

ANNOTATION

dissertation work on the topic "**Pharmacognostic study and prospects for the use in medicine of *Filipendula vulgaris*, *Filipendula ulmaria* growing in the territory of Central Kazakhstan**" for the degree of Doctor of Philosophy (PhD) on specialty 6D110400 – «Pharmacy»

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Relevance of the research topic

At present, providing the population of the Republic of Kazakhstan with relatively safe, sufficiently effective and affordable domestic medicines is one of the priority tasks of pharmacy. To implement this direction of the pharmaceutical industry, it is necessary to conduct research on the rational use of the domestic resource of natural raw materials. In accordance with the Address of the Head of State to the people and the National Development Plan of the country until 2025, the Decree of the Prime Minister of the Republic of Kazakhstan on the Comprehensive Plan for the Development of the Pharmaceutical and Medical Industry for 2020-2025, as well as the Decrees of the Government of the Republic of Kazakhstan on the Concept for the Development of the Manufacturing Industry for 2023-2029 years and about the national project "Healthy Nation", the creation of domestic medicines using medicinal plants growing in the territory of the Republic of Kazakhstan, as well as the development of a pharmaceutical cluster by increasing the competitiveness of domestic products and entering foreign markets, is becoming increasingly important.

Particular interest in herbal medicines is justified by the fact that most of them have low toxicity and a number of other advantages compared to synthetic ones; and the variety of biologically active substances contained in plants provides a wide range of pharmacological effects of phytopreparations. In this regard, the search for new types of medicinal plant raw materials is a very urgent task.

As you know, many plants have certain medicinal properties and are included in the arsenal of tools used both in folk and in modern medical practice. The main criteria for the selection of plant raw materials as a source of biologically active substances are: a high quantitative content of the main components, the availability of raw materials in nature, or a simple technology for cultivating producing plants. These plants include *Filipendula vulgaris* Moench (meadowsweet ordinary or common) and *Filipendula ulmaria* (L.) Maxim. (meadowsweet elmous or elm-leaved), which are widely distributed in the Republic of Kazakhstan.

Filipendula L. is a genus of perennial herbaceous plants from representatives of the Kazakh flora of the *Rosaceae* Juss. family. According to foreign researchers, it has been established that plants of the genus *Filipendula* L. contain biologically active substances with practically valuable properties: flavonoids, glycosides, triterpenoids, tannins, catechins and essential oils, as well as a small amount of ascorbic acid.

In recent years, interest in plants of the genus *Filipendula* L. has not decreased, since their resource potential and spectrum of pharmacological activity

are significant, and the possibilities of using modern research methods have appeared and are expanding.

It is known that the chemical composition of the plant, the quality and quantity of active substances depend on climatic conditions and the place of growth. According to the main influencing factors, the Republic of Kazakhstan is distinguished by its large territory (ninth place in the world), soil diversity and sharply continental climate. In this regard, the pharmacognostic study of *Filipendula vulgaris* Moench and *Filipendula ulmaria* (L.) Maxim. growing on the territory of Kazakhstan and the scientific substantiation of the prospects for their use in medical practice are interesting scientific tasks for the pharmaceutical industry of the Republic of Kazakhstan.

Purpose of the dissertation research: the study of anatomical and morphological features, chemical composition, biological properties and prospects for the use in medicine of *Filipendula vulgaris* and *Filipendula ulmaria*, growing in the territory of Central Kazakhstan.

Objectives of the research:

1) to conduct resource studies to determine the reserves of herb *Filipendula vulgaris* and herb *Filipendula ulmaria* of the flora of Central Kazakhstan;

2) to conduct a pharmacognostic study of herb *Filipendula vulgaris* and herb *Filipendula ulmaria*, to determine the biomorphological features and anatomical and diagnostic features of these species;

3) to develop quality indicators and standardization of medicinal plant raw materials of the species *Filipendula vulgaris* and *Filipendula ulmaria*;

4) to develop a technology for obtaining extracts from *Filipendula vulgaris* and *Filipendula ulmaria* using ultrasonic treatment and study their component composition;

5) to assess the safety and screening of certain types of biological activity of samples of extracts from *Filipendula vulgaris* and *Filipendula ulmaria*, obtained by ultrasonic method.

Methods of research:

The methods used to conduct scientific research comply with the requirements of the State Pharmacopoeia of the Republic of Kazakhstan (SP RK), the Pharmacopoeia of the Eurasian Economic Union, European Pharmacopoeia, United States Pharmacopoeia, British Pharmacopoeia, FS and other regulatory documents in force on the territory of the Republic of Kazakhstan. To develop a method, technology for obtaining a biologically active substance, draft regulatory documents and laboratory regulations, the rules of GACP, GMP, State Standards and other regulatory documents in force on the territory of the Republic of Kazakhstan were used.

Also the following methods were used: ultrasonic extraction; chemical: qualitative reactions to various classes of biologically active substances; physical and chemical: high performance liquid chromatography (HPLC/UV, HPLC/MS), chromato-mass spectroscopy (GC/MS).

Statistical processing of the results was carried out using the program "Statistica v6.1", as well as the Microsoft Excel package. The results obtained are

presented as "mean \pm standard error of the mean". To assess the differences between 2 comparison groups, a non-parametric test was used - the Mann-Whitney U-test, and for several independent groups (3 or more) - the Kruskal-Wallis test. Differences were considered significant at the achieved significance level $p \leq 0.05$. Also, to process the obtained research results, the method of variance-statistical analysis was applied using the Student's reliability criterion ($P < 0.95$) and the methods of the general pharmacopoeial monograph (GPM.1.1.0013.15, sections 3 and 4).

Objects of research: herbal raw materials: herb *Filipendula vulgaris* (common meadowsweet) and herb *Filipendula ulmaria* (elm-leaved meadowsweet), collected on the territory of Central Kazakhstan; sums of extractive substances: dense extracts of *Filipendula vulgaris* and *Filipendula ulmaria* obtained by ultrasonic method.

Subject of study: resource-study data, biomorphological features, diagnostic features, numerical indicators and chemical composition of herb *Filipendula vulgaris* and herb *Filipendula ulmaria*; method of obtaining and production technology of thick extracts of *Filipendula vulgaris* and *Filipendula ulmaria*; chemical composition and biological properties of thick extracts of *Filipendula vulgaris* and *Filipendula ulmaria*.

The main provisions of the thesis research put to the defense:

- results of determination of raw material reserves and pharmacognostic analysis of herb *Filipendula vulgaris* and herb *Filipendula ulmaria* growing in the territory of Central Kazakhstan, draft regulatory documents;
- a method for obtaining thick extracts from herb *Filipendula vulgaris* and herb *Filipendula ulmaria* by ultrasonic method and their component composition;
- results of assessment of acute toxicity, study of antimicrobial, antifungal, anti-inflammatory, antioxidant activity and cytotoxicity of thick extracts of *Filipendula vulgaris* and *Filipendula ulmaria* obtained by ultrasound.

Scientific novelty:

- for the first time, a pharmacognostic analysis and assessment of the quality indicators of medicinal plant raw-materials *Filipendula vulgaris* and *Filipendula ulmaria*, growing in the territory of Central Kazakhstan, were carried out, draft RDs were developed;
- for the first time, an assessment of the raw material reserves of herb *Filipendula vulgaris* and herb *Filipendula ulmaria* was carried out on the territory of Central Kazakhstan;
- for the first time developed a method for obtaining thick extracts of *Filipendula vulgaris* and *Filipendula ulmaria* by ultrasonic method;
- for the first time the chemical composition of dense extracts of *Filipendula vulgaris* and *Filipendula ulmaria*, obtained by ultrasonic method, was studied;
- the biological properties of the obtained extracts of *Filipendula vulgaris* and *Filipendula ulmaria* were studied for the first time;

The novelty of the conducted research is confirmed by two Kazpatent applications (QAZPATENT) for inventions:

- application No. 2023/0007.1 dated 01/06/2023 for the invention «Method for obtaining extract of meadowsweet elmous (*Filipendula ulmaria*) with antimicrobial and antioxidant activities» (status: positive result of formal examination, at the stage of substantive examination);

- application No. 2023/0082.1 dated February 7, 2023 for the invention «Method for obtaining extract of meadowsweet ordinary (*Filipendula vulgaris*) with antimicrobial and antioxidant activities» (status: positive result of formal examination, at the stage of substantive examination).

Practical significance of the research:

As a result of the research, raw material reserves of herb *Filipendula vulgaris* and herb *Filipendula ulmaria* were determined in the territory of Central Kazakhstan.

Based on the results obtained in the course of the dissertation research, medicinal plant raw-materials of two types are recommended: *Filipendula vulgaris* herba and *Filipendula ulmaria* herba for the development of medicines.

The harvesting technology and quality specification, draft regulatory documents for the types of raw materials «*Filipendula vulgaris* herba», «*Filipendula ulmaria* herba» have been developed.

A rational method has been developed for obtaining extracts of *Filipendula vulgaris* and *Filipendula ulmaria* by ultrasonic method for further drug development, which is characterized by a significant reduction in the duration and increase in the productivity of the technological process, an increase in the yield of extractives and the content of biological active substances, and the absence of toxic solvents. Laboratory regulations and draft regulatory documents for thick extract substances of *Filipendula vulgaris* and *Filipendula ulmaria* obtained by ultrasonic method have been developed. Based on the results of the dissertation research, thick extracts of *Filipendula vulgaris* and *Filipendula ulmaria* are recommended for the development of drugs with antimicrobial, antioxidant and anti-inflammatory effects.

The results of the research work on the pharmacognostic study of herb *Filipendula vulgaris* and herb *Filipendula ulmaria* have been introduced into the educational process of the School of Pharmacy of the NCJSC «Karaganda Medical University», the Faculty of Biology and Geography of the NCJSC «Karaganda University after named Academician E.A. Buketov» and the Department of Pharmaceutical Disciplines of the PI «Bolashaq Academy» of Pharmacy in the discipline «Pharmacognosy» for students of educational programs 6B10103 – «Pharmacy», 6B07201 – «Technology of Pharmaceutical Production» and 6B05102 – «Biotechnology».

Author's personal contribution. All the above experimental results of the dissertation research were obtained by the author himself, which testifies to the personal contribution of the applicant to Pharmaceutical Sciences. The author carried out studies on the study of morphological features and anatomical and histological features of the structure of herb *Filipendula vulgaris* and herb *Filipendula ulmaria*, identified and identified diagnostic features for these plants. The dissertation student obtained essential oils of herb *Filipendula vulgaris* and

herb *Filipendula ulmaria*, using the Clevenger apparatus, thick extracts of *Filipendula vulgaris* and *Filipendula ulmaria* were obtained, methods for their production by the ultrasonic method were developed. Studies of acute toxicity, screening of certain types of biological activity of the obtained extracts were carried out. Statistical processing of the obtained results was carried out and they were designed in accordance with the requirements for the dissertation work.

Conclusions:

1. The study of distribution, raw material reserves and assessment of the prospects of domestic plant species of the genus *Filipendula* L. showed that herb *Filipendula vulgaris* and herb *Filipendula ulmaria* are a renewable source of plant raw materials for the production of medicinal substances. In the Karaganda and Ulytau regions, significant reserves of raw materials were identified: the area of thickets with the participation of herb *Filipendula vulgaris* was 52.5 hectares with an operational reserve of 26.9 tons and the volume of possible collection of raw materials - 13.5 tons, while for the thickets of herb *Filipendula ulmaria* these the figures were 16.2 ha, 14.2 tons and 7.0 tons, respectively.

2. According to the results of a comparative pharmacognostic study of herb *Filipendula vulgaris* and herb *Filipendula ulmaria*, collected in the territory of Central Kazakhstan, their diagnostic anatomical and morphological features were established, allowing identification. Identification indicators were determined based on the results of histochemical and phytochemical analysis. The chemical composition of essential oils from herb *Filipendula vulgaris* and herb *Filipendula ulmaria* was studied, where the main components are: methyl salicylate (41.05% and 19.48%, respectively) and 1.8-cineol (2.85% and 3.07% respectively).

3. The harvesting technology and quality specification for herb *Filipendula vulgaris* and herb *Filipendula ulmaria* have been developed in accordance with the requirements of the SP RK, F EAEU and GACP. Draft RDs were developed for the medicinal plant raw materials of «*Filipendula vulgaris* herba», «*Filipendula ulmaria* herba». Shelf life is set to 24 months. at a temperature of 25 ± 2 °C and a relative humidity of $60\pm 5\%$.

4. A method and technology for the production of thick extracts of *Filipendula vulgaris* and *Filipendula ulmaria* have been developed and their quality parameters have been studied:

- the highest yield of the product is provided by double sonication of air-dry raw materials, crushed to a size of 5 mm, with 70% ethanol at an ultrasonic frequency of 40 kHz, for 30 minutes;

- technological and instrumental schemes of production are proposed, while the advantages of the developed technology are an increase in the productivity of the technological process by 2 times, a significant reduction in its duration by 20 times and an increase in the yield of the finished product by 3 times;

- in the composition of thick extracts, 16 phenolic compounds were identified and quantified, 6 of which are phenolic acids, 10 are flavonoids, and the dominant compounds are cynaroside with a content of 46.31 and 37.42 mg/g, apigenin - 14.15 and 16.57 mg/g, quercetin - 7.92 and 7.94 mg/g, and gallic acid - 4.85 and 4.94 mg/g, respectively;

- quality specifications for thick extract substances of *Filipendula vulgaris* and *Filipendula ulmaria* have been developed. Shelf life of thick extracts is 2 years. Draft regulatory documents for thick extract substances have been developed.

5. It has been established that thick extracts of *Filipendula vulgaris* and *Filipendula ulmaria* belong to the "Practically non-toxic" group (VI class - low toxicity). Evaluation of biological activity showed that thick extracts of the studied species of meadowsweet exhibit antimicrobial activity against strains of *S. aureus*, *E. coli* and antifungal activity against the yeast fungus *C. albicans*, have high antioxidant, anti-inflammatory, wound healing activity, in experiments in vitro show cytotoxic properties. This is the basis for further research and development of drugs with appropriate types of pharmacological activity, including antitumor activity.

Approbation of the results of the dissertation:

1) VII International scientific and practical distance conference «Management and marketing as part of the modern economy, science, education, practice» (Ukraine, Kharkiv, March 21, 2019). According to the results of participation in this conference in English, he was awarded the Grand Prix Diploma for the best report;

2) International scientific and practical conference dedicated to the memory of Professor R. Dilbarkhanov «Formation and development prospects of the scientific school of pharmacy: continuity of generations» (Kazakhstan, Almaty, June 16, 2019);

3) International scientific and practical conference “Ecology and biodiversity conservation” (Kazakhstan, Almaty, October 23-24, 2019);

4) VIII International Scientific and Practical Conference «Belikovskiy Readings» (Russia, Pyatigorsk, December 5-6, 2020);

5) International scientific conference of young scientists «Modern trends in the development of health saving technologies» (Russia, Moscow, December 17-18, 2020, ARIMAP);

6) XXVIII International scientific and practical conference of young scientists and students «Topical issues of new medicines development» (Ukraine, Kharkiv, March 18-19, 2021);

7) At an expanded meeting of the Council of the School of Pharmacy NCJSC «Karaganda Medical University» (Pr. No. 12 dated 26.06.2023).

Publications: based on the materials of the dissertation, 11 printed works were published, including: 1 article in an international scientific publication included in the international Scopus database (percentile - 58%); 4 - in the publications recommended by the Committee for Quality Assurance in the Field of Science and Higher Education of MSHE RK; abstracts of 6 reports in the materials of international conferences.

Scope and structure of the dissertation: The dissertation is presented on 145 pages of computer text and consists of an introduction; review; 6 sections describing the material and research methods; the main part containing the results and discussion of their own research; conclusions; list of references, including 148

references, of which 107 in Russian and 41 in foreign languages. The dissertation is illustrated with 42 tables and 34 figures, 7 formulas and includes 18 applications.