PHYTOCHEMICAL STUDY OF SALVIA GRANDIFLORA AND SALVIA OFFICINALIS LEAVES FOR ESTABLISHING PROSPECTS FOR USE IN MEDICAL AND PHARMACEUTICAL PRACTICE

M. Myha, **O. Koshovyi**, **O. Gamulya**, **T. Ilina**, **N. Borodina**, **I. Vlasova**

Сировинна база лікарських рослин України є достатньою тільки для половини фармакопейних видів. Велика частина ЛРС зростає у недостатній кількості та виникає потреба в їх імпортуванні. В умовах імпортозалежності та дефіциту вітчизняної рослинної сировини, пошук нових джерел біологічно активних речовин серед представників флори України є актуальним завданням сучасної фармацевтичної науки.

***Мета роботи** – провести порівняльне фітохімічне дослідження листя S. grandiflora та S. officinalis для встановлення можливості використання нефармакопейного виду у фармацевтичній та медичній практиці.*

***Матеріали та методи.** Об'єктоми дослідження було листя S. grandiflora та S. officinalis, яке було заготовлено у ботанічному саду Львівського національного університету імені І. Франка. Дослідження макро- та мікроелементного складу у листі S. officinalis та S. grandiflora проводили атомно-емісійним спектрографічним методом. Визначення якісного складу та кількісного вмісту основних груп БАР проводили методом ВЕРХ. Кількісне визначення фенольних сполук також проводили спектрофотометричним методом.*

***Результати.** В обох досліджуваних видах виявлено вміст 15 мікро- та макроелементів. У листі S. officinalis та S. grandiflora було ідентифіковано 15 амінокислот та 8 сапонінів. Методом ВЕРХ було встановлено якісний склад та кількісний вміст речовин фенольної природи у листі S. officinalis та S. grandiflora (13 та 9 сполук відповідно).*

***Обговорення.** Домінуючими мікро- та макроелементів у обох видах сировини були силіцій, фосфор, магній, кальцій, натрій та калій. Загальний вміст мікроелементів у листі S. grandiflora у 1,67 раз більший ніж у фармакопейному виді S. officinalis. Домінуючими амінокислотами в листі обох видів є глутамінова кислота, аспарагінова кислота, валін та лейцин.*

Домінуючими сапонінами у листі S. officinalis були урсолова та олеанолова кислоти, загальний вміст яких становить 75,82 %. У листі S.grandiflora домінуючими були урсолова та еускапова кислоти, загальний вміст яких становить 63,25 %.

Загальний вміст флавоноїдів найбільший в листі S. officinalis та становить 4,90 мг/г. Загальний вміст гідроксикоричних кислот найбільший в листі S. grandiflora та становить 4,49 мг/г, що на 221,18 % (в 2,21 рази) більше ніж у фармакопейному виді S. officinalis (2,03мг/г). Загальний найбільший вміст похідних кавової кислоти переважає в листі Salvia officinalis (0,77 мг/г). Найбільший вміст суми всіх виявлених сполук фенольної природи характерний для листя S. officinalis та становить 6,93 мг/г.

***Висновки.** У результаті проведеного порівняльного фітохімічного дослідження листя S. grandiflora та S. officinalis встановлено, що S. grandiflora є перспективним видом для впровадження у медичну та фармацевтичну практику саме як джерело фенольних сполук*

***Ключові слова:** рід Шавлія, нефармакопейний вид, листя, хімічний склад, фенольні сполуки*

1. Introduction

The pharmaceutical market for synthetic drugs is showing rapid growth. At the same time, there remains high level of topicality of herbal medicines research. New drugs based on biologically active substances of plant origin are emerging every year [1, 2]. The market of medicinal herbal raw materials in Ukraine is rapidly developing, as evidenced by the development and increase in the number of enterprises of all units from the cultivation and harvesting of medicinal products to the production of finished products. However, in today's conditions, the market of medicinal plants of Ukraine is dominated by imported raw materials, which exacerbates the issue of import substitution to ensure the medical safety of the country [3, 4].

About 23 % of all pharmacopoeial species of Ukraine have to be imported from abroad for the needs of the domestic pharmaceutical industry. In conditions of import dependence and scarcity of domestic medicinal plant raw materials, the search for new sources of biologically active substances among the representatives of the flora of Ukraine is an urgent task of modern pharmaceutical science [1, 5].

Particular attention is drawn to the study of representatives of the *Salvia* genus in Ukraine [6, 7]. It is the largest genus in the *Lamiacea* family. 21 species

grow in Ukraine [8–10]. The pharmaceutical market of Ukraine presents about 40 drugs, the components of which have biologically active substances (BAS) of Salvia leaves [11, 12].

Previous chemotaxonomic studies of representatives of the *Salvia* in Ukraine have shown the prospect of using raw materials of *S. grandiflora* in the pharmaceutical industry [1, 9, 13]. Therefore, it is advisable to conduct a comparative study of the leaves of this species and the galenic drug on its basis in comparison with the pharmacopoeial species - leaves of *S. officinalis* [14, 15].

The aim of the study was to conduct a comparative phytochemical study of *S. grandiflora* and *S. officinalis* leaves to determine the possibility of using non-pharmacopoeial species in pharmaceutical and medical practice.

2. Planning (methodology) of research

To achieve the aim it was necessary to solve the following problems:

– to analyse the macro- and micro-elemental, amino acid composition of *S. grandiflora* and *S. officinalis* leaves

– to study the qualitative composition and quantitative content of the main groups of biologically active substances in the leaf of the studied species

– to carry out a comparative analysis of the obtained results to determine the possibility of using non-pharmacopoeial species in pharmaceutical and medical practice.

3. Materials and methods

The object of the study was the leaves of *S. grandiflora* and *S. officinalis,* which were harvested at the Botanical Garden of Lviv National University named after Ivan Franko, under the guidance of a senior researcher, Ph.D Skibitska M. I. [16, 17].

Macro- and micronutrient composition studies in the leaves of *S. officinalis* and *S. verticillata* were carried out by atomic emission spectrographic method on a DFS-8 spectrograph at State Scientific Institution "Institute for Single Crystals" of NAS of Ukraine. The AC arc was obtained with the help of the IBC-28 generator. The spectra were recorded on PFS-02 photographic plates [18, 19].

The study of the amino acid composition of the plant raw materials of the studied species was performed by HPLC on a chromatograph firm Agilent Technologies (model 1100). For the chromatography we used column AA 200 × 2.1 mm and protective column; as mobile phase – solution A (20 mmM sodium acetate and 0.018 % triethylamine, adjusted to pH 7.2 with 1–2 % acetic acid, with the addition of 0.3 % tetrahydrofuran, and solution B (40 % CH$_3$CN, 40 % MeOH and 20 % 100 mM sodium acetate, adjusted to pH 7.2 with 1–2 % acetic acid); volumetric flow rate – 0.45 ml / min; column temperature – 40 °C; detection was carried out with a UV detector after pre-column dewatering first with o-phthalic aldehyde (OPA reagent) and then with 9-fluorenylchloroformate (FMOC reagent) for for display of proline [20, 21]. The identification of amino acids was performed by the retention time of the standards of the corresponding amino acids (TC 6-09-3147-83) [18, 22, 23].

Study of the saponin composition of the leaves of the studied species was performed by HPLC on a Shimadzu LC20 Prominence chromatograph in a modular system equipped with a four-channel pump LC20AD, thermostat STO20A columns, SIL20A automatic sampler, Bridge CST2020 diode-matrix detector and SPDM20 detector 150 mm * 4.6 mm with a grain size of 5 microns (Waters); column temperature – 30 °C; detection wavelength – 205 nm; the flow rate of the mobile phase is 1.0 ml / min; the volume of the sample injected is 20 µl. Mobile phase: methanol for HPLC: 0.2 % ammonium acetate solution (pH 6.75) (80:20). Elution mode: isocratic. The identification of the components was carried out by the retention time and the compliance of the UV spectra with the substance standards. The spectra of triterpene saponins have a maximum absorption at (200–210) nm, so detection of this group of compounds was carried out at 205 nm [24, 25].

The study of the composition of phenolic compounds was performed by HPLC on a Shimadzu LC20 Prominence chromatograph in a modular system equipped with a four-channel pump LC20AD, thermostat STO20A column, automatic SIL20A sampler, diode-matrix detector SPDM20A and ChemStation LC18 and ChemStation LC 250 mm x 4.6 mm, particle size 5 µm; column temperature – 35 °C; detection wavelength – 330 nm (for hydroxycinnamic acids, flavonoid glycosides), 370 nm (for flavonoid aglycones), 280 nm (for tannins), 340 nm (coumarins); the flow rate of the mobile phase is 1 ml / min; sample volume injected – 5 µl; mobile phase: eluent A: 0.1 % trifluoroacetic acid solution in water; eluent B: 0.1 % trifluoroacetic acid solution in acetonitrile. The identification of the components was performed by the retention time and the compliance of the UV spectra with the substance standards [23, 26–28].

The quantitative determination of phenolic compounds was also performed by spectrophotometric method. The optical density was measured on an Evolution 60S spectrophotometer (USA) at the appropriate wavelength. The content of the sum of hydroxycinnamic acid derivatives was determined in terms of rosmarinic acid at 505 nm, the content of flavonoids in terms of luteolin – at a wavelength of 410 nm, the content of the amount of phenolic compounds in terms of per gallic acid – at 270 nm. For statistical accuracy, the experiments were performed at least five times [20, 29, 30].

4. The results of the study

Analysis of macro- and micronutrient composition of leaves of S. officinalis and S. grandiflora. As a result of the analysis, the content of 15 macro- and micronutrients was identified and established (Tab. 1).

Analysis of the content of amino acids in the objects of the study. The results of the study of the amino acid composition of leaves of *S. officinalis* and *S. grandiflora* are shown in Tab. 2.

Analysis of the content of saponins in the raw materials of the studied species. The HPLC method identified and quantified the content of 8 saponins in the leaf of the studied species of the *Salvia* genus (Tab. 3).

Table 1

Macro- and micronutrient composition of leaves of *S. officinalis* and *S. grandiflora*

Element	Element content, mg / 100 g	
	Salvia officinalis	*Salvia grandiflora*
Fe	65.7	78
Si	330	1040
P	145	220
Al	32.8	130
Mn	4.7	7.8
Mg	290	390
Pb	<0.03	0.13
Ni	0.03	0.065
Mo	0.04	0.1
Ca	730	1300
Cu	0.43	0.65
Zn	14.6	28.6
Na	290	117
K	2050	3250
Sr	2.9	6.5
Total content	3956.21	6568.85

Table 2

Amino acid composition of leaves of *S. officinalis* and *S. grandiflora*

No.	Amino acid	Quantitative content, %	
		S. officinalis	*S. grandiflora*
1	Aspartic acid	0.97	1.44
2	Threonine	0.41	0.61
3	Serine	0.34	0.55
4	Glutamic acid	1.08	1.84
5	Proline	0.69	0.53
6	Glycine	0.49	0.77
7	Alanine	0.53	0.86
8	Valine	0.55	0.87
9	Isoleucine	0.42	0.66
10	Leucine	0.67	1.16
11	Tyrosine	0.28	0.52
12	Phenylalanine	0.50	0.75
13	Histidine	0.22	0.32
14	Lysine	0.49	0.74
15	Arginine	0.37	0.72

Table 3

Saponin composition of leaves of *S. officinalis* and *S. grandiflora*

No.	Compound	Retention time, min	Quantitative content of mg / g of raw material	
			S. oficinalis	*S. grandiflora*
1	Ursolic acid	17.45	7.74	4.25
2	Euscapic acid	8.53	0.83	2.48
3	Tormentic acid	12.68	1.09	0.07
4	Uvaol	22.80	0.15	1.1
5	Oleanolic acid	16.34	2.46	0.8
6	Erythrodiol	22.59	0.11	0.03
7	Betulin	14.57	0.26	1.1
8	Lupeol	48.13	0.81	0.81
Total content			13.46	10.64

Content analysis of phenolic compounds in leaves of S. officinalis and S. grandiflora. The HPLC method identified and quantified the content of 14 phenolic substances in leaves of *S. officinalis* and *S. grandiflora* (Tab. 4). Among them, 6 are substances of flavonoid nature, 8 are hydroxycinnamic acids.

The spectrophotometric method was used to determine the quantitative content of phenolic compounds in the studied objects, including derivatives of hydroxycinnamic acids, flavonoids and the sum of phenolic compounds (Table 5).

Table 4

Phenolic composition of leaves of *S. officinalis* and *S. grandiflora*

No.	Compound	Retention time, min	Quantitative content of mg / g of raw material	
			S. officinalis	*S. grandiflora*
Flavonoids				
1	Rutin	30.9–31.0	1.10	0.00
2	Apigenin-7-glucoside	36.0–36.4	0.41	0.39
3	Luteolin	47.0	0.41	0.11
4	Apigenin	52.3–52.4	0.00	0.19
5	Luteolin-7-glucoside	33.1	2.75	0.21
6	Catechin	19.4	0.22	0.18
Hydroxycinnamic acids				
7	Chlorogenic acid	20.0–20.4	0.04	0.04
8	Caffeic acid	21.8–22.0	0.20	0.19
9	Rosmarinic acid	37.8–38.2	1.02	4.26
Salvianolic acids				
10	Lithospermic acid ~	38.4	0.34	0.00
11	Salvianolic acid F	23.1	0.03	0.00
12	Salvianolic acid C	30.1	0.03	0.00
13	Salvianolic acid B	47.7	0.31	0.14
14	Salvianolic acid A	56.1	0.06	0.00
The total content of salvianolic acids			0.77	0.14
The total content of hydroxycinnamic acids			2.03	4.49
The total content of flavonoids			4.90	1.08
The total content of phenolic compounds			6.93	5.71

Table 5

Quantitative content of phenolic compounds in leaves of species *Salvia*

BAS group and used method	Quantitative content, % in raw materials	
	S.officinalis	*S. grandiflora*
Derivatives of hydroxycinnamic acids		
Spectrophotometry in terms of rosmarinic acid	0.81±0.04	2.29±0.06
Flavonoids		
Spectrophotometry in terms of luteolin	1.18±0.03	0.75±0.04
The sum of phenolic compounds		
Spectrophotometry in terms of gallic acid	2.31±0.05	1.97±0.03

5. Discussion of research results

The obtained data from the study of macro and microelement (tab. 1) indicate a significant content in both types of micro elements such as: silicon (330–1040 mg / 100 g), phosphorus (145–220 mg / 100 g), magnesium (290–390 mg / 100 g), calcium (730–1300 mg / 100 g), sodium (290–117 mg / 100g) and potassium (2050–3250 mg / 100 g). The total micro element content of *S. grandiflora* leaves is 1.67 times greater than that of the *S. officinalis* pharmacopoeial species. The content of toxic elements such as cobalt, cadmium, arsenic and mercury, lead and molybdenum are within the maximum permissible concentrations for raw materials and foodstuffs.

In the *S. officinalis* leaf, 15 amino acids were identified (tab. 2). The dominant ones are glutamic acid, aspartic acid, valine and leucine, with a total content of 43.07 %. Among the identified amino acids 8 are irreplaceable, their content is 47.93 % of the total number of amino acids. In the letter of *S. grandiflora*, 15 amino acids were also identified. Glutamic acid is dominant, aspartic acid, valine and leucine have a total content of 43.66 %. Among the identified amino acids 8 are indispensable. Their content is 48.33 % of the total number of amino acids.

In *S. officinalis* leaves, 8 saponins were identified (tab. 3). Ursolic and oleanolic acids were dominant, with a total content of 75.82 %. In *S. grandiflora's* leaves, 8 saponins were identified. Ursolic and euscapic acids were dominant, with a total content of 63.25 %.

In the leaf of *S. officinalis*, 13 substances of phenolic nature were identified (tab. 4). Among them, 5 flavonoids: rutin, apigenin-7-glucoside, luteolin, luteolin-7-glucoside, catechin; 3 hydroxycinnamic acids: chlorogenic acid, caffeic acid, rosmarinic acid and 5 derivatives of caffeic acid: lithospermic acid, salvianolic acid F, salvianolic acid C, salvianolic acid B, salvianolic acid A. Routine, apigenin-7-glucoside, luteolin, luteolin-7-glucoside, rosemary, lithospermic and salvianolic B acids were dominant.

In the *S. grandiflora* leaves were identified 9 substances of phenolic nature. Among them were 5 flavonoids: apigenin-7-glucoside, luteolin, apigenin, luteolin-7-glucoside, catechin; 3 hydroxycinnamic acids: chlorogenic acid, caffeic acid, rosmarinic acid; 1 coffee acid derivatives: salvianolic acid B. Apigenin-7-glucoside and rosmarinic acid were dominant.

The total content of flavonoids is highest in leaves of *S. officinalis* and is 4.90 mg / g. The total hydroxycinnamic acid content is highest in the leaves of *S.*

grandiflora and is 4.49 mg / g, which is 221.18 % (2.21 times) more than in the pharmacopoeial species of *S. officinalis* (2.03 mg / g). The overall highest content of coffee acid derivatives is dominated by leaves of *S. officinalis* (0.77 mg / g).

The highest content of the sum of all detected compounds of phenolic nature is characteristic of leaves of *S. officinalis* and is 6.93 mg / g.

According to the spectrophotometric study of the content of phenolic compounds (tab. 5) in the leaf of the studied species of the genus *Salvia,* it was found that the highest content of hydroxycinnamic acid derivatives is specific for *S. grandiflora* leaves, the highest content of flavonoid compounds, and the total content of phenolic compounds is specific for *S. officinalis*.

The content of phenolic compounds in the two species studied is practically at the same level, except for the hydroxycinnamic acid content. In the leaf of the non-pharmacopoeial species *S. grandiflora*, the content of the amount of hydroxycinnamic acids is 2.21 times higher. Particular attention is drawn to the high content of rosemary acid in leaves of *S. grandiflora* 4.18 times more than in leaves of *S. officinalis*. The results of qualitative and quantitative analysis of BAS in the leaf of the non-pharmacopoeial species of *S. grandiflora* indicate the prospect and possibility of its use in medical and pharmaceutical practice as a source of phenolic compounds, in particular hydroxycinnamic acids.

Study limitations. For the statistical significance of the study, it would be advisable to investigate, even wild samples of raw materials from different regions of Ukraine, and not only cultivated and harvested in the Botanical Garden of the National University of Lviv named after Ivan Franko. It was advisable to compare not only the chemical composition of the raw material, but also to compare the pharmacological activity of galenic and neogalenic agents from these raw materials.

Prospects for further research. According to the results of the studies, further screening of pharmacological studies, analysis of terpenoid composition and development of parameters for standardization of *S. grandiflora* leaves are planned.

6. Conclusions

Comparative pharmacognostic and pharmacological studies of *S. grandiflora* and *S. officinalis* leaves revealed that *S. grandiflora* is a promising species for introduction into medical and pharmaceutical practice as a source of phenolic compounds, in particular hydroxycinnamic acids.

In both studied species, was found the presence of 15 micro and macronutrients, of which dominant are silicon, phosphorus, magnesium, calcium, sodium and potassium. The total trace element content of *S. grandiflora* leaves is 1.67 times greater than that of the pharmacopoeial species of *S. officinalis*. In the leaves of *S. officinalis* and *S. verticillata*, 15 amino acids and 8 saponins were identified. HPLC determined the qualitative composition and quantitative content of phenolic substances in leaves of *S. officinalis* and *S. grandiflora* (13 and 9 compounds, respectively). The total content of flavonoids is highest in leaves of *S. officinalis* and is 4.90 mg / g. The total hydroxycinnamic acid content is highest in the leaf of *S. grandiflora* and is 4.49 mg / g, which is 221.18 % (2.21 times) more than in the pharmacopoeial species of *S. officinalis* (2.03 mg / g). The overall highest content of coffee acid derivatives is found in leaves of *S. officinalis* (0.77 mg / g). The content of phenolic compounds in the two studied species is practically at the same level, except for the hydroxycinnamic acid content. In the leaf of the non-pharmacopoeial species *S. grandiflora*, the content of the amount of hydroxycoric acids is 2.21 times higher. Particular attention is drawn to the high content of rosmarinic acid in leaves of *S. grandiflora,* which is 4.18 times more than in leaves of *S. officinalis*.

The results of the comparative phytochemical and pharmacological study of *S. officinalis* leaves and *S. grandiflora* leaves significantly extend the data on non-pharmacopoeial species and indicate the undoubted prospect of using *S. grandiflora* leaves in pharmaceutical and medical practice.

Conflict of interests

There are no conflicts of interest regarding this study.

References

1. Koshovyi, O. M. (2013). Suchasni pidkhody do stvorennia likarskykh zasobiv na osnovi roslyn rodiv Evkalipt ta Shavliia. Kharkiv: NFaU, 41.

2. Minarchenko, V. M., Butko, A. Yu. (2017). Doslidzhennia vitchyznianoho rynku likarskykh zasobiv roslynnoho pokhodzhennia. Farmatsevtychnyi zhurnal, 1, 30–36. Available at: http://nbuv.gov.ua/UJRN/pharmazh_2017_1_5

3. Nykytiuk, Yu. A. (2016). Orhanizatsiino-ekonomichni vazheli derzhavnoho stymuliuvannia importozamishchennia na rynku likarskoi roslynnoi syrovyny. Zbalansovane pryrodokorystuvannia, 4, 202–207.

4. Tildesley, N., Kennedy, D., Perry, E., Ballard, C., Wesnes, K., Scholey, A. (2005). Positive modulation of mood and cognitive performance following administration of acute doses of Salvia lavandulaefolia essential oil to healthy young volunteers. Physiology & Behavior, 83 (5), 699–709. doi: http://doi.org/10.1016/j.physbeh.2004.09.010

5. Koshevoi, O. N. (2011). Amino-acid and monosaccharide compositions of Salvia officinalis leaves. Chemistry of Natural Compounds, 47 (3), 492–493. doi: http://doi.org/10.1007/s10600-011-9976-3

6. Cherniavskyi, A. V., Terenteva, N. H. (1987). Yzuchenye vydov roda Salvia L. Flori Ukrayni pry pomoshchy dyskrymynalnoho analyza. Ukrainskyi botanichnyi zhurnal, 5 (44), 63–67.

7. Lopresti, A. L. (2016). Salvia (Sage): A Review of its Potential Cognitive-Enhancing and Protective Effects. Drugs in R&D, 17 (1), 53–64. doi: http://doi.org/10.1007/s40268-016-0157-5

8. Myha, M. M., Koshovyi, O. M., Ilina, T. V., Borodina, N. V., Skybitska, M. I. (2019). Research in phenolic compounds in leaves of non-pharmacopoeial species of the genus Salvia from Ukrainian flora. Current Issues in Pharmacy and Medicine: Science and Practice, 3, 291–297. doi: http://doi.org/10.14739/2409-2932.2019.3.184191

9. Baranauskiene, R., Dambrauskiene, E., Venskutonis, P. R., Viskelis, P. (2011). Influence of harvesting time on the yield and chemical composition of sage (Salvia officinalis L.). Foodbalt, 104–109.

10. Raal, A., Orav, A., Arak, E. (2007). Composition of the essential oil ofSalvia officinalisL. from various European countries. Natural Product Research, 21 (5), 406–411. doi: http://doi.org/10.1080/14786410500528478

11. Kovalenko, V. N. (Ed.) (2014). Kompendyum 2014 – lekarstvennie preparaty. Kyiv: MORYON, 2700.

12. Xu, J., Wei, K., Zhang, G., Lei, L., Yang, D., Wang, W. et. al. (2018). Ethnopharmacology, phytochemistry, and pharmacology of Chinese Salvia species: A review. Journal of Ethnopharmacology, 225, 18–30. doi: http://doi.org/10.1016/j.jep. 2018.06. 029

13. Firuzi, O., Miri, R., Asadollahi, M., Eslami, S., Jassbi, A. R. (2013). Cytotoxic, antioxidant and antimicrobial activities and phenolic contents of eleven Salvia species from Iran. Iranian Journal of Pharmaceutical Research, 12, 801–810. doi: http://doi.org/10.3109/13880209.2013.810650

14. Mahdizadeh, R., Moeln, S., Soltani, N., Malekzadeh, K., Moein, M. (2018). Study of molecular mechanism of Salvia species in prevention of diabetes. International Journal of Pharmaceutical Science and Research, 9, 4512–4521.

15. Wu, Y.-B., Ni, Z.-Y., Shi, Q.-W., Dong, M., Kiyota, H., Gu, Y.-C., Cong, B. (2012). Constituents from Salvia Species and Their Biological Activities. Chemical Reviews, 112 (11), 5967–6026. doi: http://doi.org/10.1021/cr200058f

16. Dobrochaeva, D. N., Kotov, M. I., Prokudin, Y. N., Barbarich, A. I. (1999). Key to Higher Plants of Ukraine. Kyiv: Naukova Dumka, 546.

17. Eidi, M., Eidi, A., Bahar, M. (2006). Effects of Salvia officinalis L. (sage) leaves on memory retention and its interaction with the cholinergic system in rats. Nutrition, 22 (3), 321–326. doi: http://doi.org/10.1016/j.nut.2005.06.010

18. Koshovyi, O. M., Komisarenko, A. M., Kovalova, A. M., Mudryk, I. M. (2005). Mikroelementnyi, aminokyslotnyi ta polisakharydnyi sklad lystia evkalipta. Fitoterapiia. Chasopys, 3, 59–62.

19. Osmachko, A. P., Kovaleva, A. M., Ili'ina, T. V., Kovalova, O. N., Komisarcnko, A. M., Akhmedov, E. Yu. (2017). Study of macro- and microelements composition of Veronica longifolia L. herb and Veronica teucrium L. herb and rhizomes, and extracts obtained from these species. Azerbaijan Pharmaceutical and Pharmacotherapy Journal, 1, 24–28. Available at: http://dspace.nuph.edu.ua/handle/123456789/20611

20. Derzhavna Farmakopeia Ukrainy. Vol. 1 (2015). Kharkiv: Derzhavne pidpryiemstvo «Ukrainskyi naukovyi farmakopeinyi tsentr yakosti likarskykh zasobiv», 1128.

21. Eidi, M., Eidi, A., Zamanizadeh, H. (2005). Effect of Salvia officinalis L. leaves on serum glucose and insulin in healthy and streptozotocin-induced diabetic rats. Journal of Ethnopharmacology, 100 (3), 310–313. doi: http://doi.org/10.1016/j.jep.2005. 03.008

22. Jassbi, A. R., Zare, S., Firuzi, O., Xiao, J. (2015). Bioactive phytochemicals from shoots and roots of Salvia species. Phytochemistry Reviews, 15 (5), 829–867. doi: http://doi.org/10.1007/s11101-015-9427-z

23. Koshovyi, O. M., Zagayko, A. L., Kolychev, I. O., Akhmedov, E. Yu., Komissarenko, A. N. (2016). Phytochemical study of the dry extract from bilberry leaves. Azerbaijan Pharmaceutical and Pharmacotherapy Journal, 1, 18–23.

24. Jash, S. K., Gorai, D., Roy, R. (2016). Salvia genus and triterpenoids. International Journal Of Pharmaceutical Sciences And Research, 7, 4710–4732. doi: http://doi.org/10.13040/ijpsr.0975-8232.7(12).4710-32

25. Shynkovenko, I. L., Ilyina, T. V., Kovalyova, A. M., Goryacha, O. V., Golembiovska, O. I., Koshovyi, O. M. (2018). Saponins of the extracts of Galium aparine and Galium verum. News of Pharmacy, 4 (96), 16–23. doi: http://doi.org/10.24959/nphj.18.2225

26. Koshovyi, O. M. (2012). Fenolnyi sklad deiakykh predstavnykiv pidrodu Sclarea rodu Salvia. Aktualni pytannia farmatsevtychnoi i medychnoi nauky ta praktyky, 3, 11–14. Available at: http://nbuv.gov.ua/UJRN/apfimntp_2012_3_5

27. Ilina, T., Kashpur, N., Granica, S., Bazylko, A., Shinkovenko, I., Kovalyova, A. et. al. (2019). Phytochemical Profiles and In Vitro Immunomodulatory Activity of Ethanolic Extracts from Galium aparine L. Plants, 8 (12), 541. doi: http://doi.org/10.3390/plants8120541

28. Kamatou, G., Viljoen, A., Steenkamp, P. (2010). Antioxidant, anti-inflammatory activities and HPLC analysis of South African Salvia species. Planta Medica, 76 (12). doi: http://doi.org/10.1055/s-0030-1264458

29. Koshevoi, O. N., Vovk, G. V., Akhmedov, E. Iu., Komisarenko, A. N. (2015). Issledovanie khimicheskogo sostava i farmakologicheskoi aktivnosti ekstraktov, poluchennykh pri kompleksnoi pererabotke listev shalfeia lekarstvennogo. Azerbaidzhanskii farmacevticheskii i farmakoterapevticheskii zhurnal, 1, 30–34.

30. Koshovyi, O. M., Perederii, Ye. O., Kovalova, A. M., Komisarenko, A. M. (2010). Doslidzhennia fenolnykh spoluk lystia shavlii likarskoi. Farmatsevtychnyi chasopys, 1, 17–19.

Mykhailo Myha, Postgraduate Student, Department of Pharmacognosy, National University of Pharmacy, Pushkinska str., 53, Kharkiv, Ukraine, 61002
E-mail: myhamykhailo@gmail.com

Oleh Koshovyi, Doctor of Pharmaceutical Sciences, Professor, Head of Department, Department of Pharmacognosy, National University of Pharmacy, Pushkinska str., 53, Kharkiv, Ukraine, 61002
E-mail: oleh.koshovyi@gmail.com

Olha Gamulya, PhD, Senior Lecturer, Department of Fundamental and Language Training, National University of Pharmacy, Pushkinska str., 53, Kharkiv, Ukraine, 61002
E-mail: olga.gamulya@gmail.com

Tetiana Ilina, Doctor of Pharmaceutical Sciences, Professor, Department of Pharmacognosy, National University of Pharmacy, Pushkinska str., 53, Kharkiv, Ukraine, 61002
E-mail: ilyinatany86@gmail.com

Natalia Borodina, PhD, Associate Professor, Department of Pharmacognosy, National University of Pharmacy, Pushkinska str., 53, Kharkiv, Ukraine, 61002
E-mail: natalijaborodina@gmail.com

Inna Vlasova, National University of Pharmacy, Pushkinska str., 53, Kharkiv, Ukraine, 61002
E-mail: innavlasova.ukraine@gmail.com