IRSTI 31.23.17:31.23.39 https://doi.org/10.26577/ijbch.2021.v14.i1.017

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Chemical study of *Artemisia austriaca* Jacq.

Abstract. Chemical study of *Artemisia austriaca* Jacq. was carried out by various methods of plant raw materials extraction. Three sesquiterpene lactones of the guaian type – arborescin, austricin, artausin and the flavonoid 5-hydroxy-7,4'-dimethoxy-6-methylflavone, were isolated and identified from the acetone extract of *Artemisia austriaca* Jacq. by column chromatography. Only arborescin and austricin were isolated from the water extract of *Artemisia austriaca* Jacq. The molecule structure of the isolated compounds was established on the basis of IR-, UV-, and NMR-spectroscopy data. The crystal and molecular structures of arborescin and austricin were studied by X-ray diffraction analysis. Arborescin and austricin are optically active compounds and have 6 and 5 asymmetric carbon atoms in their structure, respectively. Austricin is a marker component in the *Artemisia* line closely related to *Artemisia austriaca* Jacq. Isolation and identification of the sesquiterpene lactones of arborescin and austricin allows us to consider *Artemisia austriaca* Jacq. as a biogenetically close species to *Artemisia* of the subgenera *Artemisia* Less. and *Seriphidium* (Bess.) Rouy. Austricin is a promising renewable material for the development of original lipid-lowering, antioxidant and antiparasitic agents.

Key words: *Artemisia austriaca* Jacq., extraction, sesquiterpene lactones, flavonoid, biogenetic relationship, biological activity.

Introduction

Artemisia austriaca Jacq., *Asteraceae* family – perennial herbaceous plant, widespread in Central Kazakhstan, Western Siberia, Central Europe, Crimea, Iran, Caucasus, Balkans [1; 2].

In traditional medicine, *Artemisia austriaca* Jacq. is used as a wound healing, anticonvulsant, anthelmintic, antibacterial, anti-inflammatory, hemostatic agent [3; 4]. Extract of *Artemisia austriaca* Jacq. has a pronounced antioxidant, antiinflammatory activity [5; 6].

Artemisia austriaca Jacq. is considered as a promising source of biologically active compounds, among which the most important are terpenoids and phenolic compounds.

Earlier it was reported that during the flowering phase from the aerial part of *Artemisia austriaca* Jacq., growing in Turkey, an essential oil was isolated by hydrodistillation, with camphor (45.5%), 1,8-cineole (30.4%), camphene (6.5%), α-terpineol (3.2%), a-pinene (3.0%), and terpinen-4-ol (2.9%) as basic ingredients [7]. In the essential oil isolated from the aerial part of *Artemisia austriaca* Jacq., growing in Iran, the main components were camphor (15.88%), 1,8-cineole (10.75%), camphene (3.53%) and beta-fenchyl alcohol (3.03%) [8]. The component composition of the essential oil of *Artemisia austriaca* Jacq. growing in the Stavropol territory in Russia was studied by gas chromatography–mass spectrometry. The main components are α-thujone (55.26%), 1,8-cineole (12.01%), terpineol-4 (4.32%), (+)-camphor (4.11%) [9].

Artemisia austriaca Jacq., collected during the flowering phase in N.N. Grishko National Botanical Gardens of the National Academy of Sciences of Ukraine, was studied for the content of essential oils and phenolic compounds. The main components of the essential oil, obtained by hydrodistillation, were trans-verbenol (30.77%), sabinyl acetate (18.16%), pinocarvone (10.77%), 1,8-cineole (7.31%), sabinol (6.02%), terpinen-4-ol (2.98%), para-ment-1,5-dien-8-ol (3.55%). The sum of phenolic compounds in the air-dry raw material was 2.73%, the main flavonoid – rutin [10].

It is known that the quantitative content and qualitative composition of biologically active compounds in various organs of *Artemisia* and in different phases of their development is not the same and changes during the growing season, but also depends on climate conditions and methods of isolation. So, from the ethyl acetate extract of the raw materials of *Artemisia austriaca* Jacq., gathered in the Akmola region, the sesquiterpene lactones matricarin, austricin and the flavonoid cirsilineol were isolated [11], and from *Artemisia austriaca* Jacq., growing

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in Turkey, an extract was obtained with petroleum ether, from which 8α-hydroxyachylline was isolated [12].

The purpose of this work is a comparative chemical study of acetone and water extractions of the aerial part of *Artemisia austriaca* Jacq. growing in Central Kazakhstan, determination of the optimal conditions for the isolation of sesquiterpene γ-lactones and flavonoids.

Materials and methods

The individuality of the compounds was monitored by thin layer chromatography (TLC) on a TLCP-AF-A-UV plate of the "Imid" company (Russia). TLC plates were stained in a 2% aqueous solution of $KMnO_4$. For column adsorption chromatography, we used KSK silica gel with a grain size of less than 0.3 mm. Melting points were determined using an OptiMelt apparatus (United States). The IR-spectrum was recorded on an "Avatar 360" spectrometer (USA) in tablets with potassium bromide, in the range from 4000 to 500 cm^{-1}. The specific optical rotation was measured on a Polax-2L semi-automatic polarimeter (Japan) in a tube 0.5 dm in length and 3 ml in volume. NMR spectra were recorded on a Jeol Resonance-500 spectrometer (operating frequency 500.16 MHz for ^1H, 125.76 MHz for ^{13}C, d-scale).

The X-ray diffraction experiment was carried out on a Bruker KAPPA Apex II diffractometer (MoKα radiation with a graphite monochromator, CCD detector, φ, ω-scanning). Absorption was taken into account using the SADABS program. The structure of the compounds was deciphered by a direct method and refined in the anisotropic-isotropic (for H atoms) approximation using the SHELX-97 program. The positions of hydrogen atoms were determined geometrically, the parameters of hydrogen atoms were refined in the isotropic approximation of the rider model.

Raw materials. Aerial part (buds, flower baskets and leaves) of *Artemisia austriaca* Jacq. were collected in the budding and flowering phase in the vicinity of Karaganda. Herbarium specimens are kept in the herbarium fund of JSC "International Research and Production Holding "Phytochemistry" (KG) (Karaganda, Republic of Kazakhstan). For the extraction of biologically active substances of *Artemisia austriaca* Jacq., acetone and water extraction of raw materials of the aerial part was carried out.

Acetone extraction. 7 kg of flower baskets and leaves of *Artemisia austriaca* Jacq., collected in the budding phase in the vicinity of Karaganda, were extracted five times with acetone (hydromodule 1:5). The resulting sum of extractive substances (314 g) was subjected to water-alcohol treatment (ratio 1:2), while the filtrate was treated with chloroform at a ratio of 1:1. The sum of extractive substances (37 g) was chromatographed on a column with KSK silica gel in the ratio (1:30).

Isolation of sesquiterpene lactones and flavonoids.

Isolation of arborescin **(1)**. Upon elution with a benzene-ether mixture (9: 1), 1.2 g of crystalline substance (**1**) with the composition $C_{15}H_{20}O_3$ with m.p. 139-142°C, $[\alpha]^{20}_D$ +63° (c 4.24; chloroform) was isolated. The yield of compound (**1**) was 0.6% based on air-dry raw materials.

UV-spectrum (EtOH, λmax, nm): 204 (ε 18521).

IR-spectrum (KBr, νmax, cm^{-1}): 3065, 3020, 2985, 2950, 2925, 2880, 1770 (γ-lactone carbonyl), 1660 (C = C), 1450, 1385, 1325, 1300, 1275, 1250, 1230, 1190, 1175, 1130, 1120, 1110, 1070, 1040, 1025.

^1H NMR spectrum (500 MHz, $CDC1_3$, ppm, J/Hz): 1.18 (3H, d, J = 6.9, CH_3-13), 1.33 (3H, s, CH_3-14), 1.45 (1H, m , H-8β), 1.64 (1H, m, H-8α), 1.76 (1H, m, H-7), 1.93 (3H, br.s, CH_3-15), 2.08 (1H, m, H-9β), 2.14 (1H, m, H-2β), 2.18 (1H, m, H-9α), 2.76 (1H, m, H-2α), 2.95 (1H, d, J = 10.0, H-5), 3.15 (1H, dq, J = 12.3, 6.9, H-11), 4.02 (1H, t, J = 10.0, H-6), 5.55 (1H, s, H-3).

^{13}C NMR spectrum (125 MHz, $CDC1_3$, ppm): 16.1 (q, C-13), 22.0 (t, C-8), 26.4 (q, C-14), 26.5 (q, C-15), 37.1 (t, C-9), 43.3 (t, C-2), 44.5 (d, C-11), 55.9 (d, C-7), 58.1 (d, C-5), 66.1 (c, C-10), 76.0 (s, C-1), 86.2 (d, C-6), 128.4 (d, C-3), 144.3 (s, C-4), 182.2 (s, C-12).

Isolation of austricin **(2)**. Upon elution with a benzene-ether mixture (9: 1), 0.6 g of colourless crystalline substance (**2**) with the composition $C_{15}H_{18}O_4 \bullet H_2O$ with m.p. 149-151°C, $[\alpha]^{20}_D$ +13,52° (c 3.7; ethanol) and a yield of 0.03% based on air-dry raw materials was isolated.

UV-spectrum (EtOH, λmax, nm): 255 (ε 14425).

IR-spectrum (KBr, νmax, cm^{-1}): 3550 (OH-group), 1775 (γ-lactone carbonyl), 1685, 1645, 1630 (cyclopentadienone).

^1H NMR spectrum (500 MHz, DMSO-d_6, ppm, J/Hz): 1.25 (3H, d, J = 6.8, CH_3-13), 2.18 (3H, s, CH_3-15), 2.30 (3H, s, CH_3-14), 2.26 (1H, d, J = 12.0, H-11), 2.29 (1H, dd, J = 10.4, 7.4, H-7), 2.61 (1H, dd, J = 11.3, 10.4, H-9α), 2.94 (1H, dd, J = 11.3, 7.4, H-9β), 3.77 (1H, t, J = 10.6, H-8), 3.62 (1H, d, J = 10.1, H-5), 3.95 (1H, t, J = 10.4, H-6), 5.08 (OH at C-8), 6.07 (1H, s, H-3).

^{13}C NMR spectrum (125 MHz, DMSO-d_6, ppm): 15.3 (q, C-13), 18.2 (q, C-14), 20.9 (q, C-15), 39.5

(d, C- 8), 47.3 (d, C-11), 49.4 (t, C-9), 59.4 (d, C-5), 66.5 (d, C-7), 79.1 (d, C-6), 129.0 (s, C-1), 131.5 (d, C-3), 142.5 (s, C-10), 166.4 (s, C-4), 173.4 (s, C-12), 189.8 (s, C-2).

Isolation of artausin **(3)**. Upon elution with a benzene-ether mixture (1:1), 0.095 g of colourless crystalline substance (**3**) with the composition $C_{15}H_{22}O_3$ with m.p. 201-204°C (from ethanol) was isolated. The yield of compound (**3**) was 0.0005% based on air-dry raw materials).

UV-spectrum (EtOH, λmax, nm): 204 (ε 19800).

IR-spectrum (KBr, νmax, cm^{-1}): 3470, 3400 (OH group), 1750 (γ-lactone carbonyl), 1630 (C = C).

^{1}H NMR spectrum (500 MHz, $CDC1_3$, ppm, J/Hz): 1.18 (3H, d, J = 6.0, CH_3-13), 1.22 (3H, s, CH_3-15), 1.62 (2H, m, H-3α, 3β), 1.86 (3H, q, J = 1.0, CH_3-14), 1.92 (1H, m, H-8α), 2.02 (1H, m, H-2β), 2.15-2.35 (4H, m, H-1, H-5, OH-4, H-11), 2.53 (1H, dd, J = 6.0, 4.0, H-2α), 2.64 (1H, doublet of sextets, J = 16.0, H-8β), 3.20 (1H, d, J = 1.0, H-7), 4.15 (1H, dd, J = 11.0, 9.5, H-6), 5.39 (1H, m, H-9).

^{13}C NMR spectrum (125 MHz, $CDC1_3$, ppm): 14.81 (q, C-13), 18.9 (q, C-14), 22.1 (q, C-15), 24.2 (d, C-1), 26.1 (t, C-8), 35.1 (t, C-2), 37.1 (t, C-3), 45.5 (d, C-11), 47.3 (d, C-5), 59.6 (d, C-7), 67.4 (s, C-4), 77.3 (d, C-6), 123.3 (d, C-9), 141.1 (s, C-10), 174.6 (s, C-12).

Isolation of 5-oxy-7,4'-dimethoxy-6-methylflavone **(4)**. Upon elution of the system with a benzene-ether mixture in a composition of 1:1, a yellow crystalline substance of the composition $C_{18}H_{16}O_5$ with m.p. 180-183°C and a yield of 0.0007% based on air-dry raw materials was isolated.

UV-spectrum (EtOH, λmax, nm): 244 (ε 15200), 276 (ε 13600), 342 (ε 19200).

IR-spectrum (KBr, νmax, cm^{-1}): 3600-3400 (OH-group), 2846, 1670 (C=O), 1630, 1590 (aromatic ring).

^{1}H NMR spectrum (500 MHz, $CDC1_3$, ppm, J/Hz): 2.11 (3H, s, CH_3), 3.83 (3H, s, 4'-OCH_3), 3.98 (3H, s, 7-OCH_3), 6.43 (1H, s, H-3), 6.53 (1H, s, H-8), 6.95 (2H, d, J = 8.9, H-3', H-5'), 7.77 (2H, d, J = 8.9, H-2', H-6'), 13.04 (1H, s, 5-OH).

^{13}C NMR spectrum (125 MHz, $CDC1_3$, ppm): 182.97 (s, C-4); 164.46 (s, C-2), 159.18 (s, C-7), 152.41 (s, C-5), 148.86 (s, C-9), 147.9 (s, C-4 '), 111.7 (s, C-6), 129.27 (d, C-2', C-6'), 122.27 (s, C-1'), 116.87 (d, C-3', C-5'), 106.23 (s, C-10), 103.82 (d, C-3), 91.48 (d, C-8), 60.42, 55.83 (OCH_3), 9.00 (q, CH_3).

Water extraction.

2 kg of the aerial part (flower baskets, leaves) of *Artemisia austriaca* Jacq., collected in the budding phase in the vicinity of Karaganda, was infused four times with hot water (at a temperature of 80-85°C). The aqueous extracts were combined, then extracted three times with chloroform. Chloroform extracts were combined, evaporated under vacuum. 31.3 g of the sum of extractive substances were isolated.

Isolation of arborescin **(1)**.

Upon chromatography of the sum of extractive substances on a column with KSK silica gel in a sum-carrier ratio = 1:17 and eluted by the system with a benzene-ether mixture (4:1 ratio), 2.2 g of a colorless crystalline substance (**1**) of the composition $C_{15}H_{20}O_3$, mp 139-142°C, $[\alpha]^{20}_D$ +63° (c 4.24; chloroform) was isolated. The yield of compound (**1**) was 0.11% based on air-dry raw materials.

Isolation of austricin **(2)**. Elution of the column with ether yielded 0.6 g of a colorless crystalline substance (**2**) of the composition $C_{15}H_{18}O_4 \bullet H_2O$ with m.p. 149-151°C, $[\alpha]^{20}_D$ +13.52 ° (*c* 3.7; ethanol). The substance yield was 0.03% for air-dry raw materials.

Results and discussion

Aerial part (buds, flower baskets and leaves) of *Artemisia austriaca* Jacq. was exhaustively extracted with acetone and the resulting extract was evaporated under vacuum on a rotary evaporator. Chromatography of the obtained sum of extractive substances on a column with KSK silica gel by elution with a benzene-ether mixture (9:1) isolated a colorless crystalline substance of the composition $C_{15}H_{20}O_3$ (**1**).

The IR spectrum of compound (**1**) contains absorption bands in the range of 3065, 3020, 2985, 2950, 2925 (C-H), 1770 (γ-lactone carbonyl), 1660 (C=C), 1130 cm^{-1} (C-O-C epoxy group).

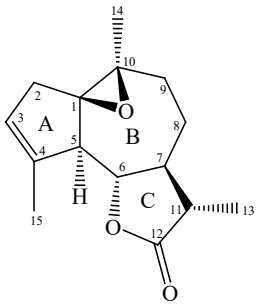
In the ^{1}H NMR spectrum of molecule (**1**), proton signals in the 1.33 ppm region are observed in the form of singlets, characteristic of the methyl group at epoxide, in the 1,18 ppm region, a doublet with a spin-spin coupling constant of 6 Hz is observed, which belongs to the secondary methyl group at C-11, and protons in the form of a broadened singlet at 1.93 ppm – the methyl group at the C-4 double bond. The signal of the proton in the region of 4.02 in the form of a triplet with a spin-spin coupling constant of 10 Hz, characteristic of the lactone proton H-6.

The ^{13}C NMR spectrum indicates the presence of 15 carbon atoms in its molecule. Thereby, signals are noted that are characteristic of the carbon atom of the carbonyl group in the region of 182.2 ppm, which belongs to the lactone group. Signals from the carbon atoms of three methyl groups are also observed (16.1 ppm; 26.5 ppm; 26.4 ppm). Two signals at 128.4 and 144.3 ppm characteristic of carbon atoms at the olefinic double bond.

According to the physicochemical constants, IR, ^{13}C-NMR-spectra and comparison with the literature, the isolated compound was identified as the sesquiterpene lactone arborescin (**1**) [13-15].

The stereochemistry of the crystal structure of the arborescin molecule (**1**) was studied by X-ray diffraction method. The structure of the molecule (**1**) is shown in Figure 1. Cycle *A* has the shape of an envelope, the atoms C2, C3, C4, C5 lie in the same plane. The conformation of cycle *B* is very close to the shape of a chair with a plane of symmetry passing through the C7 atom and the middle of the bond between the C1 and C10 atoms. The *C* lactone cycle is in a slightly distorted envelope shape. This form of the *C* lactone cycle is characteristic of sesquiterpene lactones with the *trans*-junction of the *B* and *C* cycles. The arborescin molecule (**1**) has 6 asymmetric carbon atoms C-1, C-5, C-6, C-7, C-10, C-11.

Based on the above-mentioned data, the structure of 1(10)b-epoxy-5α,7a,6b,11b(H)-guai-3(4)-en-6,12-olide corresponds to the molecule (**1**).



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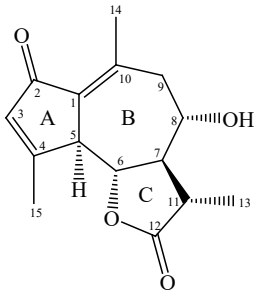


(2)

Upon further elution of the column with a benzene-ether system, a colorless crystalline substance (**2**) of the composition $C_{15}H_{18}O_4 \bullet H_2O$ was isolated.

The data of the IR- and UV-spectra of compound (**2**) made it possible to assume that its molecule contains the same dienone group as in matricarin, leucomisin, as well as a γ-lactone ring (1775 cm-1), OH-group (3550 cm^{-1}) and cyclopentadienone (1685, 1645, 1630 cm^{-1}), as evidenced by the absorption maximum at 255 nm.

Acetylation of molecule (**2**) with acetic anhydride in pyridine gave acetylaustricin, a colorless crystalline substance, with a yield of 96%. The IR-spectrum shows the absorption band of the acetyl group (1745 and 1250 cm^{-1}). The presence of the aceto group is also confirmed by the data of the PMR-spectrum, where there are signals of the protons of the methyl of the acetyl group in the form of a singlet at 2.02 ppm (3H) and the signal of the heme-acetyl proton in the form of a triplet at 5.62 ppm (1H, SSCC 6 Hz). According to the ^{13}C NMR spectrum, the values of the chemical shifts of carbon atoms for compound (**2**) and its acetyl derivative differ insignificantly, except for the C-8 signal.

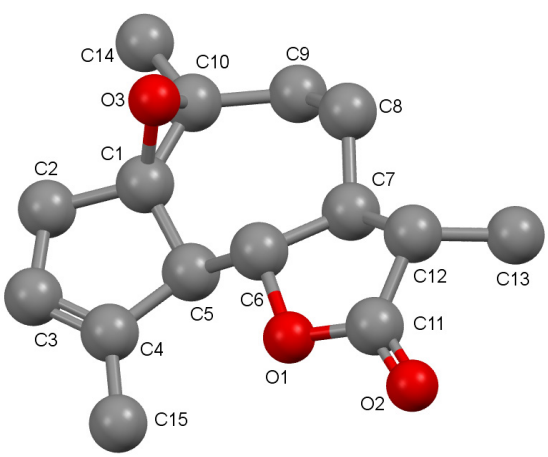
The ^{1}H NMR spectrum of molecule (**2**) is very close to the NMR spectrum of leucomisin, in comparison with which in the region of 3.77 ppm an additional signal is observed, which is the result of the superposition of the signals of the hydroxyl group and the geminal proton to it. The shift of the methyl group signal in the spectrum of austricin compared to the spectrum of leucomisin is most likely associated with its spatial proximity to hydroxyl and manifests itself as a doublet with SSCC 6.8 Hz in the region of 1.25 ppm. Three-proton singlets of methyl groups are noted at ***C***-10 and ***C***-4 in the region of 2.30 and 2.18 ppm, respectively.

The ^{13}C NMR spectrum data indicate the presence of fifteen carbon atoms in the molecule (**2**). In this case, a signal characteristic of the carbon atom of the carbonyl group is noted in the region of 173.4 ppm, which belongs to the lactone group. Four signals at 129.0, 131.5, 142.5 and 166.4 ppm are characteristic of carbon atoms at the olefinic double bond. Signals from the carbon atoms of three methyl groups (15.3 ppm, 18.2 ppm, and 20.9 ppm) are also observed.

The stereochemistry of the crystal structure of the molecule (**2**) was studied by the X-ray diffraction method. The structure of the molecule (**2**) is shown in Figure 1. The conformation of cycle A is a strongly flattened envelope: the C2, C3, C4 atoms and the exocyclic O3 atom are in the same plane, and the C1 and C15 atoms leave it in the α-side by 0.05 and 0.07 Å, respectively. The conjugated system O3, C2, C1,

C10 is actually flat. The conformation of cycle B is a slightly distorted chair: atoms C5, C6, C8, C9 are coplanar within ±0.02 Å, and atoms C1, C7, and C10 leave it their plane by 1.05, 0.70, and 1.09 Å in β, α, β-side, respectively. The conformation of the lactone ring C has the shape of an envelope (the C6, O1, C11, and C12 atoms are in the same plane and the C7 atom leaves it by 0.62 Å in the α-side). The methyl group at C11 has a quasiequatorial α-orientation. The junction of cycles B and C is trans-arrangement. The austricin molecule (**2**) has 5 asymmetric carbon atoms C-5, C-6, C-7, C-8, C-11.

Thus, the results of spectral data (IR-, PMR-, C^{13} NMR), including X-ray diffraction analysis, and comparison with the available literature data [11-12], for the isolated compound (**2**) a structure of 2-keto-8α-hydroxy-5α,7α,6β,11β(H)-guai-1(10),3(4)-diene-6,12-olide was proposed.



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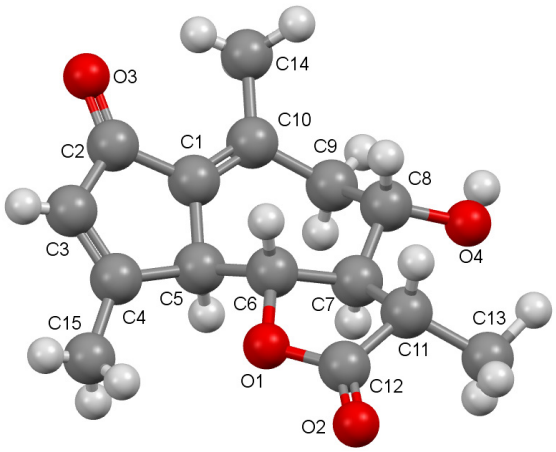


(2)

Figure 1 – Spatial structure of molecules (**1**) and (**2**) according to X-ray structural analysis.

Upon elution of the column with a benzene-ether mixture (1:1), a colorless crystalline substance (**3**) of the composition $C_{15}H_{22}O_3$ was isolated.

The IR-spectrum of compound (**3**) contains absorption bands characteristic of the hydroxyl group (3470 cm^{-1}), γ-lactone carbonyl (1750 cm^{-1}) and C=C-bonds (1630 cm^{-1}).

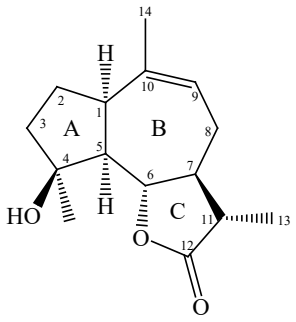
The ^{13}C NMR spectrum contains signals from 15 carbon atoms: three quartets, three triplets, six doublets, and three singlets, which characterize the guaiane skeleton.

The PMR spectrum of molecule (**3**) contains a 1.18 ppm doublet (J=6 Hz, 3H), characteristic of the secondary methyl group, a 1.22 ppm singlet (1H) – for the proton of the tertiary OH group, a 1.86 ppm quartet (J=1.0 Hz, 3H) indicates the presence of methyl at the double bond, which interacts with the vicinal olefinic proton H-9 and H-1. The doublet of sextets 2.64 ppm (J = 16.0 Hz, 1H) was assigned to the H_β proton at C-8. Upon the suppression of the signal of the olefinic proton (double resonance), the signal at 2.64 ppm changes the quintet doublet multiplicity. Multiplet 3.20 ppm (J=1.0 Hz, 1H) refers to H-7. The signal of the lactone proton appears as a doublet of 4.15 ppm doublets (J = 11.0, 9.5 Hz, 1H), which characterizes its addition at C6-C7. The multiplet in the region of 5.39 (1H signal width at half-height of intensity is 6 Hz) corresponds to an olefinic proton (splitting occurs due to its weak interaction with Me-10, H-1 and H-8 protons).

Compound (**3**) is not acetylated with acetic anhydride and is not oxidized with chromic anhydride in pyridine, that is, the hydroxyl group is tertiary. Based on the obtained data of IR- and PMR-spectra and their comparison with the literature [16] for the isolated compound (**3**), the structure of 4β-hydroxy-1α,5α,7α,6β(H)-guai-9(10)-en-6,12-olide was proposed.

Column elution with a benzene-ether mixture (1:1) yielded a colorless crystalline substance (**4**) of the composition $C_{18}H_{16}O_5$.

The IR-spectrum contains absorption bands characteristic of the hydroxyl group in the region of 3600-3400 cm^{-1}, the carbonyl group in the region of 1670 cm^{-1} and double bonds in the aromatic ring at 1630, 1590 cm^{-1}.



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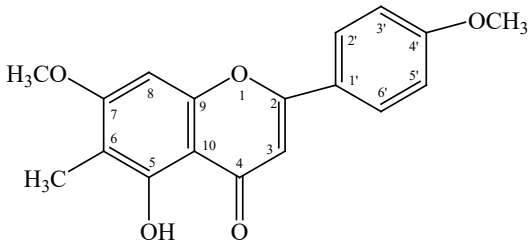

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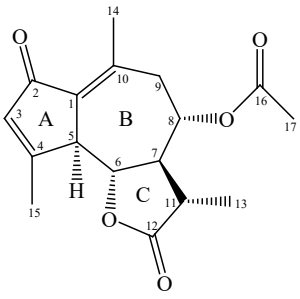

(5)

In the ^{1}H NMR spectrum, the proton signal at C-8 appears as a singlet in the region from 6.53 ppm. The proton of the OH group at C-5 resonates in a weak field in the form of a singlet at 13.04. The signals of the protons of the methoxy groups appear as singlets in the region of 3.83 (4'-OCH_3) and 3.98 ppm. (7-OCH_3). In the case of 4'-substitution, protons in positions H-2 'and H-6', as well as H-3 'and H-5' become pairwise equivalent and resonate in the form of two two-proton doublets with a coupling constant of 8.9 Hz in the region of 7.77 ppm and 6.95 ppm respectively.

The ^{13}C NMR spectrum confirms the presence of 18 carbon atoms in its molecule. The signal characteristic of the carbonyl group at C-4 is in the region of 182.97 ppm.

According to physicochemical constants, spectral data, the isolated compound (**4**) was identified as 5-oxy-7,4'-dimethoxy-6-methylflavone [17,18].

By hot water extraction of the aerial part of *Artemisia austriaca* Jacq. followed by extraction with chloroform and chromatographic separation of the sum of substances on a column with KSK silica gel (1:20), 0.11% of arborescin (**1**) and 0.03% of austricin (**2**) were isolated, calculated on air-dry raw materials.

As can be seen from the Table, the qualitative composition and quantitative content of sesquiterpene lactones, flavonoids in *Artemisia austriaca* Jacq. depend on the place of growth and the phase of development. The extraction of components from plant raw materials also depends on the method of isolation and subsequent purification of individual compounds. So, the sesquiterpene lactones arborescin (**1**), austricin (**2**), artausin (**3**) and the flavonoid 5-oxy-7,4'-dimethoxy-6-methylflavone (**4**) were isolated from the acetone extract of *Artemisia austriaca* Jacq., while from the aqueous extract isolated only sesquiterpene lactones arborescin (**1**), austricin (**2**) were isolated.

Table 1 – Results of the chemical study of *Artemisia austriaca* Jacq.

Extraction method	Chromatographic separation (sorbent, eluent)	Individual components	Yield in terms of air-dry raw materials, %
Water extraction (buds, flower baskets and leaves)	KSK brand silica gel (carrier amount 1:17)		
	Benzene ether (4:1)	arborescin (1)	0.11
	Benzene ether (1:1)	austricin (2)	0.03
Acetone extraction (buds, flower baskets and leaves)	KSK brand silica gel (carrier amount 1:30)		
	Benzene ether (9:1)	arborescin (1)	0.6
	Benzene ether (9:1)	austricin (2)	0.03
	Benzene ether (1:1)	artausin (3)	0.0005
	Benzene ether (1:1)	5-oxy-7,4'-dimethoxy-6-methylflavone (4)	0.0007

Sesquiterpene lactones of the guaian structure arborescin (**1**), austricin (**2**), and artausin (**3**) are common in the *Asteraceae* family of the *Absinthium* DC section [19-23].

In addition, the results obtained suggest that the biogenetic precursor of dienone guaianolide austricin (**2**) can be matricarin (**5**) synthesized in the plant organism by the mevalonate-isopentylpyrophosphate-farnesylpyrophosphate pathway.

According to the literature data [19-25], austricin (**2**) is biosynthesized in the following species of *Artemisia*: *Artemisia lanata* Willd., *Artemisia cana* Pursh ssp. Cana, *Artemisia klotzchiana* Bess., *Artemisia leucodes* Schrenk, *Artemisia lercheana* Web. ex Stechm., *Artemisia tilesii* Ldb, *Artemisia tridentate* Nutt. ssp. Tridentate, *Artemisia vermicularis* Trin., *Artemisia sericea* Wb. ex Stechm., *Artemisia jacutica* Drob., and arborescin **(1)** – in *Artemisia arborescens* L., *Artemisia judaica* L., which allows us to consider them as biogenetically related species to *Artemisia austriaca* Jacq.

Sesquiterpene lactones of the guaian series with a dienone fragment are considered as agents with hypolipidemic, antioxidant, and antiparasitic activities [26-28]. Therefore, austricin (**2**) is a promising renewable material for the development of new medicinal substances.

Conclusion

Thus, a chemical study of *Artemisia austriaca* Jacq., three sesquiterpene lactones of the guaian type and flavonoid have been identified, which can be of interest as biologically active substances, as well as an initial material for the synthesis of new practically valuable compounds. The sesquiterpene lactone austricin can be considered as a potential source of a new lipid-lowering, antioxidant and antiparasitic agent. Austricin is a marker component in the *Artemisia* line closely related to *Artemisia austriaca* Jacq.

The qualitative composition and quantitative content of biologically active substances in *Artemisia austriaca* Jacq. depend not only on the place of growth, the phase of plant development, but also on the method of their isolation from plant raw materials.

Acknowledgments

The work was carried out under the grant project AP09260624, funded by the Science Committee of the MES of the Republic of Kazakhstan.

References

1 Pavlov N.V. (1966) Flora of Kazakhstan. [Flora Kazakhstana] Alma-Ata: Science., vol.9, pp.9-10.

2 Komarova V.L. (1961) Flora of USSR [Flora SSSR] Leningrad: Moscow, Vol. 26. pp.31-32.

3 Sokolov P.D. (1993) Plant resources of the USSR. Flowering plants, their chemical composition, use. *Asteraceae* Family. [Rastitel'nyye resursy SSSR. Tsvetkovyye rasteniya, ikh khimicheskiy sostav, ispol'zovaniye. Semeystvo Asteraceae]. S.-Petersburg: Science, 350 p.

4 Mercan U., Oner A., Onture H. (2008) Investigation of acute liver toxicity and anti-inflammatory effects of *Artemisia austriaca* Jacq. Pharmacol., no1, pp. 131-138.

5 Grudzinskaya L.M., Gemedzhieva N.G., Nelina N.V., Karzhaubekova Zh.Zh. (2014) Annotated list of medicinal plants of Kazakhstan. [Annotirovannyy spisok lekarstvennykh rasteniy Kazakhstana] Almaty, pp.27.

6 Ozgen U., Mavi A., Terzi Z. (2004) Antioxidant activities and total phenolic compounds amount of same *Asteraceae* species. Turkish Journal of Pharm Sci., vol.1, no3.-pp.203-216.

7 Güvenalp Z., Çakir A., Harmandar M., Gleispach H. (1998) The essential oils of *Artemisia austriaca* Jacq. and *Artemisia spicigera* C. Koch. from Turkey. Flavour and Fragrance Journal, vol. 13, no 1, pp. 26–28. https://doi.org/10.1002/(SICI)1099-1026(199801/02)13:1<26::AID-FFJ686>3.0.CO;2-P

8 Razavi S.M., Nourouzi Z., Ghasemiian A., Ghorbani A., Latifi S. (2014) Chemical composition of the essential oil of *Artemisia austriaca* Jacq. growing wild in Iran. Turkish Journal of Biochemistry / Turk Biyokimya Dergisi, vol. 39, Is. 3, pp. 368-372.

9 Konovalov D.A., Konovalov Yu.B. (2006) Component composition of essential oil of *Artemisia austriaca* Jacq. growing in the Stavropol Territory [Komponentnyy sostav efirnogo masla polyni avstriyskoy, proizrastayushchey v Stavropol'skom kraye] Kuban Scientific Medical Bulletin, №10, pp. 38-39.

10 Ivaschenko I.V., Rakhmetov D.B., Slastiya E.A., Ivashchenko O.A. (2014) Chromatographic analysis of the essential oil and phenolic compounds of *Artemisia austriaca* when introduced into Zhytomyr Polesie [Khromatograficheskiy analiz efirnogo masla i fenol'nykh soyedineniy *Artemisia austriaca* pri introduktsii v Zhitomirskom Poles'ye]

In collection: Ecosystems, their optimization and protection. Simferopol: TNU, Iss.10, pp.99-105.

11 Kikhanova Z.S., Iskakova Z.B., Dzhalmakhanbetova R.I., Seilkhanov, T.M., Ross S.A., Suleimen E.M. (2013) Constituents of *Artemisia austriaca* and their biological activity. Chemistry of Natural Compounds, vol. 49, no. 5, pp. 967–968. https://doi.org/10.1007/s10600-013-0796-5

12 Melikoglu G. (1988) A sesquiterpene lactone from *Artemisia austriaca*. J. Fac. Pharm. Istanbul Univ., 32, pp. 9-11

13 Mazur Y., Meisels A. (1956) The structure of arborescine, a new sesquiterpene from *Artemisia arborescens*. Chemistry and Industry, pp. 492-493.

14 Fraga B.M. (2013) Natural Sesquiterpenoids. Journal Natural Product Reports, vol.30, pp.1226-1264; 2012, vol.29, pp.1334-1366; 2011, vol.28, pp.1580-1610; 2010, vol.27, pp.1681-1708; 2009,Vol.26, pp.1125-1155; 2008, vol.25, pp.1180-1209; 2007, vol.24, pp.1350-1381; 2006, vol.23, pp.943-972.

15 Sulsen V., Martino V. (2018) Sesquiterpene lactones. Advances in their chemistry and biological aspects. Springer International Publishing AG, Cham, Switzerland, 381p. ISBN: 978-3-319-78274-4

16 Fischer N.H., Olivier E.J., Fischer H.D. (1979) The Biogenesis and Chemistry of Sesquiterpene Lactones. Fortschr. Chem. Org. Naturst., vol. 38, pp. 47-390. http://dx.doi.org/10.1007/978-3-7091-8548-3_2

17 Klyshev L.K., Bandyukova V.A., Alyukina L.S. (1978) Flavonoids of plants [Flavonoidy rasteniy] – Scince, Alma-Ata, 220 p.

18 Korulkin D.Yu., Abilov Zh.A., Muzychkina R.A., Tolstikov G.A. (2007) Natural flavonoids [Prirodnyye flavonoidy]. Novosibirsk: Geo, 232 p. ISBN 978-5-9747-0119-1

19 Aguilar J.M., Collado I.G., Macías F.A., Massanet G.M., Rodríguez-Luis F., Fronczek F.R., Waikins S.F. (1988) Sesquiterpene lactones from *Artemisia lanata.*Phytochemistry, vol. 27, Is. 7, pp. 2229–2233. https://doi.org/10.1016/0031-9422(88)80132-8

20 Grandolini G., Casinovi C.G., Betto P., Fardella G., Menichini, F., Gabriele, R., Barbetti P., Kajtar-Peredy M., Radics L. (1988) A sesquiterpene lactone from *Artemisia arborescens*. Phytochemistry, vol. 27, Is. 11, pp. 3670–3672. https://doi.org/10.1016/0031-9422(88)80792-1

21 Appendino G., Gariboldi P. (1982) The stereochemistry of matricin and 4-epimatricin, proazulene sesquiterpene lactones from *Artemisia arborescens*. Phytochemistry, vol.21, Is.10, pp. 2555–2557. https://doi.org/10.1016/0031-9422(82)85255-2

22 Rybalko K.S., Bankovskiy A.I., Sheichenko V.I. (1969) Natural sesquiterpene lactones [Prirodnyye seskviterpenovyye laktony] In book: Medicinal plants. – Moscow: Kolos, vol.15, pp. 168-331.

23 Rybalko K.S. (1978) Natural sesquiterpene lactones [Prirodnyye seskviterpenovyye laktony].-Moscow: Medicine, 320 p.

24 Adekenov S.M., Mukhametzhanov M.N., Kupriyanov A.N., Aituganov K.A. (1980) Lactones from *Artemisia sericea* [Laktony iz Artemisia sericea]. Chemistry of Natural Compounds, no3, pp. 421-422.

25 Benesheva V., Nazarenko M.V., Sleptsova, L.V. (1969) Sesquiterpene γ-lactones from *Artemisia jacutica*. Chemistry of Natural Compounds, vol. 5, no. 3, pp. 160. https://doi.org/10.1007/BF00636021

26 Rodnova E.A., Ivanov V.V., Ledyukova S.I., Chuchalin V.S., Ratkin A.V., Rakhimova B.B., Khabarov I.A., Adekenov S.M. (2012) The hypolipidemic effect of leucomisin in the model of acute ethanol-induced hyperlipidemia [Gipolipidemicheskoye deystviye leukomizina na modeli ostroy giperlipidemii indutsirovannoy etanolom] Bulletin of Siberian Medicine, vol.12, no 1, pp. 43-48.

27 Ivanov V.V., Ratkin A.V., Pfarger Yu.A., Kaidash O.A., Ryazantseva N.V., Adekenov S.M., Chuchalin V.S. (2014) The hypolipidemic effect of the sesquiterpene γ-lactone of achillin on the cell culture of rat hepatoma [Gipolipidemicheskoye deystviye seskviterpenovogo g-laktona akhillina na kletochnoy kul'ture krysinoy gepatomy] Bulletin of Siberian Medicine, vol.13, no 5, pp. 28-35.

28 Adekenov S.M. (2019) Study of antiopisthorchiasis activity of sesquiterpene lactones and their derivatives. Fitoterapia, vol. 133, pp. 200-211. https://doi.org/10.1016/j.fitote.2018.12.017