

4. Konovalenko I. S., Karpenko M. O. Development of soft dosage form based on polymers of acrylic acid in combination with antimicrobial agents derived from nitrofurans. Modern achievements of pharmaceutical technology and biotechnology: material IX international scientific-practical conference, which is dedicated to the 45th anniversary of the Department of pharmaceutical technology of drugs (Kharkiv, 11-12 November 2021). Kh.: NUPh Publishing House, 2021. P. 20.
5. Tran TTD, Tran PHL. Insoluble Polymers in Solid Dispersions for Improving Bioavailability of Poorly Water-Soluble Drugs. *Polymers (Basel)*. 2020 Jul 28;12(8):1679. doi: 10.3390/polym12081679. PMID: 32731391; PMCID: PMC7466147.

JUSTIFICATION OF THE EXTRACTION CONDITIONS OF BIOLOGICALLY ACTIVE SUBSTANCES OF UROLOGICAL PHYTOCOMPOSITION

**Benlebbar R., Ryndina M. R., Romanovska I. O., Goncharenko A. A., Melnyk I. S., Semchenko K. V., Konovalenko I. S., Kriukova A. I.
National University of Pharmacy, Kharkiv, Ukraine**

Introduction. Kidney diseases are the most complex from a clinical and epidemiological point of view. Analysis of uro- and nephrological morbidity in Ukraine according to official statistics in recent years showed an increase in the absolute number of registered patients with diseases of the genitourinary system by 25.8% annually. This is largely due to the important role of the kidneys in maintaining human physiological functions. Phytotherapy, as a method of safe basic treatment of many diseases through the harmonization of natural detoxification processes, is aimed at improving the functional state of the kidneys and can significantly increase both the effectiveness and safety of basic pharmacotherapy due to the advantages of the following nature: polymodality of effects, absence of xenobiotic metabolites, effects of drug therapy.

In this regard, the development of new phytomedicine for the treatment of kidney diseases and the increase in the range of nephroprotective agents on the pharmaceutical market is particularly relevant.

One of the important groups of medicinal substances for phytotherapy of arterial hypertension is the group of flavonoids, which have capillary-stabilizing, anti-edematous, anti-inflammatory and antioxidant activity.

The search for affordable, cost-effective and official medicinal plant raw materials for the treatment of this pathology, which would show the necessary pharmacological effects, led to the well-known medicinal plant raw materials - three-lobed beggartick herb, woundwort herb, and common agrimony herb. The peculiarity of this phytocomposition lies in its ability to strengthen the integral local-reflex action, which is accompanied by the expansion of blood vessels (tissue trophicity, fluid outflow and not a sharp decrease in blood pressure are improved) and has a venotonic effect [1].

The aim of the study. Studying the conditions for extracting a phytochemical composition with urological action, which is included three-lobed beggartick herb, woundwort herb, and common agrimony herb.

Research methods. Organoleptic, physico-chemical, pharmacotechnological, instrumental research of phytochemical composition.

Main results. Flavonoids, triterpene saponins, and tannins are one of the main active ingredients for the - three-lobed beggartick herb, woundwort herb, and common agrimony herb. Therefore, one of the main goals in the development of the composition of the collection and its optimal use as an infusion is the selection of optimal conditions and extraction modes to obtain, as a result, a phytochemical composition that will be maximally enriched with these biologically active substances.

During the development of the technology of collection from three-lobed beggartick herb, woundwort herb, and common agrimony herb, the influence of various technological factors that can have a significant impact on the yield of active substances was investigated, such as:

- selection of the extraction method;
- selection of the extractant and its concentration; temperature regime;
- ratio of used raw materials and selected extractant (extraction module);
- extraction time [2].

To extract active substances from the presented raw materials, the maceration method was used in a boiling water bath for 2 hours (120 minutes) at a temperature of 100 ° C using a reflux condenser.

One of the main criteria for the most complete extraction of biologically active substances from medicinal plant raw materials is the selection of the optimal extractant [3]. We can single out the following general requirements for extractants:

- They should have a selective effect - maximally remove the necessary active substances or their complex from raw materials, but at the same time remove various ballast substances as little as possible.
- Wetting plant material and have the necessary desorbing effect to penetrate through the walls of plant cells.
- Do not enter into chemical interaction and do not change the pharmacological properties of the active substances.
- To be pharmacologically indifferent, when included in the finished product, convenient to use from the point of view of safety and taking into account flammability, explosion and fire hazards, as well as harmful effects on the body of personnel.
- To be cheap, accessible and economical [4].

Aglycones of flavonoids are polar compounds that are well soluble in alcohols, acetone, and diethyl ether. Moreover, their glycosides are more polar - they dissolve in hot water, alcohol, but are not soluble in chloroform, benzene, and ether. Based on the above, ethanol was chosen as the extractant for the three-lobed beggartick herb, woundwort herb, and common agrimony herb. At the same time, to determine its concentration, it was decided to use several alcohol-water solutions with subsequent selection of one of them. Ethanol with concentrations of 40 % and 70 % was used.

The influence of the extraction module (ratio of raw materials and extractant) on the final yield of extractive substances was also determined in parallel. The ratio was used to prepare the extract 1:5, 1:10, 1:15, 1:20.

There are several ways to intensify extraction processes. Based on literature data, the effect of ultrasound significantly accelerates the extraction process and ensures a more complete extraction of the necessary components from the raw materials, for the intensification of the ultrasonic mode of extraction for the release of active substances from a series of three-lobed beggartick herb, woundwort herb, and common agrimony herb. The extraction process was carried out using the same extractants and extraction modules, which were previously established experimentally using the ultrasound of the bathroom with a frequency of 50-60 Hz [5].

The process time was chosen in the range from 5 minutes to 25 minutes with an interval of 5 minutes. The temperature regime was maintained in the range from 40 °C to 50 °C, since this temperature completely excludes the possibility of decomposition of thermolabile substances, and also accelerates the process of extraction of difficult-to-access biologically active substances. Selected parameters of the ultrasonic extraction process and a summary of the comparative characteristics of both methods are presented below in Table 1 and Table 2, respectively.

Table 1

Parameters of the process of ultrasonic extraction of three-lobed beggartick herb, woundwort herb, and common agrimony herb

Raw materials	Extractant	Extraction module	Extraction time, min	Extraction temperature, °C
Three-lobed beggartick herb (<i>Bidens tripartita</i> L.)	Ethanol 70 %	1:20	25	40...50
Woundwort herb (<i>Solidago canadensis</i> L.)	Ethanol 40 %	1:20	20	40...50
Common agrimony herb (<i>Agrimonia eupatoria</i> L.)	Ethanol 40 %	1:20	25	40...50

Table 2

Parameters of the extraction method for the yield of biologically active substances

Raw materials	The yield of extractives during maceration in a water bath, %	Yield of extractives using ultrasound, %
Three-lobed beggartick herb (<i>Bidens tripartita</i> L.)	19.50 ± 0.25	33.30 ± 0.85
Woundwort herb (<i>Solidago canadensis</i> L.)	27.50 ± 0.74	43.80 ± 0.57
Common agrimony herb (<i>Agrimonia eupatoria</i> L.)	17.50 ± 0.65	34.00 ± 0.74

When analyzing the data obtained on ultrasonic extraction, it can be concluded that the yield of extractives when using ultrasound is significantly higher than when maceration in a boiling water bath is used for all types of raw materials under study.

Using the method of thin-layer chromatography, it was established that ultrasound at the stage of extraction does not affect the qualitative composition of biologically active substances in the extracts. For the development of extraction modes and the technology of obtaining dry extracts, along with the separate extraction of 3 types of raw materials, experiments were carried out on the extraction of a mixture of raw materials of three-lobe beggartick herb, woundwort herb, and common agrimony herb. At the same time, alcohol-water extractants in concentrations of 40 % and 70 % were also used. The output of extractive substances and the content of biologically active substances in the extracts and in the raw materials are presented in the Table 3.

Table 3

Comparison of phytocomposition extraction and individual types of plant raw materials

The content of biologically active substances in total and individual extraction from phytocomposition					
Substances	Extractant		Substances	Extractant	
	Eth. 40 %	Eth.70 %		Eth.40 %	Eth.70 %
flavonoids	0.93 ± 0.03	flavonoids	flavonoids	1.12 ± 0.07	3.28 ± 0.01
saponins	0.81 ± 0.12	saponins	saponins	1.30 ± 0.02	0.62 ± 0.04
tannins	3.05 ± 0.07	tannins	tannins	3.61 ± 0.10	2.01 ± 0.11

Conclusions. Based on the obtained results, it is possible to conclude:

1. During the separate extraction of three-lobe beggartick herb, woundwort herb, and common agrimony herb the concentration of extractive substances in the extracts is higher than when extracting a mixture of medicinal plant raw materials. 2. With separate extraction, a higher yield of target biologically active substances from raw materials is achieved, 97–98 %, while with mixture extraction, the yield was 81 %.

References

1. Lubinus Badillo FG, Cala OLO, Vera Campos SN, Villarreal Ibañez ED. Relationship Between Urolithiasis and Fatty Liver Disease: Findings in Computed Tomography. *Tomography*. 2020 Mar;6(1):1–4. doi: 10.18383/j.tom.2020.00020. PMID: 32280744; PMCID: PMC7138524.

2. Крюкова А.І., Кваша Д. М. Вивчення процесу екстракції трави звіробою в присутності поверхнево активних речовин. Сучасні досягнення фармацевтичної технології і біотехнології: матеріали ІХ Міжнародної науково-практичної конференції (м. Харків, 11-12 листопада 2021 р.). Х.: Вид-во НФаУ, 2021. –С. 118-121.

3. Kutsevol E. Study of ultrasonic extraction of corn columns with stigmas.

Kutsevol E., Konovalenko I. Fundamental and applied research in the field of pharmaceutical technology: materials of the I International scientific-practical conference (Kharkiv, October 13, 2021). Kh.: NUPh Publishing House, 2021. P. 23–24.

4. Коноваленко І. С., Половко Н. П. Фармакотехнологічні дослідження сухого екстракту зі збору для фітотерапії клімактеричного синдрому. Матеріали науково-практичної конференції «Сучасні проблеми фармакології, косметології та ароматології». Факультет стоматології і фармації МГУ, Одеса, 24.09.2021 р. С. 12–17.

5. Chemat, F. Ultrasound assisted extraction of food and natural products. Mechanisms, techniques, combinations, protocols and applications. A review. F. Chemat, N. Rombaut, A.–G. Sicaire et al. Ultrasonics sonochemistry. 2017. Vol. 34. P. 540– 560.

References

1. Lubinus Badillo FG, Cala OLO, Vera Campos SN, Villarreal Ibañez ED. Relationship Between Urolithiasis and Fatty Liver Disease: Findings in Computed Tomography. *Tomography*. 2020 Mar;6(1):1–4. doi: 10.18383/j.tom.2020.00020. PMID: 32280744; PMCID: PMC7138524.

2. Kryukova A.I., Kvasha D. M. Vyvchennya protsesu ekstraktsiyi travy zvirobouyu v prysutnosti poverkhnevo aktyvnykh rechovyn. Suchasni dosyahnennya farmatsevychnoyi tekhnolohiyi i biotekhnolohiyi: materialy IKH Mizhnarodnoyi naukovo-praktychnoyi konferentsiyi (m. Kharkiv, 11-12 lystopada 2021 r.). KH.: Vydvo NFaU, 2021. – S. 118-121.

3. Kutsevol E. Study of ultrasonic extraction of corn columns with stigmas. Kutsevol E., Konovalenko I. Fundamental and applied research in the field of pharmaceutical technology: materials of the I International scientific-practical conference (Kharkiv, October 13, 2021). Kh.: NUPh Publishing House, 2021. P. 23–24.

4. Konovalenko I. S., Polovko N. P. Farmakotekhnolohichni doslidzhennya sukhoho ekstraktu zi zboru dlya fitoterapiyi klimakterychnoho syndromu. Materialy naukovo-praktychnoyi konferentsiyi «Suchasni problemy farmakolohiyi, kosmetolohiyi ta aromolohiyi». Fakul'tet stomatolohiyi i farmatsiyi MHU, Odessa, 24.09.2021 r. S. 12–17.

5. Chemat, F. Ultrasound assisted extraction of food and natural products. Mechanisms, techniques, combinations, protocols and applications. A review. F. Chemat, N. Rombaut, A.–G. Sicaire et al. Ultrasonics sonochemistry. 2017. Vol. 34. P. 540– 560.