DOI 10.1007/s10600-020-03132-w
Chemistry of Natural Compounds, Vol. 56, No. 4, July, 2020

FLAVONOIDS FROM THE AERIAL PART OF *Alhagi persarum* OF THE FLORA OF UZBEKISTAN AND THEIR BIOLOGICAL ACTIVITY

S. Z. Nishanbaev,[1,2*] Kh. M. Bobakulov,[1,2] D. A. Narbutaeva,[1] S. F. Aripova,[1] Z. A. Khushbaktova,[1] and N. D. Abdullaev[1]

Previously, volatile compounds in the hexane and C_6H_6 extracts and the compositions of essential oils obtained by steam- and hydrodistillation from the aerial part of *Alhagi persarum* Boiss. & Buhse (Fabaceae) collected during full flowering were analyzed by us using GC-MS. Also, mono- and sesquiterpenoids and their derivatives, aldehydes, and hydrocarbons and their functional derivatives were identified [1–3].

Quercetin, isorhamnetin, quercetin-3-*O*-α-L-rhamnopyranoside, quercetin-3-*O*-α-L-arabinofuranoside, quercetin-5,3′,4′-trimethoxy-3-*O*-β-D-galactopyranosido-(2→1)-α-L-rhamnopyranosido-7-*O*-α-L-rhamnopyranoside, isorhamnetin-3-*O*-β-D-glucopyranoside, and isorhamnetin-3-*O*-α-L-arabinopyranoside were isolated from a population of *A. persarum* growing in Kazakhstan [4]. Also, the polysaccharide composition of this plant was studied [5]. However, phenolic compounds from *A. persarum* have not until now been studied.

The dried aerial part of *A. persarum* (Fabaceae) collected in June 2016 during full flowering in Jizzakh Oblast, Republic of Uzbekistan, was studied. The species was determined by Cand. N. Yu. Beshko, Institute of Botany, AS, RUz.

Dried and ground aerial part of *A. persarum* (2.0 kg) was extracted (5×) at room temperature with EtOH (70%). The combined aqueous EtOH extract was concentrated to 0.5 L, diluted with hot H_2O (1:1), and back-extracted sequentially with $CHCl_3$ (5 × 400 mL), EtOAc (5 × 400 mL), and *n*-BuOH (6 × 400 mL).

The EtOAc fraction (20 g) was chromatographed over a column (3.0 × 115 cm) of silica gel using gradient elution by $CHCl_3$–MeOH in various proportions (10:1, 9:1, 7:1, 5:1, 3:1, 1:1). Rechromatography of the separate eluates over Sephadex LH-20 using elution by MeOH–H_2O (8:2) isolated five pure flavonoids (**1**–**5**). A comparison of spectral data of the isolated compounds (UV, IR, NMR) with the literature and a direct comparison with authentic samples identified them as naringenin (**1**, 68 mg), isorhamnetin (**2**, 210 mg), isomyricetin (**3**, 88 mg), narcissin (**4**, 230 mg), and genistin (**5**, 103 mg).

Naringenin (1), $C_{15}H_{12}O_5$, mp 250–251°C. UV spectrum (C_2H_5OH, λ_{max}, nm): 290 and 326 (sh). IR spectrum (KBr, ν, cm^{-1}): 3410–3114 (OH), 3282 (phenolic OH), 1631 (C=O γ-pyrone), 1602, 1519 (C=C), 1312, 1250 (C–O), 1157, 1083, 1013, 889, 832. ^{1}H NMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 2.62 (1H, dd, J = 17.1, 3.0, H-3a), 3.21 (1H, dd, J = 17.1, 12.8, H-3e), 5.37 (1H, dd, J = 12.8, 3.0, H-2), 5.83 (2H, br.s, H-6, 8), 6.74 (2H, d, J = 8.6, H-3′, 5′), 7.26 (2H, d, J = 8.6, H-2′, 6′), 9.65 (1H, br.s, OH), 12.01 (1H, s, 5-OH). ^{13}C NMR spectrum (100 MHz, DMSO-d_6, δ, ppm): 78.59 (C-2), 42.11 (C-3), 196.54 (C-4), 163.63 (C-5), 95.96 (C-6), 166.83 (C-7), 95.14 (C-8), 163.08 (C-9), 101.89 (C-10), 129.00 (C-1′), 128.53 (C-2′, 6′), 115.32 (C-3′, 5′), 157.85 (C-4′).

Isolated compound **1** was identified as 5,7,4′-trihydroxyflavanone (naringenin) (**1**) [6], which is widely distributed among flavonoids from plants of the genus *Alhagi* [7].

Isorhamnetin (2), $C_{16}H_{12}O_7$, mp 303–305°C. UV spectrum (C_2H_5OH, λ_{max}, nm): 255, 266, 370. IR spectrum (KBr, ν, cm^{-1}): 3450 (OH), 2927 (OCH_3), 1667 (>C=O), 1605, 1575, 1518 (ArH), 842, 817. Compound **2** was identified as 3,5,7,4′-tetrahydroxy-3′-methoxyflavonol [8].

1) S. Yu. Yunusov Institute of the Chemistry of Plant Substances, Academy of Sciences of the Republic of Uzbekistan, Tashkent, e-mail: sabir78@rambler.ru; 2) Tashkent Institute of Irrigation and Agricultural Mechanization Engineers, 39 Kary Niyazov St., Tashkent, 100000, Uzbekistan. Translated from *Khimiya Prirodnykh Soedinenii*, No. 4, July–August, 2020, pp. 628–629. Original article submitted January 6, 2020.

 ©2020 Springer Science+Business Media, LLC

TABLE 1. Antihypoxic Activity of Total Flavonoids from the Aerial Part of *Alhagi persarum* as Compared to Rutin and Luteolin (M ± m, n = 6)

Experimental conditions	Normobaric hypoxic hypoxia		Hemic hypoxic hypoxia	
	lifespan, min	effect, %	lifespan, min	effect, %
Control	14.3 ± 0.326	–	8.3 ± 0.203	–
Total flavonoids, 100 mg/kg	20.3 ± 1.011*	42.6	12.5 ± 0.32*	51.0
Rutin, 100 mg/kg	19.0 ± 1.202*	33.4	11.0 ± 0.36*	33.0
Luteolin, 100 mg/kg	18.6 ± 1.12*	30.8	10.5 ± 0.39*	27.0

*Statistically significant vs. corresponding control for $p < 0.05$.

Isomyricetin (3), $C_{15}H_{12}O_5$, mp 250–252°C. UV spectrum (C_2H_5OH, λ_{max}, nm): 258, 366. IR spectrum (KBr, ν, cm^{-1}): 3529–3182 (OH), 3301 (phenolic OH), 1654 (α,β-unsaturated CO), 1602, 1562, 1493 (C=C), 1320, 1251, 1201 (C–O), 1158, 1067, 1042, 996, 857. ^{1}H NMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 2.98–3.31 (5H, m, H-2″, 3″, 4″, 5″, 6″a), 3.55 (1H, br.d, J = 11.4, 6″b), 4.22, 4.91, 5.05, 5.16 (1H each, br.s, OH), 5.42 (1H, d, J = 7.7, H-1″), 6.14 (1H, d, J = 2.1, H-6), 6.32 (1H, d, J = 2.1, H-8), 7.14 (2H, s, H-2′, 6′), 9.13, 10.81 (1H each, br.s, OH), 12.61 (1H, s, 5-OH). ^{13}C NMR spectrum (100 MHz, DMSO-d_6, δ, ppm): 156.23 (C-2), 133.52 (C-3), 177.44 (C-4), 161.30 (C-5), 98.67 (C-6), 164.13 (C-7), 93.39 (C-8), 156.30 (C-9), 104.01 (C-10), 120.09 (C-1′), 108.57 (C-2′, 6′), 145.42 (C-3′, 5′), 136.68 (C-4′), 100.90 (C-1″), 73.96 (C-2″), 76.62 (C-3″), 69.97 (C-4″), 77.71 (C-5″), 61.15 (C-6″) [9].

Narcissin (4), $C_{28}H_{32}O_{16}$, mp 179–180°C. UV spectrum (C_2H_5OH, λ_{max}, nm): 257, 360. IR spectrum (KBr, ν, cm^{-1}): 3380 (OH), 2938 (OCH_3), 1655 (C=O), 1605, 1508 (C=C), 1358, 1210, 1060.

Compound **4** was identified as isorhamnetin-3-*O*-β-D-rutinoside, which was isolated previously from *Alhagi canescens* (Regel) B.Keller & Shap. [8].

Genistin (5), $C_{21}H_{20}O_{10}$, mp 253–254°C. UV spectrum (C_2H_5OH, λ_{max} nm): 235, 264, 305. IR spectrum (KBr, ν, cm^{-1}): 3424, 2927 (OH), 1657 (C=O γ-pyrone), 1620, 1575, 1513 (C=C) and 1179, 1075, 1048 (C–O). ^{1}H NMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 3.10–3.70 (6H, m, H-2″, 3″, 4″, 5″, 6″), 4.87 (1H, d, J = 7.1, H-1″), 6.17 (1H, d, J = 2.1, H-6), 6.33 (1H, d, J = 2.1, H-8), 7.05 (2H, d, J = 8.7, H-3′, 5′), 7.44 (2H, d, J = 8.7, H-2′, 6′), 8.31 (1H, s, H-2), 12.85 (s, 5-OH). ^{13}C NMR spectrum (100 MHz, DMSO-d_6, δ, ppm): 154.44 (C-2), 121.95 (C-3), 180.09 (C-4), 162.04 (C-5), 99.18 (C-6), 164.66 (C-7), 93.86 (C-8), 157.67 (C-9), 104.44 (C-10), 124.31 (C-1′), 130.15 (C-2′, 6′), 116.12 (C-3′, 5′), 157.34 (C-4′), 100.37 (C-1″), 73.31 (C-2″), 76.70 (C-3″), 69.77 (C-4″), 77.12 (C-5″), 60.76 (C-6″).

Compound **5** was identified as genistein-7-*O*-β-D-glucopyranoside [10].

Thus, the phytochemical studies isolated for the first time from the aerial part of *A. persarum* compounds **1** and **3**–**5**. Flavonols narcissin (**4**) and its aglycon isorhamnetin (**2**) are produced in major amounts in practically all plant species of the genus *Alhagi* and are chemotaxonomic markers.

The pharmacological studies showed that total flavonoids isolated from the aerial part of *A. persarum* exhibited both antioxidant properties in *in vitro* tests and antihypoxic activity (determined under acute normobaric hypoxia and hemic hypoxia conditions [11]).

The results showed that total flavonoids from the aerial part of *A. persarum* exhibited pronounced antihypoxic activity as compared to rutin and luteolin and prolonged the lifespan of animals by 30.8–42.6% (Table 1).

The lifespan increase of animals under hemic hypoxia conditions after administering the compounds was 27.0–51.0%. Their inhibitory effect on lipid peroxidation in *in vitro* tests was from 66.7 to 77.0% in practically the same range as the antioxidant activity. Total flavonoids from the aerial part of *A. persarum* were the most active. Their activity was comparable to that of the reference drug vitamin E (85.0%).

REFERENCES

1. S. Z. Nishanbaev, Kh. M. Bobakulov, B. S. Okhundelaev, S. A. Sasmakov, N. D. Abdullaev, and S. F. Aripova, *Khim. Rastit. Syr'ya*, No. 4, 125 (2018).
2. S. Z. Nishanbaev, Kh. M. Bobakulov, A. M. Nigmatullaev, I. D. Shamyanov, B. S. Ohundedaev, and N. D. Abdullayev, *Chem. Nat. Compd.*, **52**, 167 (2016).

3. S. Z. Nishanbaev, I. D. Sham′yanov, Kh. M. Bobakulov, and Sh. Sh. Sagdullaev, *Khim. Rastit. Syr′ya*, No. 4, 5 (2019).
4. B. K. Eskalieva and G. Sh. Burasheva, *Chem. Nat. Compd.*, **38**, 102 (2002).
5. D. R. Rakhimov and A. Dzhumamuratova, *Chem. Nat. Compd.*, **29**, 674 (1993).
6. O. S. Evseeva, O. A. Andreeva, E. T. Oganesyan, and M. V. Aroyan, *Fundam. Res.*, No. 6, 96 (2014).
7. V. P. Singh, Y. Bineeta, and V. B. Pandey, *Phytochemistry*, **51**, 587 (1999).
8. S. Z. Nishanbaev, Kh. M. Bobakulov, N. Yu. Beshko, I. D. Sham′yanov, and N. D. Abdullaev, *Khim. Rastit. Syr′ya*, No. 1, 77 (2017).
9. M. T. Ikramov, F. A. Mavasheva, E. Kh. Batirov, and V. M. Malikov, *Chem. Nat. Compd.*, **26**, 226 (1990).
10. I. V. Shilova, A. A. Semenov, N. I. Suslov, E. I. Korotkova, A. N. Vtorushina, and V. V. Belyakova, *Khim.-farm. Zh.*, **43** (4), 7 (2009).
11. L. D. Luk′yanov (ed.), *Methodical Recommendations for Experimental Study of Drugs Proposed for Clinical Trials as Antihypoxic Agents* [in Russian], Moscow, 1990.