

ANNOTATION

of the dissertation work on the topic «**Фармакогностическое изучение видов рода *Allium* флоры Казахстана и перспективы их использования**»
for the degree of Doctor of Philosophy (PhD) in the specialty
6D110400 – Pharmacy by **Kadyrbaeva Gulnara Mukhametovna**

Relevance of the research topic. As part of the implementation of the National Project "Healthy Nation" for 2021-2025, the main task of the domestic pharmaceutical industry is import substitution, which consists in the development and creation of domestic medicines of a full production cycle in the country and bringing the share of domestic pharmaceutical products from 17% to 50%.

As part of the implementation of the comprehensive plan for the development of the pharmaceutical industry for 2020-2025, the issue of organizing the production of medicines using medicinal plants growing on the territory of the Republic of Kazakhstan has received the status of a state priority.

The search for promising medicinal plants as sources of biologically active substances and the development of herbal pharmaceutical substances based on them is relevant.

In this regard, of particular interest are plants of the genus *Allium*, growing on the territory of the Republic of Kazakhstan, which are valuable sources of biologically active compounds, many types of which have long been used in folk medicine as diuretics, hemostatic, anti-inflammatory, bactericidal agents. Based on the above, the pharmacognostic study of some plants of the genus *Allium* of the flora of Kazakhstan and the study of pharmacological activity is promising.

The purpose of the study: pharmacognostic study of *Allium galanthum*, *Allium turkestanicum* and prospects for the creation of herbal pharmaceutical substances based on them.

Research objectives:

To establish diagnostic morphological and anatomical signs of *Allium galanthum* and *Allium turkestanicum*.

Conduct a comprehensive phytochemical study of *Allium galanthum* and *Allium turkestanicum* and establish the main groups of biologically active compounds;

To standardize raw materials of *Allium galanthum* and *Allium turkestanicum* in accordance with pharmacopoeia requirements;

To develop the optimal technology of extracts based on *Allium galanthum* and *Allium turkestanicum*, to standardize the extracts obtained;

To study the profile of the biological activity of the obtained extracts;

Objects of research: *Allium galanthum* leaves and bulbs, *Allium turkestanicum* bulbs and extracts based on them.

Research methods: macroscopic, microscopic, phytochemical, commodity science, physico-chemical, microbiological, statistical methods.

Scientific novelty:

For the first time:

- diagnostic morphological and anatomical features of *Allium galanthum* and *Allium turkestanicum* have been identified as a result of a comparative morphological and anatomical study, allowing identification of the studied species;
- a comparative phytochemical study of *Allium galanthum* and *Allium turkestanicum* were carried out using modern physico-chemical methods (HPLC-MS, GC-MS); these studies allowed us to establish the values of primary and secondary metabolism products, elemental composition for identification. HPLC-ESI-QTOF-MS/MS assays revealed up to 17 main compounds, which 15 substances belonging to various classes of natural compounds were identified: simple organic acids, flavonoids and their glycosides, which make up the main group of metabolites in the tested extracts. It was found that the plants *Allium galanthum*, *Allium turkestanicum* and are characterized by variability of flavonoid compounds. The thirteen flavonoids and their glycosides are common to the studied genus. The identified substances are chemical markers of the studied plants and are used in standardization. Extracts of diethyl ether were analyzed using GC-MS and 25, 22 and 17 volatile compounds were identified in the leaves and bulbs of *A. galanthum* and bulbs of *A. turkestanicum*, respectively.

- screening pharmacological studies of the studied plants of the genus *Allium* were carried out. It was revealed that all the studied species have low toxicity and a certain level of biological activity: antimicrobial, antioxidant, tyrosinase and are promising for introduction into medical practice, as sources of raw materials: leaves and bulbs of *Allium galanthum* and bulbs of *Allium turkestanicum*.

The priority of the conducted research is protected by the patent of the Republic of Kazakhstan for a utility model: "A method for obtaining an extract with antimicrobial and antioxidant activities from the plant *Allium galanthum*" (patent No. 7156).

The main provisions of the dissertation research submitted for defense:

- Results of a comprehensive pharmacognostic study of *Allium galanthum* and *Allium turkestanicum*: phytochemical, morphological and anatomical tests for the development of approaches to standardization;

- Results of experimental substantiation of the development of optimal technology for the production of herbal pharmaceutical substances based on *Allium galanthum* and *Allium turkestanicum* with antimicrobial, antioxidant and tyrosinase activities.

Practical significance of the study. The technology of collecting, harvesting and storing *Allium galanthum* bulbs and leaves, *Allium turkestanicum* bulbs were introduced by Phytoleum LLP, Esik, Kazakhstan.

A quality specification of *Allium galanthum* bulbs and leaves and *Allium turkestanicum* bulbs have been developed, on the basis of which a draft regulatory documentation for medicinal plant raw materials has been developed.

The technology of the production process of pilot-industrial series of extracts from herbal medicinal raw materials of leaves and bulbs of *Allium galanthum* and bulbs of *Allium turkestanicum* have been developed at the pharmaceutical enterprise "Phytoleum" LLP.

The technology of cultivation of the studied plants has been developed in accordance with the principles of the GACP standard "Good Agricultural and Collection Practice for starting materials of herbal origin".

The results obtained during the dissertation research are applied in the scientific and educational process of the Lublin Medical University (Department of Pharmacognosy) and the departments of the School of Pharmacy of the Kazakh National Medical University.

The use of *Allium galanthum* and *Allium turkestanicum* in medical practice as antimicrobial, antioxidant agents is justified.

Personal contribution of the author. All the results of the dissertation research were obtained by the author independently, which indicates the personal contribution of the applicant to the science in the field of pharmacy.

The reliability of the results, the main provisions submitted for defense, conclusions and conclusions formulated in the dissertation work is justified by a significant amount of experimental material, fully confirmed by the results of their own research conducted in laboratory and production conditions, using modern instruments and accurate measurement methods, as well as comparison with the literature data.

Approbation of the work. The main provisions of the dissertation work were reported and published in the materials of international scientific and practical conferences: International scientific and practical Conference "Modern methods of correction of acne and other skin problems in cosmetology practice" (Kharkiv, Ukraine, 2018); VI All-Russian scientific and practical conference with International participation "Innovations in the health of the nation" (St. Petersburg, Russia, 2018); VII scientific and practical conference with International participation "Priorities of pharmacy and dentistry – from theory to practice" (Almaty, Kazakhstan, 2018); IV International scientific and practical conference "Global science and innovation 2019: Central Asia" (Astana, Kazakhstan, 2019); XIV International scientific and practical conference "Years of Rural Development, Tourism and Folk Crafts (2019-2021)" (Dushanbe, Tajikistan, 2019); VIII International Scientific and Practical Conference "Priorities of pharmacy and dentistry – from theory to practice" (Almaty, Kazakhstan, 2019); International conference "Modern science. Management and standards of scientific research" (Prague, Czech Republic, 2020).

Information about publications. According to the research results, 14 scientific papers have been published, including: an article in an international peer-reviewed scientific journal included in the Scopus database and the Web of Science Core Collection – 1; articles in journals recommended by the Committee for Quality Assurance in Education and Science of the Ministry of Education and Science of the Republic of Kazakhstan - 4; articles and abstracts in collections of International scientific and practical conferences (Russian Federation, Czech Republic, Ukraine, Kazakhstan) - 7; articles in international journals (Russia) – 1; utility model patents - 1.

The volume and structure of the dissertation. The volume and structure of the dissertation. The dissertation work is presented on 151 pages of typewritten

text in a computer set, contains 37 tables, 80 figures, a list of references, including 212 sources, as well as 20 appendices. The work consists of an introduction, a literature review, a section devoted to research materials and methods, three sections of own research, findings and conclusions.

Conclusion. The dissertation work is devoted to the pharmacognostic study, standardization of raw materials *Allium galanthum* and *Allium turkestanicum*, optimal technology for obtaining extracts and studying the profile of their biological activity.

Evaluation of the prospects of studying domestic plant species of the genus *Allium* has shown that *Allium galanthum* and *Allium turkestanicum* are of scientific and practical interest as a renewable source of plant raw materials for the production of plant substances.

Diagnostic anatomical and morphological signs were established, allowing to identify *Allium galanthum* and *Allium turkestanicum*. The indicators of identification of *Allium galanthum* and *Allium turkestanicum* were determined according to the indicators: A. macroscopy, B. microscopy.

Analysis of HPLC-ESI-QTOF-MS/MS allowed preliminary identification of the main signals recorded in the obtained chromatograms. Flavonoids and their glycosides make up the main group of metabolites in the raw materials *Allium galanthum* and *Allium turkestanicum*.

The quality indicators for raw materials *Allium galanthum* and *Allium turkestanicum*, their acceptance criteria were established, the standardization of *Allium galanthum* and *Allium turkestanicum* was carried out in accordance with the requirements of the SPh RK.

As a result of long-term stability tests of raw materials, the shelf life of 24 months has been established. at a temperature of 25 ± 2 ° C and a relative humidity of $60 \pm 5\%$.

It was found that the analyzed extracts of nonpolar diethyl ether exhibit stronger biological activity compared to aqueous and water-ethanol extracts of different ratios. The first extracts proved to be strong antimicrobial agents not only against the gram-positive bacteria tested, but also inhibited the growth of several strains of gram-negative bacteria and yeast, possibly due to the presence of 16-gentriacontanone (palmiton) and 1-tritriacantanol among other components of the extracts.

The presence of flavonoids, oxygen-saturated long-chain alkanes, certainly influenced the increased antiradical potential of the extracts. It has also been proven that extracts of the diethyl ether of the *Allium galanthum* bulb inhibit mouse tyrosinase up to 54% of its activity, which can confirm its promising whitening properties.

The confirmed antiradical properties of the tested extracts, when added to cosmetics, may exhibit soothing properties against the negative effects of environmental stressors that affect skin function and lead to an increase in the generation of reactive oxygen species. Finally, the antimicrobial potential of the tested samples will be important for the preservation of pharmaceutical products,

as well as for inhibiting the development of bacterial infections on the surface of the skin prone to irritation and acne.

Thus, the results of the research described in the dissertation work confirm the use of extracts of *A. turkestanicum* and *A. galanthum* in the pharmaceutical industry