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MINOR FLAVONOLS FROM *Dracocephalum multicaule*

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Plants of the genus *Dracocephalum* L. (Lamiaceae) that contain flavonoids are widely used in folk medicine of various countries as sedative, antibacterial, anti-inflammatory, antitumor, and other agents. Their pharmacological activity has been confirmed experimentally [1, 2].

A study of the flavonoid composition of the aerial part of the herbaceous perennial *Dracocephalum multicaule* Montbr. et Auch. ex Benth. [3] isolated 13 bioactive flavones, flavonols, and flavone glucosides [4-6].

In continuation of the study of the flavonoid composition of the aerial part of this plant, column chromatography (CC) of the $CHCl_3$ fraction of the aqueous extract (13 mg) over silica gel L (40/100 mesh) with subsequent preparative TLC on Silufol UV-254 plates (×4) using C_6H_6:ether (6:1) isolated calicopterin (5,4′-dihydroxy-3,6,7,8-tetramethoxyflavone, **1**, 5.5 mg), which was identified by comparison of the TLC and mixed melting point with an authentic sample, and yellow needle-like crystals (2.6 mg), mp 248-251°C (C_6H_6), molecular ion in the mass spectrum (EI, 70 eV, *m/z*, *I*rel, %): 314 (100), of a flavonoid (IR spectrum) with a positive cyanidine Mg/HCl reaction. This indicated the presence of two OH and two OMe groups in its structure.

UV spectra with diagnostic additives according to the literature method [7] [MeOH, λ_{max} (relative intensities, nm): 257 sh (0.30), 268 (1.00), 290 sh (0.70), 321 sh (0.53), 348 (0.62)] showed that the sample might have been a mixture of two structurally similar phloroglucinol compounds according to the first (348 nm) and second (268 nm) bands and the ratio of intensities in the initial MeOH solution and with added $AlCl_3$ and $AlCl_3$ + HCl in addition to NaOMe (formation of a third band at 331 nm and a bathochromic shift of the first to 394 nm with increased intensity) and NaOAc (272, 329, 398 sh nm). These were isokaempferide (5,7,4′-trihydroxy-3-methoxyflavone, **2**) and kumatakenin (5,4′-dihydroxy-3,7-dimethoxyflavone, **3**), which contains 3-OMe, 5-OH, 7-OMe (in addition to 7-OH), and 4′-OH groups [8-10].

The mass spectrum of the sample showed ions with *m/z* 314 (100) $[M]^+$, 167 (18) $[A_1 + H]^+$, 166 (5) $[A_1]^+$, 121 (30) $[B_2]^+$, 118 (5) $[B_1]^+$, and 105 (10) of kumatakenin (**3**) with $[M - H]^+$, $[M - H_2O]^+$, $[M - H_3O]^+$, $[M - OCH_3]^+$, and $[M - CH_3CO]^+$ characteristic of 3-methoxyflavone fragmentation [11-14]. However, there was no molecular ion for **2** with *m/z* 300 and ions with *m/z* 272 (8) $[M - CO]^+$, 271 (30) $[M - COH]^+$ (also in the mass spectrum of **3** [12, 13]), 269 (3), 257 (4) $[M - CH_3CO]^+$, 153 (2) $[A_1 + H]^+$, 152 (3) $[A_1]^+$ (B_1 and B_2 ions like for **3**) may have belonged to **2** but were weak. This might have been due to the conditions under which the spectra were recorded. The small amount of sample did not enable its NMR spectrum to be obtained.

PMR spectra of the acetates of isokaempferide (**4**) and kumatakenin (**5**), minor side products obtained from CC (conditions given above) of total acetates (Ac_2O/Py) of mixtures of the apigenin (5,7,4′-trihydroxyflavone, **6**) and isokaempferide in addition to cirsimaritin (5,4′-dihydroxy-6,7-dimethoxyflavone, **7**) and kumatakenin, respectively, provided additional confirmation that isokaempferide (**2**) and kumatakenin (**3**) were native flavonols of *D. multicaule*. Compounds **6** and **7** were isolated earlier from *D. multicaule* [4, 5].

Isokaempferide triacetate (5,7,4′-triacetoxy-3-methoxyflavone, **4**), $C_{22}H_{18}O_9$, mp 154-156°C ($CHCl_3$) (lit. [15] mp 161-163°C), *m/z* 426 (17) $[M]^+$, fragmentation of 3-methoxyflavone. PMR spectrum (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 2.35 (6H, s, 7-OAc, 4′-OAc), 2.47 (3H, s, 5-OAc), 3.84 (3H, s, 3-OMe), 6.81 (1H, d, J = 2.2, H-6), 7.25 (2H, m, J_1 = 8.9, J_2 = 2.0, H-3′, H-5′), 7.30 (1H, d, J = 2.2, H-8), 8.10 (2H, m, J_1 = 8.9, J_2 = 2.0, H-2′, H-6′).

Kumatakenin diacetate (5,4′-diacetoxy-3,7-dimethoxyflavone, **5**), $C_{21}H_{18}O_8$, mp 140-143°C (lit. [16] mp 141-143°C), *m/z* 398 (20) $[M]^+$, fragmentation of 3-methoxyflavone. PMR spectrum (100 MHz, $CDCl_3$, δ, ppm, J/Hz): 2.32 (3H, s,

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4′-OAc), 2.49 (3H, s, 5-OAc), 3.87 (3H, s, 7-OMe), 3.83 (3H, s, 3-OMe), 6.63 (1H, d, J = 2.3, H-6), 6.88 (1H, d, J = 2.3, H-8), 7.27 (2H, dd, J_1 = 9.0, J_2 = 2.0, H-3′, H-5′), 8.10 (2H, dd, J_1 = 9.0, J_2 = 2.0, H-2′, H-6′).

Isokaempferide and kumatakenin were isolated previously in the *Lamiaceae* family from *Salvia glutinosa* L. [17] and *Ballota hirsuta* Benth. [18] and were observed in *D. kotschyii* Boiss. [19].

The studies showed that a characteristic feature of *D. multicaule* is the presence of hydroxylated flavones (apigenin and luteolin) and their glucosides (cosmosiin, apigenin 5-*O*-β-D-glucopyranoside and cinaroside) [5, 6] in addition to mono- (acacetin, genkwanin [5], isokaempferide), di- (cirsimaritin, kumatakenin), tri- (xanthomicrol, penduletin), tetra- (gardenin B, calicopterin), and pentamethoxylated (4′-methylcalicopterin) [4] flavones and flavonols with a 4′-*O*-substituted B-ring (besides luteolin and its derivatives). Starting with cirsimaritin and further (tri- and more methoxylated flavones and flavonols), flavonoids are 6-oxygenated. This defines their evolutionary path [20]. Calicopterin, xanthomicrol, gardenin B, and 4′-methylcalicopterin are also 8-oxygenated.

It is difficult to overestimate the value of determining the chemical composition of flavonoids that are biologically active, UV protectors of plants, and taxonomic markers at the species subgenetic level. In addition, their morphological features can be used to determine the species.

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