg) were extracted (3×) with EtOH (80%) at room temperature. The combined extracts were evaporated *in vacuo* to an aqueous residue that was worked up sequentially with hexane, $CHCl_3$, hexane–EtOAc, and EtOAc.

Recrystallization of the hexane–EtOAc extract from aqueous EtOH produced **2** (4′-methoxyisoscutellarein), $C_{16}H_{12}O_6$, mp 270–272°C, R_f 0.81. Alkaline hydrolysis of **2** formed 4-methoxybenzoic acid [4].

Recrystallization of the EtOAc extract from EtOH produced **3**, acid hydrolysis (5% H_2SO_4, 5 h) of which cleaved **3** into the aglycon, AcOH, D-glucose, and D-allose. Aglycon, $C_{16}H_{12}O_6$, mp 270–272°C (EtOH), R_f 0.81. Compound **3** was isolated earlier from the subterranean organs of *S. annua* [5].

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