Determination of chemical composition of the *Ligularia narynensis* root by gas chromatography-mass spectrometry

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Ligularia is a medicinally important herb of the family Compositae. *Ligularia narynensis* is a perennial herb growing in the mountains, rich in sesquiterpenes, triterpenes, lignans, alkaloids, and steroids. In this work chemical constituents of the root part of medicinal plant *L. narynensis* from Kazakhstan have been determined for the first time. The constituents of the root part of *L. narynensis* were extracted with hexane and analyzed by gas chromatography – mass spectrometry (GC-MS). Thirty compounds were detected, and their concentrations were determined by the method of normalization of peak areas. Among them, the major components are (9Z,12E)-octadeca-9,12-dienoic acid (16.7%), ethyl (9Z,12Z)-octadeca-9,12-dienoate (11.1%), n-hexadecanoic acid (11.0%), (3a,5a,5b,8,8,11a-hexamethyl-1-prop-1-en-2-yl-1,2,3,4,5,6,7,7a,9,10,11,11b,12,13,13a,13b-hexadecahydrocyclopenta[a]chrysen-9-yl) acetate (9.1%), [(3R)-4,4,6a,6b,8a,11,11,14b-octamethyl-1,2,3,4a,5,6,7,8,9,10,12,12a,14,14a-tetradecahydropicen-3-yl] acetate (5.1%). Presence of these bioactive constituents may indicate that the plant extract possesses anti-inflammatory, antimicrobial and anticancer activities, which can serve as a basis for the development of new phytopreparations.

Keywords: *Ligularia narynensis*; hexane extract; liposoluble constituents; GC-MS.

Газ хроматография – масс-спектрометрия әдісімен *Ligularia narynensis* тамырларының химиялық құрамын анықтау

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Ligularia – терапиялық маңызды шөпті өсімдік. *Ligularia narynensis* сесквитерпен, тритерпен, лигнан, алкалоид және стероидтарға бай тауда өсетін көпжылдық өсімдік. Бұл жұмыста Қазақстанда өсетін *L. narynensis* дәрілік өсімдігі тамырларынан химиялық компоненттерінің талдауы бірінші рет жүргізілді. *L. narynensis* өсімдігі тамыр бөлігінен майда ергіш заттар гексанмен экстрагирленген және газды хроматография – масс-спектрометрияның (ГХ-МС) әдісімен талданды. Отыз қосылыс сарапталды және олардың концентрациялары пик аудандарын қалыпқа келтіру әдісімен анықталды, олардың ішінде негізгі (9Z,12E)-октадека-9,12-диен қышқылы (16,7%), этил (9Z,12Z)-октадека-9,12-диеноат (11,1%), n-гексадекан қышқылы (11,0%), (3a,5a,5b,8,8,11a-гексаметил-1-проп-1-ен-2-ил-1,2,3,4,5,6,7,7a,9,10,11,11b,12,13,13a,13b-гексадекагидроциклопента[a]хризен-9-ил) ацетат (9,1%), [(3R)-4,4,6a,6b,8a,11,11,14b-октаметил-1,2,3,4a,5,6,7,8,9,10,12,12a,14,14a-тетрадекагидропицен-3-ил] ацетат (5,1%) болып табылады. Осы биологиялық белсенді компоненттердің болуы өсімдік сығындысы қабынуға қарсы, микробқа қарсы және ісікке қарсы белсенділікке ие екенін көрсетуі мүмкін, бұл жаңа фитопрепараттарды әзірлеуге негіз бола алады.

Түйін сөздер: *Ligularia narynensis*; гександі экстракт; майда ергіш заттар; ГХ-МС.

Определение химического состава корней *Ligularia narynensis* методом газовой хроматографии – масс-спектрометрии

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Ligularia является терапевтически важным травянистым растением из семейства Compositae. *Ligularia narynensis* – многолетнее растение, произрастающее в горах, богатое сесквитерпенами, тритерпенами, лигнанами, алкалоидами и стероидами. В данной работе впервые был исследован химический состав корней лекарственного растения Казахстана *L. narynensis*. Жирорастворимые компоненты из корневой части *L. narynensis* были экстрагированы гексаном и проанализированы методом газовой хроматографии – масс-спектрометрии (ГХ-МС). Обнаружено тридцать соединений и их концентрации определены методом нормализации площадей пиков, среди которых основными составляющими являются (9Z,12E)-октадека-9,12-диеновая кислота (16,7%), этил (9Z,12Z)-октадека-9,12-диеноат (11,1%), n-гексадекановая кислота (11,0%), (3a,5a,5b,8,8,11a-гексаметил-1-проп-1-ен-2-ил-1,2,3,4,5,6,7,7a,9,10,11,11b,12,13,13a,13b-гексадекагидроциклопента[a]хризен-9-ил) ацетат (9,1%), [(3R)-4,4,6a,6b,8a,11,11,14b-октаметил-1,2,3,4a,5,6,7,8,9,10,12,12a,14,14a-тетрадекагидропицен-3-ил] ацетат (5,1%). Наличие этих биологически активных компонентов, может свидетельствовать о том, что растительный экстракт обладает противовоспалительной, противомикробной и противоопухолевой активностью, что может послужить основой для разработки новых фитопрепаратов.

Ключевые слова: *Ligularia narynensis*; гексановый экстракт; жирорастворимые компоненты; ГХ-МС.

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1. Introduction

Ligularia is a medicinally important herb of the family Compositae containing about 180 Eurasian species, 17 species growing in mountains of Kazakhstan [1]. Some species in this genus have been used for a long time as folk remedies for their antibacterial, anticancer, and antitumor activities [2-5]. More than 27 *Ligularia* species have been used as traditional Kazakh and Chinese medicinal herbs for the treatment of fever, pain, inflammation, intoxication, cough phlegm, removing blood stasis, emetic, diuresis, cholagogue [6,7]. Previous studies confirmed the presence of sesquiterpenes, triterpenes, sinapyl alcohol derivatives, lignans, alkaloids, and steroids in *Ligularia* [8]. Eremophilane sesquiterpenes are considered as the major secondary metabolites and taxonomic markers of *Ligularia* genus. More than 500 eremophilane sesquiterpenes have been reported from this genus [9,10].

Ligularia narynensis is a *perennial* herb growing in Almaty region of Kazakhstan and in Xinjiang province of China. Gao et al. [2,7,11,12] determined the structures of oplopane-type sesquiterpenes, a new 8-O-4'-type neolignan-, oplopane- and guaiane-type sesquiterpenoids, monoterpenoids from the roots of *L. narynensis*.

We have previously reported the chemical investigation results on total bioactive components from root part of *L. narynensis* such as organic acids, flavonoids, moisture content, total ash, and extractives content. Together with eleven macro-, microelements from the ash of plant were determined by using method of multi-element atomic emission spectral analysis. And same time, twenty amino and eight fatty acids were quantified in this plant [13]. In addition, fifty nine liposoluble constituents in chloroform extract from the root part of *L. narynensis* have been identified by gas chromatography-mass spectrometry (GC-MS) method [14].

In our continuously study of the plant, thirty liposoluble constituents in hexane extract from medicinal plant *L. narynensis* have been determined by GC-MS method which grown in Almaty region of Kazakhstan for the first time.

2. Experiment

2.1 Plant material

The root part of plant *L. narynensis* was collected in September 2017 from the Zailiysky Alatau Mountains of Almaty region and identified by Dr. Alibek Ydyrys. Specimens (1217-BN-17) were deposited in the Herbarium of Laboratory Plant Biomorphology, Faculty of Biology and Biotechnology, al-Farabi Kazakh National University, Almaty, Kazakhstan.

2.2 Extraction

The dried and powdered *L. narynensis* (100 g) was extracted three consecutive portions of 95% ethanol. Volume of each portion was 800 mL. Extraction time of each portion was 7 days. Filtered extracts were combined and concentrated under reduced pressure with a vacuum rotary evaporator R-300s (Buchi, Switzerland). A residue was dissolved in 150 mL of water and extracted with 150 mL of hexane (99%, China). Then the dry extract (133 mg) was stored at 4°C. For GC-MS analysis, 1 mg of dry extract was dissolved in 1 mL of hexane.

2.3 GC-MS conditions

Analyses were conducted on Agilent 7890A/5975C gas chromatograph coupled to mass spectrometer equipped with a 7683B auto injector (Agilent Technologies, USA). Separation was carried out with a HP-5MS fused silica capillary column (0.25 mm x 30 m, 0.25 µm film, J&W Scientific, USA). The

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injection port temperature was 310°C. The injection volume was 1 µL, split ratio 5:1. Helium (99.99 %, China) was used as the carrier gas at a rate of 1.0 mL/min. The column temperature was held at 50°C for 10 min, increased by 10°C/min to 300°C, and then held for 40 min. Mass spectra were obtained by electron impact (EI) ionization at 70 eV in scan mode (*m/z* 30-1000 amu). Solvent delay was 3 min. The detector, ion source and transfer line temperature were set to 150, 230 and 250°C, respectively.

2.4 Identification and quantitation

The compounds were identified using NIST14 library. Mass fraction of each detected compound was estimated using normalization of peak areas. The sample was analyzed three times. All data are expressed as the mean ± standard deviation of three replicate measurements.

3. Results and discussion

The liposoluble constituents present in hexane extract from the root part of *L. narynensis* were analyzed by GC-MS for the first time (Figure 1). Thirty compounds were detected on a chromatogram with a NIST MS library match >70% (Table 1). The prevailing constituents are: (9Z,12E)-octadeca-9,12-dienoic acid (16.7%), ethyl (9Z,12Z)-octadeca-9,12-dienoate (11.1%), n-hexadecanoic acid (11.0%), (3*a*,5*a*,5*b*,8,8,11*a*-hexamethyl-1-prop-1-en-2-yl-1,2,3,4,5,6,7,7*a*,9,10,11,11*b*,12,13,13*a*,13*b*-hexadecahydrocyclopenta[a]chrysen-9-yl) acetate (9.1%), [(3*R*)-4,4,6*a*,6*b*,8*a*,11,11,14*b*-octamethyl-1,2,3,4*a*,5,6,7,8,9,10,12,12*a*,14,14*a*-tetradecahydropicen-3-yl] acetate (5.1%). Table 1 report the composition of the liposoluble constituents of *L. narynensis.*

The earlier reports on the essential oil from *L. virgaurea* has been reported to possess 4-methyl-1-(1-methylethyl) 3-cyclohexen-1-ol (14.4%), 2-methyl-heptane (9.8%), 3-methyl-heptane (8.3%), heptane (7.9%), 4-methyl-1-(methylethyl)-bicyclo [3,1,0] hex-2-ene (7.8%), 3-methyl-hexane (6.4%), 2-methyl-hexane (5.5%) and limonene (4.7%) [15]. *L. stenocephala* growing in Korea was reported to possess *α*-pinene (41.1%), limonene (17.7%), 2,7-bis(spirocyclopropane) bicycle [2.2.1] heptan-5-one (13.2%), *o*-anisaldehyde (5.9%) and phellandrene (5.2%) as the major constituents of its oil [16]. The oil from *L. persica* (from Iran) contained (Z)-*β*-ocimene (12.5%), *cis*-*m*-mentha-2,8-diene (8.8%), *α*-eudesmol (8.7%), valencene (5.9%) and 14-hydroxy-*δ*-cadinene (5.7%) as the major constituents [17].

On correlating the liposoluble constituents' composition of these species, it appears that *L. virgaurea, L. stenocephala* and *L. persica* are chemotaxonomically not related to *L. narynensis.* These results indicated that the differences in the volatile profiles of the species are primarily qualitative. Taken together, these data suggest that *L. narynensis* may play very important role in the development of new phytopreparations.

The main liposoluble constituent of *L. narynensis* (9Z,12E)-octadeca-9,12-dienoic acid (16.7%) have been reported to have antimicrobial activity [18]. And second major liposoluble constituent ethyl (9Z,12Z)-octadeca-9,12-dienoate (11.1%) has a hypocholesterolemic, nematicide, antiarthritic, hepatoprotective, antiandrogenic, hypocholesterolemic, 5-alpha reductaseinhibitor, antihistaminic, anticoronary, insectifuge, antieczemic, antiacne activities [19]. n-Hexadecanoic acid (11.0%) might function as an anti-inflammatory agent [20]. Furthermore, this acid has an inhibitory activity. These findings further confirm the medicinal value of plant and its anticancer cytotoxic potential [21,22].

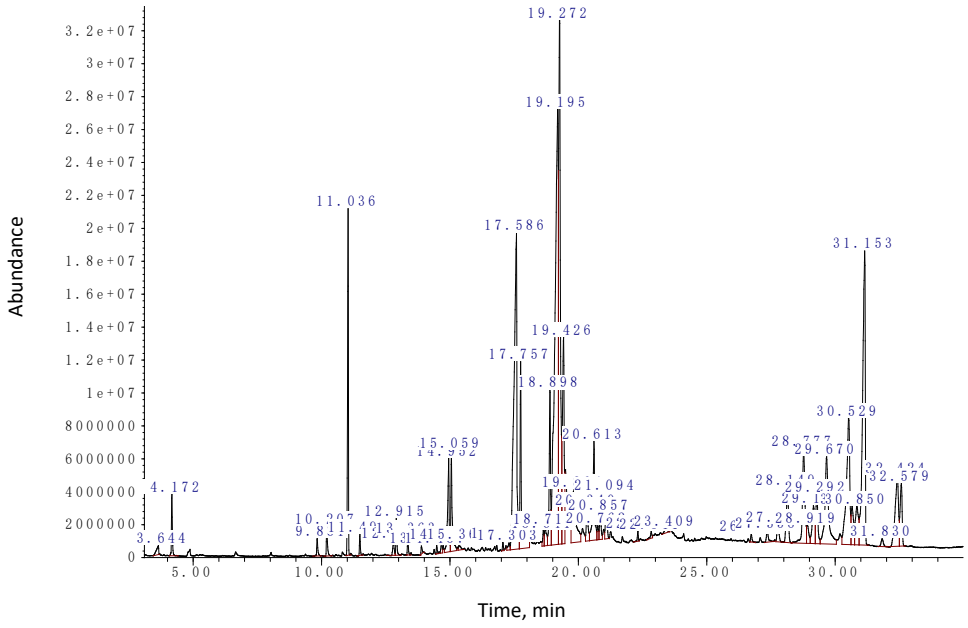

Figure 1 – Total ion (*m/z* 30-1000) chromatogram of hexane extract from the root part of *L. narynensis*

Table 1 – The liposoluble constituents from the root part of *L. narynensis*

Peak No.	Constituent	Cas No.	Retention time, min	Molecular formula	Molecular weight, amu	Content[a], %	NIST Match, %
1	2-Methoxy-4-vinylphenol	7786-61-0	9.831	$C_9H_{10}O_2$	150	0.23±0.03	94
2	2,6-Dimethoxyphenol	91-10-1	10.207	$C_8H_{10}O_3$	154	0.39±0.01	98
3	Phenoxybenzene	101-84-8	11.036	$C_{12}H_{10}O$	170	3.4±0.1	87
4	Dimethylbenzene-1,2-dicarboxylate	131-11-3	11.494	$C_{10}H_{10}O_4$	194	0.22±0.03	97
5	1-Chloro-4-phenoxybenzene	7005-71-3	13.363	$C_{12}H_9ClO$	204	0.22±0.02	97
6	4-Hydroxy-3,5-dimethoxybenzaldehyde	134-96-3	13.892	$C_9H_{10}O_4$	182	0.09±0.01	96
7	2,6-Dimethoxy-4-[(E)-prop-1-enyl]phenol	20675-95-0	14.487	$C_{11}H_{14}O_3$	194	0.10±0.01	98
8	1-Tetradecanoic acid	544-63-8	15.362	$C_{14}H_{28}O_2$	228	0.15±0.01	93
9	Methyl hexadecanoate	112-39-0	17.067	$C_{17}H_{34}O_2$	270	0.10±0.01	98
10	n-Hexadecanoic acid	57-10-3	17.586	$C_{16}H_{32}O_2$	256	11.0±0.8	99
11	Ethyl hexadecanoate	628-97-7	17.757	$C_{18}H_{36}O_2$	284	3.1±0.5	99
12	Methyl (10E,12Z)-octadeca-10,12-dienoate	21870-97-3	18.641	$C_{19}H_{34}O_2$	294	0.23±0.03	99
13	Methyl (9Z,11E)-octadeca-9,11-dienoate	79790-32-2	18.713	$C_{19}H_{34}O_2$	294	0.46±0.04	87
14	(9Z,12E)-Octadeca-9,12-dienoic acid	506-21-8	19.195	$C_{18}H_{32}O_2$	280	16.7±1.0	99
15	Ethyl (9Z,12Z)-octadeca-9,12-dienoate	6114-21-2	19.272	$C_{20}H_{36}O_2$	308	11.1±0.9	99
16	Octadecanoic acid	57-11-4	19.426	$C_{18}H_{36}O_2$	284	4.4±0.9	95
17	1,4-Dimethyl-7-(1-methylethyl)-azulen-2-ol	18937-66-1	19.834	$C_{15}H_{18}O$	214	2.5±0.3	74
18	2-Butyl-5-hexyloctahydro-1H-indene	55044-33-2	20.762	$C_{19}H_{36}$	264	0.23±0.03	94
19	Bis(2-ethylhexyl) benzene-1,2-dicarboxylate	117-81-7	22.321	$C_{24}H_{38}O_4$	390	0.12±0.01	96
20	Ethyl docosanoate	5908-87-2	22.841	$C_{24}H_{48}O_2$	368	0.12±0.02	95
21	(9Z,12Z)-1,3-Dihydroxypropan-2-yl octadeca-9,12-dienoate	3443-82-1	23.409	$C_{21}H_{38}O_4$	354	0.15±0.02	97
22	(2*S*)-2,5,7,8-Tetramethyl-2-[(4*S*,8*S*)-4,8,12-trimethyltridecyl]-3,4-dihydrochromen-6-ol	1406-18-4	26.740	$C_{29}H_{50}O_2$	430	0.13±0.01	97
23	(3*S*,8*S*,9*S*,10*R*,13*R*,14*S*,17*R*)-17-[(2*R*,5*R*)-5,6-Dimethylheptan-2-yl]-10,13-dimethyl-2,3,4,7,8,9,11,12,14,15,16,17-dodecahydro-1*H*-cyclopenta[a]phenanthren-3-ol	474-62-4	27.774	$C_{28}H_{48}O$	400	0.41±0.04	99
24	(3*b*,24*S*)-Stigmast-5-en-3-ol	83-47-6	28.777	$C_{29}H_{50}O$	414	2.8±0.3	99
25	(3*S*,4*aR*,6*aR*,6*bS*,8*aR*,12*aR*,14*aR*,14*bR*)-4,4,6*a*,6*b*,8*a*,11,11,14*b*-Octamethyl-1,2,3,4*a*,5,6,7,8,9,10,12,12*a*,14,14*a*-tetradecahydropicen-3-ol	559-70-6	29.160	$C_{30}H_{50}O$	426	1.14±0.08	99
26	(6aR,6bS,8aR,12aS,14aR,14bR)-4,4,6a,6b,8a,11,11,14b-Octamethyl-2,4a,5,6,7,8,9,10,12,12a,14, 14a-dodecahydro-1H-picen-3-one	638-97-1	29.292	$C_{30}H_{48}O$	424	1.27±0.07	94
27	(3*S*,4*aR*,6*aR*,6*bS*,8*aR*,11*R*,12*S*,12*aR*,14*aR*,14*bR*)-4,4,6*a*,6*b*,8*a*,11,12,14*b*-Octamethyl-2,3,4*a*,5,6,7,8,9,10,11,12, 12*a*,14,14*a*-tetradecahydro-1*H*-picen-3-ol	638-95-9	29.670	$C_{30}H_{50}O$	426	3.9±0.5	93
28	[(3R)-4,4,6a,6b,8a,11,11,14b-Octamethyl-1,2,3,4a,5,6,7,8,9,10,12,12a,14,14a-tetradecahydropicen-3-yl] acetate	1616-93-9	30.529	$C_{32}H_{52}O_2$	468	5.1±0.5	97
29	(3S,8aS)-5,8a-Dimethyl-3-prop-1-en-2-yl-2,3,4,4a,7,8-hexahydro-1H-naphthalene	84238-29-9	30.665	$C_{15}H_{24}$	204	1.11±0.09	90
30	(3a,5a,5b,8,8,11a-Hexamethyl-1-prop-1-en-2-yl-1,2,3,4,5,6,7,7a,9, 10,11,11b,12,13,13a,13b-hexadecahydrocyclopenta[a]chrysen-9-yl) acetate	1617-68-1	31.153	$C_{32}H_{52}O_2$	468	9.1±0.6	95

[a] Data are expressed as means ± standard deviation of three replicate measurements

4. Conclusion

In this work, the investigation of the liposoluble constituents from the roots of *L. narynensis* of Kazakhstan have been made for the first time. As the results of this study, thirty liposoluble compounds were quantified from medicinal plant in which the major constituents are (9Z,12E)-octadeca-9,12-dienoic acid (16.7%), ethyl (9Z,12Z)-octadeca-9,12-dienoate (11.1%), n-hexadecanoic acid (11.0%), (3*a*,5*a*,5*b*,8,8,11*a*-hexamethyl-1-prop-1-en-2-yl-1,2,3,4,5,6,7,7*a*,9,10,11,11*b*,12,13,13*a*,13*b*-hexadecahydrocyclopenta[a]chrysen-9-yl) acetate (9.14%), [(3*R*)-4,4,6*a*,6*b*,8*a*,11,11,14*b*-octamethyl-1,2,3,4*a*,5,6,7,8,9,10,12,12*a*,14,14*a*-tetradecahydropicen-3-yl] acetate (5.10%). Presence of these bioactive constituents may indicate that the plant extract possesses anti-inflammatory, antimicrobial and anticancer activities. The results can be used in future investigations of *L. narynensis*, to improve the knowledge about this plant, and to provide a venue to develop and debate new ideas. Further phytochemical study of the root part of *L. narynensis* opens prospects for the creation of new plant-based preparations. The practice of using medicinal plants in recent years is expanding due to their low cost, complex therapeutic effect on the body, low toxicity and the possibility of long-term use without side effects. The development of this direction through introduction of medicinal plants into medical practice and expansion of the assortment of phytopreparations is quite promising.

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