

ABSTRACT

Candidate for the degree of Doctor of Philosophy (Ph.D.) in the educational program «6D072100 – Chemical technology of organic substances»

TOKTARBEK MERUYERTKOZHA

«Development of the method for obtaining a biologically active complex from plants of the genus *Petrosimonia*»

General work description. The dissertation work is devoted to the analysis of the chemical composition of biologically active complexes of plants of the genus *Petrosimonia*: *Petrosimonia triandra*, *Petrosimonia glaucescens*, *Petrosimonia brachiata* and *Petrosimonia sibirica* of the *Chenopodiaceae* family, consideration of optimal conditions for the isolation of complexes and individual compounds, substantiation of the structure of individual compounds, study of biological activity complexes and individual compounds.

Relevance of the research work. Throughout human history, the people of the world have used plant-based raw materials for nutrition and treatment. Even though the field of health care was little developed at that time, people knew the various properties of plants and used them in traditional medicine for their health. There are about 6,000 species of plants growing on the territory of our country, only a small amount is used for the benefit of the people. Therefore, the preparation of domestic highly effective biologically active complexes in the food industry and the field of pharmaceuticals have become one of the main issues in our country.

Plants are the main source of molecules that create new medicines, so some foreign companies are interested in plant-based medicinal raw materials that show anti-inflammatory activity. And the chemical composition and biological properties of plants showing anti-inflammatory activity have not been fully studied. Anti-inflammatory drugs reduce tissue damage and interfere with the pathophysiological process of inflammation. Finding molecules from plants that exhibit anti-inflammatory activity requires research and effort.

Today, pharmaceutical production in Kazakhstan has not well developed; we are still dependent on imports because we do not have enough medicines for public health. The impact of some drugs on the human body is sometimes small, and because most of them are synthesized, they are not completely removed from the body, residues of drugs accumulate in some important organs like the liver and kidneys, and as a result, people's health deteriorates further.

The World Health Organization (WHO) estimates that approximately 65% of the world's population incorporates traditional medicine into medical care. Researching the composition of medicinal herbs used by our ancestors, determining their activity, using them for public health, modernizing traditional medicine, and meeting the needs of pharmaceutical production is an urgent issue. The action of medicinal plants depends on their composition.

The degree of knowledge of the problem. The works of Wen Sun (2015) and Ying Wang (2016) presented the chemical compositions and biological activities of the plant species *Petrosimonia sibirica*, which grows in the Xinjiang of northwest China. According to research by Chinese scientists, steroids, alkaloids, quinones, flavonoids and phenolic acids were found from the *Petrosimonia sibirica*, and it was found that plant exhibits antibacterial activity. However, the lack of information about the degree of study of other plant species of the genus *Petrosimonia* has aroused great interest, so since 2017 we have been conducting research on the identification and isolation of biologically active substances from plants of the genus *Petrosimonia*.

Purpose of the research work. Development of the method for obtaining a biologically active complex from plants of the genus *Petrosimonia*.

Tasks set to achieve the goal:

- Conducting a comparative qualitative and quantitative analysis of the main groups of biologically active substances of plants of the genus *Petrosimonia* species: *triandra*, *glaucescens*, *brachiata* and *sibirica*, which belong to the *chenopodiaceae* family.

- Development of a scientific basis and proposal of a technological block-scheme for the isolation and separation of a biologically active complex (BAC), as well as compounds contained in the objects under study.

- Establishment of the structures of individual compounds using modern physicochemical methods.

- Screening of obtained extracts, biologically active complexes and individual compounds.

Metrological support of scientific research work.

The structure of substances isolated from some plants of the genus *Petrosimonia* was identified using modern methods: one-dimensional: $^1\text{H-NMR}$ - AVANCE NEO-400, AVANCE NEO-500 at 400, 500 MHz and $^{13}\text{C-NMR}$, BB, DEPT - AVANCE NEO-400, AVANCE NEO-500 at 100, 125 and 150 MHz; two-dimensional: NMR $^1\text{H-}^{13}\text{C}$ HSQC, HMBC, $^1\text{H-}^1\text{H}$ COSY-45 $^\circ\text{C}$, NOESY, and also installed: optical rotation on the polarimetry R-2000, UV (Shimadzu UV-240, Japan), IR -spectroscopy (Bruker Vector 22, Japan) and EI-MS (JEOL 600H-1, Inlet: Direct Probe), FAB-MS (JEOL 600H-2, Inlet: Direct Probe), ESI-MS (Burker Compass Data Analysis 4.2), using HR-EI-MS (JEOL 600H-2, Inlet: Direct Probe); melting point (Melting point Buchi M-560), at the H.E.J. Research Institute of Chemistry, International Center for Chemical and Biological Sciences, University of Karachi, Pakistan and conducted in the laboratories of the Department of Chemistry and Technology of Organic Substances, Natural Compounds and Polymers, Al-Farabi Kazakh National University, Akmaty, Kazakhstan.

Description of the main results of the study.

1. For the first time, a fundamental study of some plant species of the genus *Petrosimonia* was carried out in order to identify new sources of biologically active compounds and complexes. The results of a comparative analysis of plants of the genus *Petrosimonia* species: *triandra*, *glaucescens*, *brachiata* and *sibirica*, belonging to the family *Chenopodiaceae*, collected in the Almaty region of the

Republic of Kazakhstan, are presented; the qualitative composition and quantitative content of the main groups of biologically active substances are determined.

2. A scientific basis for the separation of individual substances has been developed, a technological block diagram has been proposed, and the material balance for obtaining a dry extract has been calculated. 58 substances were found in the studied objects, 14 of which were identified by gas-liquid chromatography, 20 compounds using an amino acid analyzer.

3. The scientific basis for identifying the main groups of biologically active substances is proposed. Using the method of classical maceration and the modern method of supercritical liquid CO₂ extraction, 16 extracts were obtained. To isolate biologically active substances from plants of the genus *Petrosimonia*, silica gel, column chromatography with Sephadex, preparative thin-layer chromatography and preparative high-performance liquid chromatography were used; the isolation of alkaloids was carried out on a C18 ODS-H80 sorbent. As a result of the research work, 24 substances were isolated:

5 alkaloids: *N*-[(2*S*)-2-(4-hydroxyphenyl)-2-hydroxyethyl]-3-(3,4-dimethoxyphenyl)-(2*E*)-prop-2-enamide, *N*-*cis*-feruloylloctopamine, *N*-*trans*-feruloylloctopamine, *N*-[(2*S*)-2-(3,4-dihydroxyphenyl)-2-hydroxyethyl]-3-(3,4-dimethoxyphenyl)-(2*E*)-prop-2-enamide and allantoin, including one unpublished compound (N-[(2*S*)-2-(4-hydroxyphenyl)-2-hydroxyethyl]-3-(3,4-dimethoxyphenyl)-(2*E*)-prop-2-enamide) and (*S*)-allantoin, 1 alkanol (n-hexadecanol), 1 ester (4-hydroxyphenethyl tetradecanoate), 5 steroid compounds and 12 polyphenol compounds. To establish the structures of the isolated compounds, modern physicochemical methods were used (UV, IR, FAB-MS, EI-MS, ESI-MS, HR-EI-MASS, ECD, ¹³C-NMR, ¹H-NMR, HMBC, HSQC, COSY-45 °C and NOESY).

4. Two total (hexane and ethyl acetate) extracts obtained by maceration from a plant of the genus *Petrosimonia* have high anti-inflammatory and antibacterial effects.

Scientific novelty of the work.

For the first time, in-depth scientific studies of some species of plants of the genus *Petrosimonia* have been presented, the following promising plant species have been identified: *Petrosimonia triandra*, *Petrosimonia glucescens*, *Petrosimonia brachiata* and *Petrosimonia sibirica*, growing in saline and brackish zones of the country, comparative analyzes of the qualitative composition and quantitative content of biologically active substances in the studied species have been carried out.

For the first time, a scientific basis for the isolation and separation of biologically active complexes from these plant species has been developed, using methods of supercritical fluid CO₂ extraction and maceration.

For the first time, 24 substances were isolated from a plant of the genus *Petrosimonia*, among them the alkaloid *N*-[(2*S*)-2-(4-hydroxyphenyl)-2-hydroxyethyl]-3-(3,4-dimethoxyphenyl)-(2*E*)-prop-2-enamide is a new compound not described in the literature.

For the first time, the alkaloids *N*-[(2*S*)-2-(4-hydroxyphenyl)-2-hydroxyethyl]-3-(3,4-dimethoxyphenyl)-(2*E*)-prop-2-enamide, *N*-cis-feruloylloctopamine, *N*-trans-feruloylloctopamine and *N*-[(2*S*)-2-(3,4-dihydroxyphenyl)-2-hydroxyethyl]-3-(3,4-dimethoxyphenyl)-(2*E*)-prop-2-enamide were separated from a plant of the genus *Petrosimonia* using the C-18 ODS-H80 adsorbent.

For the first time, two total (hexane and ethyl acetate) extracts based on steroids, fatty acids, polyphenols and alkaloids obtained by maceration from a plant of the genus *Petrosimonia* have very high anti-inflammatory and antibacterial effects.

The novelty of the results obtained.

Articles have been published in Kazakh and foreign publications. The results of biological screening are protected by the utility model of the Republic of Kazakhstan «Method for producing an agent with antibacterial action» №. 7680 (December 23, 2022, Bulletin No. 51).

The main provisions of the dissertation submitted for defense:

1. The results of the analysis of the main groups of biologically active substances in some plant species of the genus *Petrosimonia*: *triandra*, *glaucescens*, *brachiata* and *sibirica*, of the *chenopodiaceae* family;

2. Optimal methods for the isolation and separation of biologically active substances from some plant species of the genus *Petrosimonia*, the *chenopodiaceae* family;

3. Structures of alkaloids and isolated substances using modern methods;

4. Results of tests on the biological activity of extracts and substances obtained from some studied plant species of the genus *Petrosimonia*.

Practical significance of the work.

New plant sources of biologically active substances have been identified - plants of the genus *Petrosimonia*, belonging to the *chenopodiaceae* family. A study on biological activity established that the obtained conditional extracts have anti-inflammatory and antibacterial effects. The results obtained can help increase the share of promising and affordable domestic drugs and meet the needs of pharmaceutical production.

Connection of work with state scientific programs. The dissertation work was carried out within the framework of the following research projects:

- AP08052551-OT-22 «Chemical research and activity of natural compounds of some plant species in Kazakhstan» (2020-2022).

- AP05131716-OT-20 «Development of scientific bases for isolating new domestic drugs from plant materials for medicine and agriculture» (2018-2020).

Publications. Based on the results of the dissertation work, 9 scientific articles were published, including 3 articles in international publications with impact factor, 2 articles in publications presented by the Committee for Quality Assurance in the field of Science and Higher Education of the Ministry of Science and Higher Education of the Republic of Kazakhstan, abstracts of 3 reports in collections of international conferences and utility model of the Republic of Kazakhstan №. 7680 (December 23, 2022, Bulletin No. 51) «Method of obtaining a medicinal product with antibacterial action».

Individual contribution of the doctoral student to the preparation of each article. Toktarbek Meruyertkozha is the first author of «Sterols and flavonoids from the pelitohalophytes *Petrosimonia glaucescens* and *Climacoptera brachiata*» (Chemistry of Natural Compounds – 2019. - Vol. 55. - №. 3. – P. 547-548, Q3) and «Phenolic compounds from the plant *Petrosimonia triandra*» (Chemistry of Natural Compounds - 2021. - Vol. 57. - №. 3. - P. 536-538, Q4). The researcher was directly involved in planning all experiments, processing the results obtained, and preparing articles.

In addition, Toktarbek Meruyertkozha was involved in preparing articles in accordance with the requirements of the journal and improving the article after each stage of review.

In the articles «Phytochemical analysis of *Petrosimonia sibirica* grown in Kazakhstan» (International Journal of Biology and Chemistry – 2018. - Vol. 11. - No. 2. – P. 314-318, IRSTI 31.23.99) and «Phytochemical analysis of some Kazakh plant species of the genus *Petrosimonia*, family *Chenopodiaceae*» (Chemistry of plant raw materials - 2022. - №. 4. P.241-248) Toktarbek M. became the second author, was engaged in obtaining experimental data, processing experimental results, collecting literature for compiling articles.

The doctoral student took direct part in international scientific conferences with the aim of summarizing materials and abstracts of 3 reports, obtaining experimental data, processing and interpreting experimental results.