Chemistry of Natural Compounds, Vol. 49, No. 1, March, 2013 [Russian original No. 1, January–February, 2013]

FLAVONOIDS FROM *Teucrium orientale*

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UDC 547.972

Teucrium orientale L. (Oriental germander, Lamiaceae) is a grayish-green perennial herb with short protruding hairs that is indigenous to Armenia [1]. It is known to have hypotensive and antioxidant action [2, 3]. Flavones from *Teucrium* species exhibit anticonvulsant, antibacterial, and cytotoxic activity [4, 5].

The flavone eupatorin was isolated previously from the flowering aerial part of *T. orientale* [6]. Eupatorin was also isolated from *T. pseudochamaepitys* L. [4] of the *Teucrium* section [7]. An isomer of eupatorin, cirsilineol, was found in other species of this section (*T. brevifolium* Schreber, *T. fruticans* L., and *T. orientale* L. var. *orientale*) [3, 7, 8].

Herein we communicate results from a study of the flavonoid composition of the flowering aerial part of *T. orientale* from four habitats and a more detailed study of a collection in the vicinity of Tatev monastery (Syunik Oblast, RA). Dried plant (450 g) was extracted with MeOH (80%). The condensed extract was diluted with H_2O (2:1). The filtrate was extracted with C_6H_6 (residue mass 2.5 g), $CHCl_3$ (2.2g), and EtOAc (2.0 g).

Flavonoids with R_f 0.53 and 0.42 (Silufol UV-254, $CHCl_3:Et_2O$, 17:3, system 1) were detected in the initial fractions by column chromatography (CC) over silica gel (SG) L (40/100 mesh) of the C_6H_6 residue using $CHCl_3:Et_2O$ (2%). The PMR spectra of these fractions showed polymethoxylated flavonoids with 4′- and 3′,4′-substituted B-rings. This excluded the possibility that they contained 5-demethylsinensetin, a marker of the section *Teucrium* [7]. The eluate containing $CHCl_3:Et_2O$ (4%) isolated light-yellow crystals of **1** (154 mg), mp 191–192°C, R_f 0.31 (system 1) and R_f 0.51 ($CHCl_3$:MeOH, 19:1, system 2), which gave a positive test (Mg/HCl) for flavones. It was identified based on physicochemical properties as the native compound (IR, UV, PMR, ^{13}C NMR, 2D NMR, and mass spectra) and the diacetate (PMR, mass spectra) of eupatorin (5,3′-dihydroxy-6,7,4′-trimethoxyflavone), $C_{18}H_{16}O_7$. Mass spectrum *m/z* 344 (M^+, 100) [6].

Subsequent fractions from CC upon elution by $CHCl_3$ and $CHCl_3$:MeOH (1→4%) on TLC using systems 1 and 2 detected for the first time for this species cirsimaritin (**2**, 5,4′-dihydroxy-6,7-dimethoxyflavone), cirsiliol (**3**, 5,3′,4′-trihydroxy-6,7-dimethoxyflavone), apigenin (**4**, 5,7,4′-trihydroxyflavone), and luteolin (**5**, 5,7,3′,4′-tetrahydroxyflavone). CC fractions of the C_6H_6 and $CHCl_3$ residues eluted by $CHCl_3$:MeOH (2%) afforded crystals of **3** (8 mg), mp 275–277°C, R_f 0.27 (system 2). UV spectrum (MeOH, λ_{max}, nm): 253, 276, 343. It was identified as cirsiliol, $C_{17}H_{14}O_7$. Mass spectrum: *m/z* 330 (M^+, 100). PMR spectrum of **3** (300 MHz, DMSO-d_6:CCl_4, 1:3, δ, ppm, J/Hz): 3.78 (3H, s, OMe), 3.94 (3H, s, OMe), 6.52 (1H, s, H-3), 6.67 (1H, s, H-8), 6.85 (1H, d, J = 8.3, H-5′), 7.32 (1H, dd, J = 8.3, 2.3, H-6′), 7.35 (1H, d, J = 2.3, H-2′), 8.95 (1H, br.s, 3′-OH), 9.41 (1H, br.s, 4′-OH), 12.81 (1H, br.s, 5-OH). ^{13}C NMR spectrum of **3**: (75.46 MHz, δ, ppm): 55.7 (MeO-7), 59.4 (MeO-6), 90.4 (C-8), 102.4 (C-3), 113.1 (C-2′), 115.5 (C-5′), 118.2 (C-6′), 121.4 (C-1′), 131.8 (C-6), 145.4 (C-3′), 149.4 (C-4′), 152.4 (C-5 and C-9), 158.1 (C-2), 164.0 (C-7), 181.7 (C-4).

The C_6H_6 and $CHCl_3$ residues from *T. orientale* collected during flowering in the vicinity of Aghveran (Kotayk Oblast, RA) and Artanish villages (Gegharkunik Oblast, RA) afforded a compound with the same physicochemical and spectral properties as eupatorin [6]. The qualitative compositions of the residues (TLC using systems 1 and 2) of the aforementioned collections were also identical.

The EtOAc residue of *T. orientale* from Tatev monastery contained three glycosides. CC over SG L (40/100 mesh) using EtOAc:MeOH:H_2O (98:1.5:0.5) isolated light-yellow crystals (25 mg) of **6** with R_f 0.46 (EtOAc:MeOH:H_2O, 9:1:0.5, system 3), mp 237–238°C, $[\alpha]_D^{20}$ –59° (*c* 0.5, EtOH). UV spectrum (MeOH, λ_{max}, nm): 257, 269sh, 300sh, 360. It was identified as hyperoside (quercetin-3-*O*-*β*-D-galactopyranoside), $C_{21}H_{20}O_{12}$. Mass spectrum *m/z* 302 (M^+_{agl}, 48) [9]. PMR spectrum of **6** (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 3.33 (1H, td, $J_{5,6}$ = 6.0, $J_{5,4}$ = 0.9, H-5″), 3.40 (1H, dd, $J_{6a,6b}$ = 11.0, J = 6.0, H-6b″), 3.41 (1H, dd, $J_{2,3}$ = 9.5, $J_{3,4}$ = 3.4, H-3″), 3.51 (1H, dd, $J_{6a,6b}$ = 11.0, $J_{5,6a}$ = 6.0, H-6a″), 3.66 (1H, dd,

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0009-3130/13/4901-0106

$J_{2,3}$ = 9.5, $J_{1,2}$ = 7.7, H-2″), 3.73 (1H, dd, $J_{3,4}$ = 3.4, $J_{4,5}$ = 0.9, H-4″), 5.04 (1H, d, $J_{1,2}$ = 7.7, H-1″), 6.14 (1H, d, J = 2.1, H-6), 6.42 (1H, d, J = 2.1, H-8), 6.80 (1H, d, J = 8.5, H-5′), 7.48 (1H, dd, J = 8.5, 2.2, H-6′), 7.70 (1H, d, J = 2.2, H-2′), 8.83 (1H, br.s, 3′-OH), 9.09 (1H, br.s, 4′-OH), 10.34 (1H, br.s, 7-OH), 12.30 (1H, br.s, 5-OH). ^{13}C NMR spectrum of **6** (75.46 MHz, δ, ppm): 59.7 (C-6″), 67.5 (C-4″), 71.7 (C-2″), 73.2 (C-3″), 75.3 (C-5″), 93.2 (C-8), 98.5 (C-6), 102.9 (C-1″), 103.7 (C-10), 114.9 (C-5′), 116.3 (C-2′), 121.2 (C-6′), 133.6 (C-3), 144.3 (C-3′), 148.2 (C-4′), 156.2 (C-2), 156.5 (C-9), 161.2 (C-5), 164.0 (C-7), 177.3 (C-4).

Acid hydrolysis of **6** (H_2SO_4, 5%) produced quercetin with R_f 0.63 (system 3), mp 313–316°C. UV spectrum (MeOH, λ_{max}, nm): 255, 269sh, 300sh, 369. Galactose was detected by PC. CC fractions of the EtOAc residue also contained cinaroside (**7**, luteolin-7-*O*-*β*-D-glucopyranoside) (TLC, system 3).

A study of the short- and long-haired varieties of *T. orientale* (near Geghard monastery, Kotayk Oblast, RA) detected eupatorin in the short-haired variety. Hyperoside was absent in the EtOAc residue of the MeOH extract of both varieties, in contrast with the sample from Tatev monastery (TLC, system 3).

The studies suggested that eupatorin and the flavonol glycoside hyperoside were definitive for the chemotype *T. orientale*. Cirsiliol (**3**) and hyperoside (**6**) were isolated for the first time from *T. orientale*.

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