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Saponins of the extracts of *Galium aparine* and *Galium verum*

Aim. To determine the qualitative composition and the quantitative content of saponins in the liquid extracts of the herb of cleavers (*Galium aparine* L.) and lady's bedstraw (*Galium verum* L.).

Materials and methods. Extracts of the herb of cleavers and lady's bedstraw were obtained by the triple extraction of the raw material with 96 % ethanol when heating with the subsequent concentration of the combined extracts to the ratio of the raw material : the finished product of 1 : 1. Saponins were studied by the method of high-performance liquid chromatography (HPLC).

Results and discussion. As a result of the chromatographic study of extracts of the herb of cleavers and lady's bedstraw it has been found that they contain 6 and 7 saponins, respectively. The compounds belong to ursane (ursolic, euscaphic, tormentic acids and uvaol), oleanane (oleanolic acid) and lupane (betulin and lupeol) type. In the extract from the herb of cleavers the compounds of ursane derivatives (50 mg/ml) prevail, the dominant compound is euscaphic acid (3.34 mg/ml); in the extract from the herb of lady's bedstraw there are saponins of lupane derivatives (2.50 mg/ml), lupeol (1.60 mg/ml) is predominant.

Conclusions. The results obtained indicate the prospects for further in-depth study of the chemical composition and biological activity of the liquid extracts from the herb of cleavers and lady's bedstraw.

Key words: cleavers; lady's bedstraw; liquid extract; saponins; HPLC

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Сапоніни екстрактів *Galium aparine* та *Galium verum*

Мета роботи – одержання, дослідження якісного складу та вмісту сапонінів у екстрактах рідких трави підмаренника чіпкого (*Galium aparine* L.) та підмаренника справжнього (*Galium verum* L.).

Матеріали та методи. Екстракти трави підмаренника чіпкого та підмаренника справжнього отримували шляхом триразової екстракції сировини 96 % спиртом етиловим при нагріванні з подальшим концентруванням об'єднаних витяжок до співвідношення сировина : готовий продукт 1 : 1. Сапоніни досліджували методом високоефективної рідинної хроматографії (ВЕРХ).

Результати та їх обговорення. В результаті хроматографічного дослідження екстрактів трави підмаренника чіпкого та підмаренника справжнього виявлено, що в них містяться 6 та 7 сапонінів відповідно. Сполуки відносяться до урсанового (урсолова, еускафова, тормантинова кислоти та уваол), олеананового (олеанолова кислота) та лупанового (бетулін та лупеол) типу. В екстракті з трави підмаренника чіпкого в цілому переважають сполуки урсанового ряду (50 мг/мл), домінуючою сполукою є еускафова кислота (3,34 мг/мл); у екстракті з трави підмаренника справжнього – сапоніни лупанового ряду (2,50 мг/мл), домінуючою сполукою є лупеол (1,60 мг/мл).

Висновки. Отримані результати свідчать про перспективність подальшого поглибленого дослідження хімічного складу та біологічної активності екстрактів рідких з трави підмаренника чіпкого та підмаренника справжнього.

Ключові слова: підмаренник чіпкий; підмаренник справжній; екстракт рідкий; сапоніни; ВЕРХ

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Сапонины экстрактов *Galium aparine* и *Galium verum*

Цель работы – получение, изучение качественного состава и содержания сапонинов экстрактов жидких травы подмаренника цепкого (*Galium aparine* L.) и подмаренника настоящего (*Galium verum* L.).

Материалы и методы. Экстракты травы подмаренника цепкого и подмаренника настоящего получали путем трехкратной экстракции сырья 96 % спиртом этиловым при нагревании с дальнейшим концентрированием объединенных извлечений до соотношения сырье : готовый продукт – 1 : 1. Сапонины исследовали методом высокоэффективной жидкостной хроматографии (ВЭЖХ).

Результаты и их обсуждение. При хроматографическом изучении экстрактов травы подмаренника цепкого и подмаренника настоящего выявлено, что в них содержатся 6 и 7 сапонинов соответственно. Соединения относятся к к урсановому (урсоловая, эускафовая, тормантиновая кислоты и уваол), олеананову (олеаноловая кислота) и лупановому (бетулин и лупеол) типу. В экстракте из травы подмаренника цепкого больше содержится сапонинов типа урсана (3,50 мг/мл), а доминирующим соединением является эускафовая кислота (3,34 мг/мл). В экстракте из травы подмаренника настоящего превалируют сапонины типа лупана (2,50 мг/мл) и доминирующим соединением является лупеол (1,60 мг/мл).

Выводы. Полученные результаты свидетельствуют о перспективности дальнейшего углубленного изучения химического состава и фармакологической активности экстрактов жидких из травы подмаренника цепкого и подмаренника настоящего.

Ключевые слова: подмаренник цепкий; подмаренник настоящий; экстракт жидкий; сапонины; ВЭЖХ

Among the representatives of *Galium* L. genus of *Rubiaceae* Juss. family cleavers (*Galium aparine* L.) and lady's bedstraw (*Galium verum* L.) belong to plants with the largest raw material base, they are distributed throughout the temperate zone of Europe, Asia and North America [1].

The herb of cleavers and lady's bedstraw is used for liver diseases, edemas, involuntary urination, painful uri nation, kidney stone disease, inflammation of the kidneys and bladder, inflammation of the stomach, intestines. Oil infusions of the cleavers herb are used externally for skin diseases, rashes, eczema, shingles, skin cancer [2-6].

A considerable number of works of scientists in many countries is devoted to the study of the chemical composition of the herb of *G. aparine* and *G. verum* [7-10]. Mainly phenolic compounds and terpenoids in the composition of essential oils were studied. In the samples of the herb of *G. verum* from Moldova a steroid compound of *β*-sitosterol and triterpenoid – oleanolic acid were found [11], in the samples from China there were α-amyrin derivatives: ursolic acid, ursolic aldehyde and rubifolic acid [12]. Among other types in the herb of *G. rivale* the derivatives of oleanolic acid – rivalosides A-E and momordin IIb were identified [13-15].

Many scientific publications are devoted to the study of such pharmacological activity of triterpenic acids as anti-inflammatory, antimicrobial, antiviral, cytotoxic, as well as their effect on the cardiovascular system [16-20].

The aim of this work was to study saponins in the extracts of the herb of *G. aparine* and *G. verum*.

Materials and methods

The raw material was collected at the flowering stage of plants in June, 2017: the herb of cleavers – in the Botanical garden of the National University of Pharmacy (NUPh, Kharkiv, Ukraine), the herb of lady's bedstraw – near the village of Rus'ki Tyshky of the Kharkiv region.

To obtain the liquid extracts 10.0 g of the air-dry crushed raw material was placed in a flask, 100 ml of 96 % ethanol was added and heated with a reflux condenser on a boiling water bath for 30 min. After cooling the content of the flask was filtered, and the volume of the resulting solution was measured. The procedure was repeated twice under the same conditions. The filtrates were combined and concentrated under vacuum in a rotary vacuum evaporator to the ratio of the raw material – finished product of 1 : 1; thus, 10 ml of the liquid extract was obtained.

The qualitative composition and quantitative content of saponins were studied by the method of high-performance liquid chromatography (HPLC) on a Shimadzu LC20 Prominence liquid chromatograph in the modular system equipped with the 4-channel pump LC20AD, the column thermostat CTO20A, the automatic sampler SIL20A, the diode array detector SPDM20A and Chem Station LC20 in the following chromatographic conditions: the X-Bridge C18 chromatographic column with the size of 150 × 4.6 mm and the particle size of 5 µm (Waters company); the column temperature – 30 °C; the detection wavelength – 205 nm; the flow rate of the mobile phase – 1.0 ml/min; the injection volume – 20 µl; the mobile phase – methanol for HPLC : 0.2 % solution of ammonium acetate (pH 6.75) in the ratio of 80 : 20; the elution mode – isocratic.

Table 1

The chromatographic analysis of solutions of the reference samples

Compounds	Retention time, min	λ_{max}, nm
Euscaphic acid	8.53	200
Tormentic acid	12.68	200
Betulin	14.57	200, 234, 322
Oleanolic acid	16.25	200
Ursolic acid	17.29	200
Uvaol	22.80	200
Lupeol	48.13	203, 230

Identification of the components was carried out by the retention time and compliance of UV spectra with reference substances [21-23]. Triterpenic saponins was detected at 205 nm based on their absorption maximum at 200-210 nm.

The quantitative determination of individual components in ethanol extracts of the raw material was carried out using the external solutions of reference samples (Tab. 1).

The content of substances in the liquid extracts was calculated by the formula:

$$\text{X, mg/ml} = \frac{A_{pr} \cdot m_{st} \cdot P}{A_{st} \cdot V_{st} \cdot 100},$$

where: A_{pr} – is the peak area of the substance on the chromatogram of the test solution; A_{st} – is the peak area of the substance on the chromatogram of the reference solution; m_{st} – is the weight of the standard sample of the substance in the reference sample solution, mg; V_{st} – is dilution of the reference solution, ml; P – is purity of the reference sample, %.

Results and discussion

The liquid extracts obtained are a thick green liquid with a specific odor.

The chromatographic analysis of saponins in the extract from the herb of cleavers 20 saponins were found, 6 saponins of them were identified; in the extract from the herb of lady's bedstraw there were 26 saponins, 7 of them were identified (Fig. 1-2, Tab. 2).

The chromatographic separation of oleanolic acid and ursolic acid is often hindered by the similarity of their chemical structure. On this basis the optimal chromatographic conditions and the type of the stationary column phase were selected, they allowed to achieve the separation index of these pentacyclic triterpenic acids of approximately 1.2. The retention time for oleanolic acid was 16.247 min, for ursolic acid – 17.288 min (Fig. 3).

As a result of the studies conducted the content of 6 and 7 saponins, respectively, was identified and determined in the liquid extracts of the herb of cleavers and lady's bedstraw (Tab. 2).

The compounds identified belong to ursane (ursolic, euscaphic, tormentic acids and uvaol), oleanane

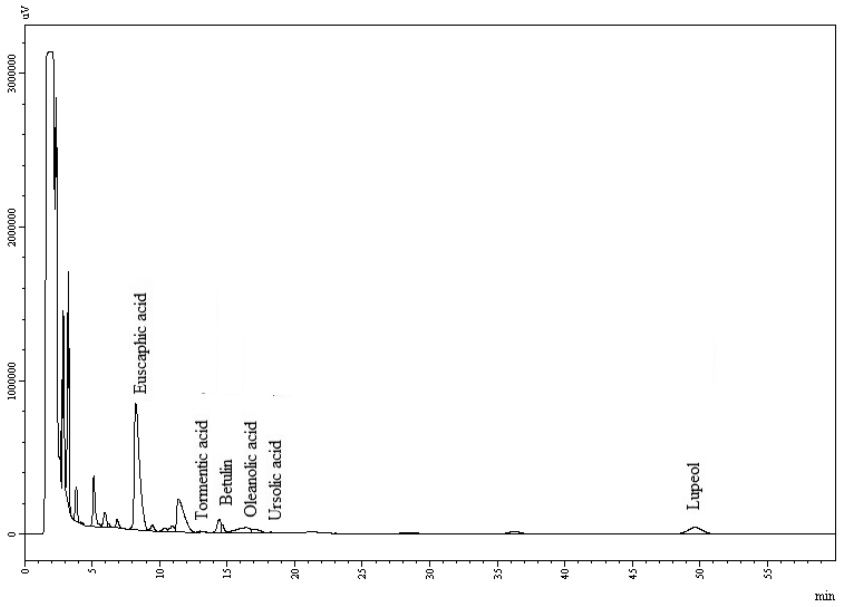


Fig. 1. The scheme of the chromatogram of saponins in the extract of Cleavers

Table 2

Saponins of the liquid extracts of the herb of cleavers and lady's bedstraw

Compounds	*Galium aparine* L.		*Galium verum* L.	
	Retention time, min	The content of the substance in the extract, mg/ml	Retention time, min	The content of the substance in the extract, mg/ml
Euscaphic acid	8.22	3.34	8.44	0.87
Tormentic acid	12.97	0,02	13.03	0.004
Betulin	14.60	0.62	14.45	0.89
Oleanolic acid	16.30	0,21	16.43	0.48
Ursolic acid	17.28	0.13	17.47	1.04
Uvaol	-	0.00	22.98	0.01
Lupeol	49.68	1.20	49.40	1.60
In total		5.52		4.894

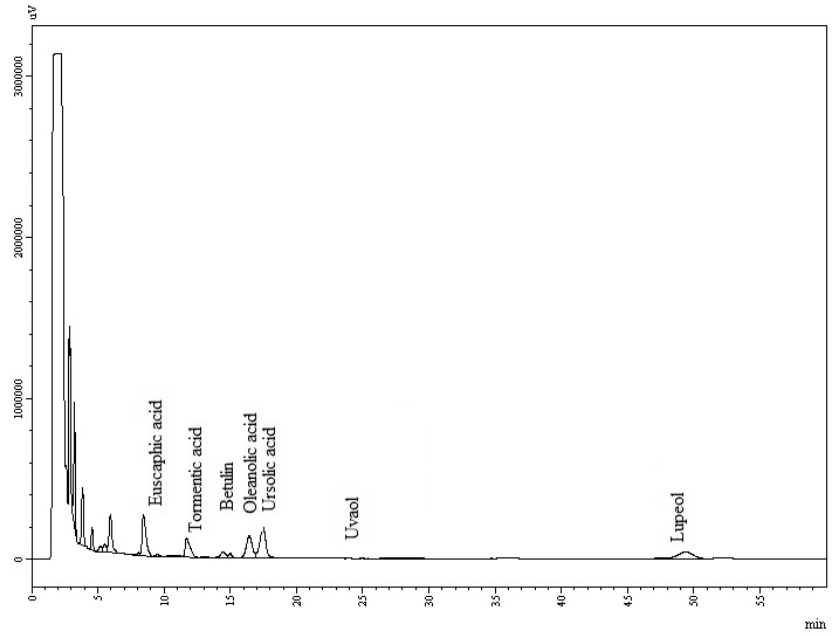


Fig. 2. The scheme of the chromatogram of saponins in the extract of Lady's bedstraw

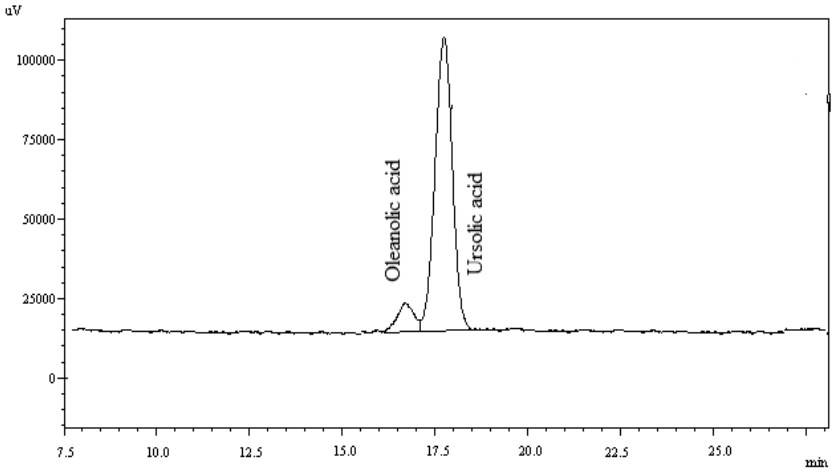


Fig. 3. The typical chromatogram of the mixture of reference compounds of ursolic acid and oleanolic acid for separation

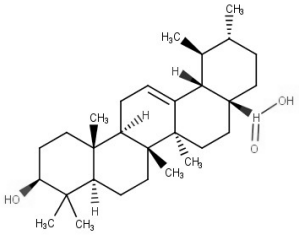
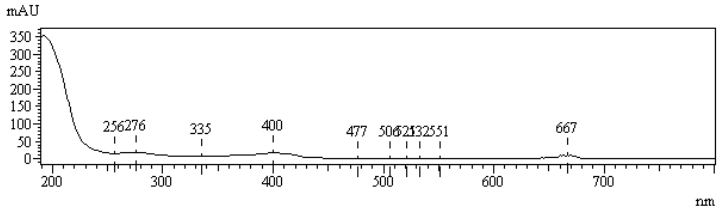
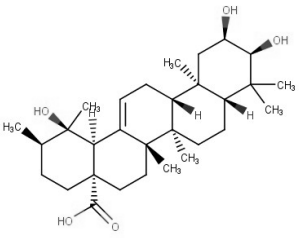
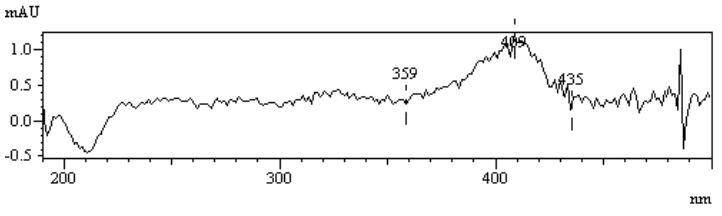
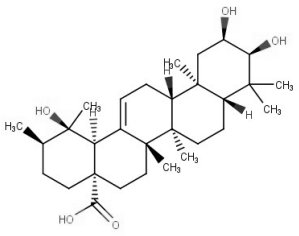
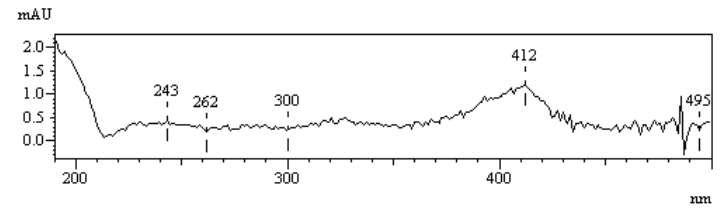
(oleanolic acid) and lupane (betulin and lupeol) type. The UV spectra of compounds are presented in Tab. 3

It has been found that the qualitative composition of saponins in the liquid extracts of lady's bedstraw and cleavers is similar. Of saponins identified only the extract of lady's bedstraw contains uvaol. Quantitatively, euscaphic acid (3.34 mg/ml) prevails in the extract of cleavers, whereas in the extract of lady's bedstraw lupeol (1.60 mg/ml) is dominant.

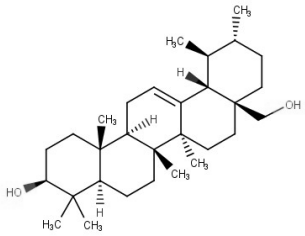
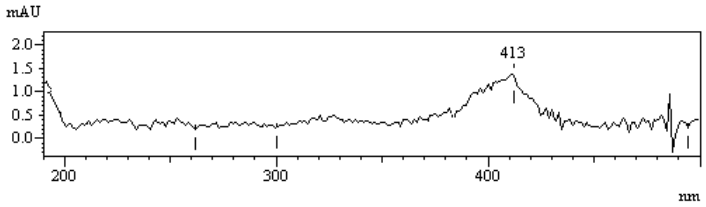
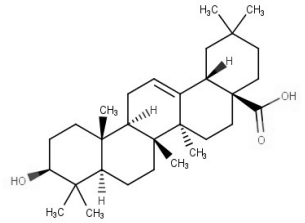
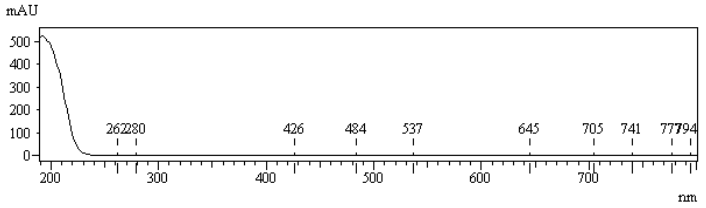
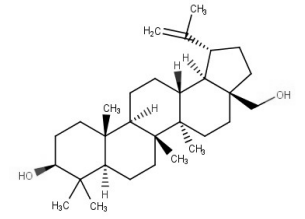
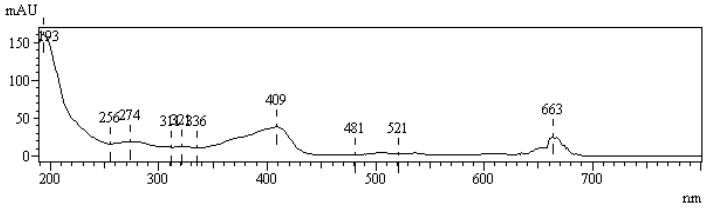
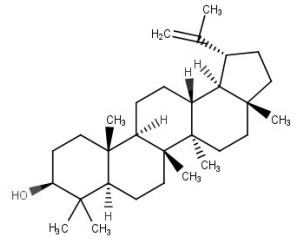
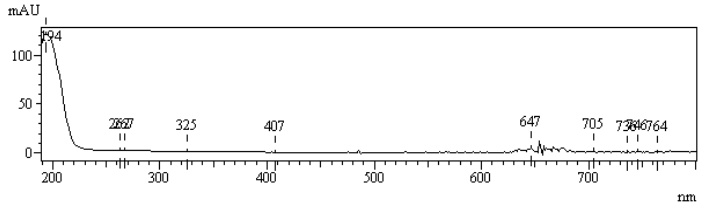
In the extract of cleavers ursane derivatives are dominant; their content is 3.50 mg/ml, the content of lupane derivatives is 1.82 mg/ml, oleanane – 0.21 mg/ml.

Table 3

Characteristics of saponins identified in the extracts of the herb of cleavers and lady's bedstraw

Compounds	Two-dimensional structural formula	UV-spectrum
1	2	3
Ursolic acid		
Euscaphic Acid		
Tormentic acid		

Continuation of the Table 3

1	2	3
Uvaol		
Oleanolic acid		
Betulin		
Lupeol		

In the extract of lady's bedstraw lupane derivatives prevail; their content is 2.50 mg/ml, the content of ursane derivatives is 1.92 mg/ml, oleanane – 0.48 mg/ml.

The results of the study confirm the data of the previous works on the presence of triterpenoids of the ursane type – ursolic acid in lady's bedstraw [12].

For the first time euscaphic acid, tormentic acid, betulin and lupeol were found in cleavers and lady's bedstraw. Uvaol was identified for the first time in lady's bedstraw.

The presence of the dominant compounds – euscaphic acid, lupeol, ursolic acid and betulin in the extract of cleavers and lady's bedstraw creates the basis for predicting such types of the pharmacological activity as hypoglycemic, anti-inflammatory, antimicrobial, antiprotozoal, anti-tumor, antiviral, antiproliferative, anti-angiogenic and hypocholesterolemic ones [24-28].

The dominance of euscaphic acid in the liquid extract from the herb of cleavers suggests the expediency of studying its hypoglycemic activity, while the dominance of lupeol together with ursolic acid in the liquid extract from the herb of lady's bedstraw indicates the prospects of the study of its anti-tumor action.

CONCLUSIONS

1. In the liquid extracts obtained from the herb of cleavers and lady's bedstraw the content of 6 and 7 saponins, respectively, has been identified and determined; they belong to ursane (ursolic, euscaphic, tormentic acids and uvaol), oleanane (oleanolic acid) and lupane (betulin and lupeol) type. Uvaol has been detected only in the extract from the herb of lady's bedstraw.

2. In the extract of cleavers ursane derivatives are dominant; their content is 3.50 mg/ml. In the extract of lady's bedstraw lupane derivatives prevail; their content is 2.50 mg/ml.

Conflict of Interests: authors have no conflict of interests to declare.

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