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PHENOLIC COMPOUNDS FROM THE AERIAL PART OF *Filipendula ulmaria*

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*The new natural compound salicyl alcohol 7-*O*-β-D-(6′-*O*-benzoyl)glucopyranoside, which we called isopopulin, and the known compounds gaulterin, gallic acid, quercetin, spireoside, and astragalin were isolated from the aerial part of* Filipendula ulmaria *(L.) Maxim. The chemical structures of the isolated phenolic compounds were studied using UV, ^{1}H and ^{13}C NMR spectroscopy; mass spectrometry; and chemical transformations.*

Keywords: *Filipendula ulmaria* (L.) Maxim., phenolic compounds, simple phenols, flavonoids.

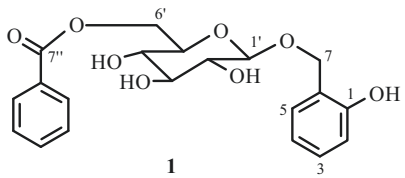
Filipendula ulmaria (L.) Maxim. (Rosaceae) is broadly distributed in European Russia and western and eastern Siberia [1, 2]. Currently, the herb of *F. ulmaria* is included in pharmacopoeias of many countries [3]. Flowers of *F. ulmaria* are the only pharmacopoeial type of raw material in the Russian Federation (Pending Monograph 42-1777-87, Meadowsweet flowers) [4].

Preparations based on *F. ulmaria* raw material possess broad spectra of biological activity, including anti-inflammatory, antimicrobial, hepatoprotective, antioxidant, and nootropic [2–10]. The chemical composition of the aerial part of *F. ulmaria* is represented by phenols (gaulterin, spirein, salicylic acid, gallic acid, ethyl gallate, 4-methoxybenzoic acid, salicylaldehyde), a coumarin (esculetin), flavonoids (kaempferol, quercetin, isoquercitrin, avicularin, spireoside, quercetin 4′-*O*-*β*-D-galactopyranoside, rutin), and triterpene saponins (oleanolic and ursolic acids) [2, 4–6, 11, 12].

The aim of the present work was to study the constituent composition of the aerial part of *F. ulmaria* collected in Alekseevka, Samara Region, in July 2021 during flowering.

Chromatographic studies isolated from the aerial part of *F. ulmaria* the phenolic compounds **1**–**6**.

The ^{1}H NMR spectrum of **1** exhibited resonances for nine aromatic protons of salicylic alcohol and a benzene ring at 7.44 ppm (2H, dd, J = 2.0, 8.0, H-2″, H-6″), 7.26–7.35 (4H, m, H-3, H-3″, H-4″, H-5″), 7.13 (1H, dt, J = 2.0, 8.0, H-4), 6.68 (1H, d, J = 8.0, H-2), and 6.48 (1H, d, J = 8.0, H-5). Also, the ^{1}H NMR spectrum of **1** had two 1H doublets at 5.25 and 5.10 ppm with spin−spin coupling constant (SSCC) 13.0 Hz for CH_2OH groups of salicylic alcohol. A resonance for glucose C-6′ at 66.53 ppm in the ^{13}C NMR spectrum of **1** confirmed that the glucose CH_2OH group (C-6) was esterified by benzoic acid. A free phenolic group in **1** was confirmed by a 1H singlet for the phenolic OH of salicylic alcohol at 9.95 ppm in the ^{1}H NMR spectrum of **1**. This indicated that the glucose was bonded to the CH_2OH group of salicylic alcohol.



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This conclusion was confirmed by **1** having a free phenolic OH on C-1, in contrast to populin, and appearing as an orange spot under TLC conditions upon treatment by a basic solution of diazobenzenesulfonic acid. Therefore, **1** had the structure salicylic alcohol 7-*O*-*β*-D-(6′-*O*-benzoyl)glucopyranoside and was a new natural compound that we called isopopulin. Previously, populin with a structure close to that of isopopulin was isolated and had a glucose bonded to the phenolic OH group of salicylic alcohol. It is interesting that **1** and populin had significantly different melting points of 269–272°C and 179–180°C, respectively.

Compounds **2** and **3** were identified using UV, NMR, and mass spectral data as gaulterin and gallic acid, which were reported from *F. ulmaria* [2, 5, 6, 11]; flavonoids **4**–**6**, as quercetin (**4**), spireoside (**5**), and astragalin (**6**), which were isolated by us for the first time from the aerial part of *F. ulmaria*.

EXPERIMENTAL

The chemical structures of the compounds isolated from the aerial part of *F. ulmaria* were studied using UV, ^{1}H and ^{13}C NMR spectroscopy. ^{1}H and ^{13}C NMR spectra were taken on a JNM-ECX 400 instrument (399.78 MHz for ^{1}H; 100.52 MHz for ^{13}C). High-resolution mass spectra were recorded on a Bruker maXis impact instrument using electrospray ionization (ESI). Spectra were recorded in 10-mm cuvettes on a Specord 40 spectrophotometer (Analytik Jena AG, Germany) in the range 190–500 nm. Acid hydrolysis of phenolic and flavonoid glycosides **1**, **2**, **5**, and **6** used HCl (2%) on a boiling-water bath for 2 h. Enzymatic hydrolysis of flavonoids **5** and **6** used an aqueous solution of *β*-glucosidase (Sigma). Monosaccharides in acid hydrolysates of the glycosides were identified by paper chromatography using the solvent system *n*-BuOH–glacial AcOH–H_2O in a 4:1:2 ratio (anilinium phthalate reagent).

Extraction and Isolation of the Compounds. Air-dried aerial part of *F. ulmaria* (200 g) collected during flowering was extracted with EtOH (70%). The combined aqueous EtOH extract was evaporated under vacuum to a thick residue (60 g) that was placed onto KSK silica gel 50/100 (Russia), dried, and separated by chromatography over silica gel. The eluents were $CHCl_3$ and $CHCl_3$–EtOH mixtures (97:3, 95:5, 93:7, 90:10, 85:15, 80:20, 70:30, 60:40, 50:50). Eluates were divided into fractions of approximately equal volumes (200 mL each).

Fractions obtained by elution with $CHCl_3$–EtOH (70:30) isolated crystalline **1**, which was purified by rechromatography over polyamide (0.4% yield) using H_2O as the eluent. Further elution of this chromatography column by 40% EtOH produced **3** (0.2% yield). Fractions obtained upon elution by $CHCl_3$–EtOH (60:40) isolated crystalline **2**, which was purified by rechromatography over polyamide (0.7% yield) using H_2O as the eluent. Fractions obtained by elution with $CHCl_3$–EtOH (93:7) isolated crystalline **4**, which was purified by rechromatography (0.1% yield) over polyamide using EtOH (70%) as the eluent. Fractions obtained by elution with $CHCl_3$–EtOH (80:20) produced a mixture of **5** and **6** that was separated by rechromatography (0.3% and 0.05% yields, respectively) over polyamide using EtOH (40% and 70%) as eluents.

Structural studies of isopopulin (**1**) used databases such as CAS Common Chemistry, PubChem, ChemSynthesis, and others.

Isopopulin [salicylic alcohol 7-*O*-*β*-D-(6′-*O*-benzoyl)glucopyranoside] (1), white crystalline compound, $C_{20}H_{22}O_8$, mp 269–272°C (EtOH). UV (EtOH, λ_{max}, nm): 233, 288. ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 9.95 (1H, s, 1-OH), 7.44 (2H, dd, J = 2.0, 8.0, H-2″, 6″), 7.26–7.35 (4H, m, H-3, 3″, 4″, 5″), 7.13 (1H, dt, J = 2.0, 8.0, H-4), 6.68 (1H, d, J = 8.0, H-2), 6.48 (1H, d, J = 8.0, H-5), 5.27 (1H, d, J = 13.0, H-7), 5.10 (1H, d, J = 13.0, H-7), 5.01 (1H, d, J = 7.0, Glc H-1′), 2.8–4.9 (9H, m, 6H Glc and 3H of three glucose hydroxyls on C-2′, 3′, C-4′). ^{13}C NMR (100 MHz, DMSO-d_6, δ, ppm): 166.32, 155.81, 136.76, 131.72, 128.81, 128.28, 128.28, 112.39, 109.86, 106.39, 104.43, 104.38, 100.88, 77.16, 76.97, 73.91, 70.08, 66.53, 66.18. HR-ESI-MS *m/z* 413.2661 $[M + Na]^+$ (calcd for $C_{20}H_{22}O_8Na$, 413.3748).

Gaulterin (methylsalicylate 2-*O*-*β*-D-primeveroside) (2), $C_{19}H_{26}O_{12}$, mp 278–280°C (EtOH). UV (EtOH, λ_{max}, nm): 243, 286, 315 (sh). Spectral data for gaulterin agreed with those in the literature [5].

Gallic acid (3), $C_7H_6O_5$, mp 219–221°C (EtOH). UV (EtOH, λ_{max}, nm): 278. Spectral data for gallic acid agreed with those in the literature [5].

Quercetin (3,5,7,3′,4′-pentahydroxyflavone) (4), $C_{15}H_{10}O_7$, mp 314–315°C (aq. EtOH). UV (EtOH, λ_{max}, nm): 257, 268 sh, 375; + NaOAc 273, 386; + NaOAc + H_3BO_3 273, 390; +A1C1$_3$ 273, 425; +A1C1$_3$ + HCl 270, 401. Spectral data agreed with the literature [5].

Spireoside (quercetin 4′-*O*-*β*-D-glucopyranoside) (5), $C_{21}H_{22}O_{12}$, mp 228–230°C (aq. EtOH). UV (EtOH, λ_{max}, nm): 260, 274 sh, 372; +NaOAc 276, 384; +NaOAc + H_3BO_3 276, 384; +A1C1$_3$ 265, 274, 424; +A1C1$_3$ + HCl 265, 274, 424. Spectral data agreed with the literature [5].

Astragalin (3,5,7,4′-tetrahydroxyflavone 3-*O*-*β*-D-glucopyranoside) (6), $C_{21}H_{20}O_{11}$, mp 173–176°C (aq. EtOH). UV (EtOH, λ_{max}, nm): 269, 355; + NaOAc 274, 368; + NaOAc + H_3BO_3 272, 356; +$AlCl_3$ and +$AlCl_3$ + HCl 275, 306, 396. ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 12.38 (1H, s, 5-OH), 10.79 (1H, s, 7-OH), 9.50 (1H, s, 4′-OH), 8.10 (2H, d, J = 9.0, H-2′, 6′), 7.15 (2H, d, J = 9.0, H-3′, 5′), 6.41 (1H, d, J = 2.5, H-8), 6.16 (1H, d, J = 2.5, H-6), 5.34 (1H, d, J = 7.0, Glc H-1″), 2.9–4.8 (6H, m, 6H Glc). ^{13}C NMR (100 MHz, DMSO-d_6, δ, ppm): 176.57 (C-4), 164.59 (C-7), 161.23 (C-5, 9), 156.75 (C-2), 147.29 (C-4′), 136.81 (C-3), 129.69 (C-2′, 6′), 124.91 (C-1′), 116.65 (C-3′, 5′), 103.61 (C-10), 101.93 (Glc C-1″), 98.75 (C-6), 94.02 (C-8), 77.81 (C-5″), 76.67 (C-3″), 73.79 (C-2″), 70.17 (C-4″), 61.22 (C-6″). HR-ESI-MS *m/z* 447.0930 $[M - H]^-$ (calcd 447.3701); *m/z* 449.1079 $[M + H]^+$; 471.0898 $[M + Na]^+$; 487.0846 $[M + K]^+$.

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