ABSTRACT
of the dissertation work of Arailym Beibitkyzy Mukanova
on the topic «Development of pharmaceutical justification of new phytopreparations from the herb of Pale yellow scabious (*Scabiosa ochroleuca* L.)» presented for the degree of Doctor of Philosophy (PhD) in the specialty "Pharmacy" 6D110400

The development of healthcare infrastructure to ensure efficient operation is one of the main tasks of the healthcare system and improving the health of the population (Resolution of the Government of the Republic of Kazakhstan dated June 12, 2024 No. 454 «Concept for the Development of Healthcare Infrastructure for 2024-2030»).

Strengthening the health of the population is a priority direction of the state's health policy. According to the Comprehensive Plan for the Development of the Pharmaceutical and Medical Industry for 2020-2025 (On Amendments and Supplements to the Decree of the Prime Minister of the Republic of Kazakhstan No. 132 of October 6, 2020), one of the main priorities is the creation of the production of medicinal products based on plants growing in the Republic of Kazakhstan.

In order to achieve the goals and objectives of the development of the pharmaceutical industry, it is necessary to conduct full-fledged scientific and practical research on the use of a rational, resource-saving method of domestic natural raw materials as a source of biologically active substances. Despite the dynamic growth of the pharmaceutical industry in the Republic of Kazakhstan, the issue of import dependence is acute. This is evidenced by the presence of manufacturing countries in Kazakhstan and the structure of the pharmaceutical market, since the share of domestic production of medicines in the republic is only 14.9% [1].

Considering the above, it is of particular interest to study the phytochemical composition of some promising plant species of the genus Scabiosa growing in the country.

According to the flora of the USSR, about 100 species of the genus *Scabiosa* L. belong to the *Dipsaceae* family, which are widespread in the Mediterranean countries and belong to the *Caprifoliaceae* family. Some species are distributed to the Far East, and the southern border of the breed borders the mountains of East Africa. In Kazakhstan, from Altai to the Northern Tien Shan, there are 7 species of the genus Scabiosa L., two of which are in Central Kazakhstan: *Scabiosa isetensis* L. (Lomelosia isetensis (L.) Sojak) and *Scabiosa ochroleuca* L. [2-4].

Plant species of the genus *Scabiosa* are widely used as antibacterial, anti-inflammatory, antioxidants, desensitization and anticonvulsants.

Expanding the range of plant raw materials and creating new herbal preparations from *Scabiosa ochroleuca* L. raw materials based on innovative technologies is a promising area of pharmaceutical research.

Research objective: Justification, standardization and determination of the safety and biological activity of extracts of the herb *Scabiosa ochroleuca* L. using modern technologies.

Research tasks:

1. Extraction of *Scabiosa ochroleuca* L. herb using ultrasonic and microwave methods.
2. Determination of the chemical composition of *Scabiosa ochroleuca* L. extracts.
3. Development of a rational technology and feasibility study for *Scabiosa ochroleuca* L. extracts.
4. Determination of quality indicators and shelf life of extracts obtained from *Scabiosa ochroleuca* L. herb.
5. Evaluation of the overall safety and biological activity of the extract obtained from *Scabiosa ochroleuca* L. herb.

Research methods: Pharmacopoeial and non-pharmacopoeial methods (physical, physico-chemical, pharmaceutical-technological, pharmacological, biological), informational-analytical, statistical, as well as marketing methods of analysis.

Objects of research: Medicinal plant raw materials - *Scabiosa ochroleuca* L. herb; concentrated extracts of *Scabiosa ochroleuca* L. obtained by ultrasonic and microwave methods.

Subject of research: Rational technology for obtaining extracts from raw materials of *Scabiosa ochroleuca* L., study of their chemical composition, safety, stability and pharmacological properties.

Issues proposed for the defense of the dissertation

– The results of the study of the rational technology of extracts from *Scabiosa ochroleuca* L. plant raw materials, the chemical composition and stability of finished products, and the determination of shelf life.

– The results of safety assessment and determination of biological activity of extracts obtained by innovative methods; Technical and economic justification of production of *Scabiosa ochroleuca* L. extract obtained by microwave extraction method and Scabiosa ochroleuca L extract obtained by ultrasonic extraction method.

Description of the main results of the study

The analysis of medicines in the pharmaceutical market of Kazakhstan for 2024 showed dependence on imports. The share of domestically produced products amounted to 14.9% of the total volume of registered medicines. The share of herbal medicines was only 1.44% of the total number of registered medicines, which indicates a decrease in the share of herbal medicines on the market: in 2015, this figure was more than 4%. This may be due to a combination of factors, including a decrease in sales, devaluation of the tenge, and changes in the wishes of producers and consumers.

As a result of determining the component composition of extracts obtained by maceration using six different concentrations of aqueous alcohol solutions from 20% to 70% from the carbon dioxide extraction residue of *Scabiosa ochroleuca* L., it was found that this residue is rich in biologically active substances such as ketones,

pyrimidine derivatives, glucopyranosides, extreme carboxylic acids, essential fatty acids, monosaccharides, phytosterols, and monosaccharides. Among the water-alcohol extracts obtained, alcohol extracted at 70% proved to be the richest in the content of biologically active substances: 11 substances were identified in its composition.

In order to develop an optimal technology for obtaining extracts from the plant *Scabiosa ochroleuca* L., pharmaceutical and technological parameters of raw materials were experimentally determined: specific gravity, bulk density, seed mass, porosity, separability, free volume of the raw material layer, extractant absorption coefficient (for water and 70% ethyl alcohol), average size - 5.5 mm, and absorption coefficient water – 2.87. Alcohol absorption coefficient (for 70% ethyl alcohol) – 2.26. The studied raw materials have high volume characteristics (bulk weight, porosity).

As a result of the study, the technological parameters for the raw materials of *Scabiosa Ochroleuca* L. were established, and the factors ensuring the maximum yield of the amount of flavonoids were selected: A 70% ethyl alcohol solution was used as an extractant, and the degree of grinding of the raw materials was 5 mm, the ratio of raw materials: the extractant is 1:10, the ultrasonic extraction time is 25 minutes at a frequency of 40 kHz (patent for invention No. 34786 dated 12/25/2020), the microwave extraction time is 3 minutes, and the power is 360 Watts (patent for invention No. 34786 dated 12/25/2020). Based on the data obtained, extraction technologies have been substantiated and developed using innovative approaches aimed at intensifying the technological process, which makes it possible to obtain products in two ways with a maximum yield of biologically active substances.

Extracts were obtained from the *Scabiosa ochroleuca* L. herb by maceration with ultrasonic and microwave activation. The Wiley 7th edition and NIST'02 libraries were used to discover the obtained mass spectra (the total number of spectra in the libraries is more than 550 thousand).

As a result, in terms of the number of main compounds identified during the study of the component composition of extracts from *Scabiosa ochroleuca* L. herb, 46 compounds were detected in microwave extraction, and 43 compounds in ultrasonic extraction.

The validation of the method for quantitative determination of catechol and hydroquinone in extracts obtained from the aerial part of *Scabiosa ochroleuca* L. was carried out. The average error of determination of the result is 4.24 ±1.14 % for catechol and 9.96 ±1.09 % for hydroquinone in the ultrasonic extract of *Scabiosa ochroleuca* L.

The microelement composition of the obtained extracts was determined. According to the results of the study, the microelement composition of *Scabiosa ochroleuca* L. extracts was found to contain in large quantities: zinc (10.15 mg/g), copper (3.44 mg/g), and iron (16.95 mg/g) in the ultrasonic extract; manganese (9.20 mg/g), and zinc (9.94 mg/g) in the microwave alcohol extract.

According to the quantitative determination of polyphenols and phenolcarboxylic acids, the highest amount of polyphenols is found in the microwaved alcoholic extract (18.41 %). The ultrasonic extract contains a large

amount of phenolcarboxylic acids, including caffeic acid (9.34 %), and gallic acid (8.50 %), while the microwave extract contains caffeic acid (9.17 %), gallic acid (8.34 %), and chlorogenic acid (6.35 %).

In accordance with the requirements of the Ministry of Health of the Republic of Kazakhstan and the Order of the Minister of Health of the Republic of Kazakhstan dated February 16, 2021 No. DSM-20 RK "On approval of the Rules for coordinating a regulatory document on the quality of medicines developed by a drug manufacturer and with a state expert organization when conducting an examination of medicines", the following quality criteria and permissible limits for Scabiosa ochroleuca L. extracts have been approved: description, identification, dry residue, loss on drying, heavy metals, quantitative determination, packaging, labeling, transportation, storage, shelf life, main pharmacological action. A quality specification for Scabiosa ochroleuca L. extracts has been developed, and a draft regulatory document has been prepared.

Scabiosa ochroleuca L. extracts were subjected to separation with different solvent systems, thin layer chromatography (TLC), and high performance liquid chromatography (HPLC).

As a result of the study, the extracts were separated into five fractions in order to separate different groups of compounds that may have antimicrobial and antioxidant activity: petroleum ether, dichloromethane, ethyl acetate, butanol, and water. By performing thin-layer chromatography on the obtained fractions, we determined that the ethyl acetate and dichloromethane fractions contained more flavonoids.

The ethyl acetate and dichloromethane fractions of extracts from *Scabiosa ochroleuca* L. herb were analyzed by high-performance liquid chromatography (HPLC). The standard samples for the determination of flavonoids and phenolic carboxylic acids in the extract were catechin, naringin, and gallic acid at a concentration of 0.1 mg/ml (analytical standard, Sigma-Aldrich, USA).

Thus, during the study of the ethyl acetate and dichloromethane fractions of *Scabiosa ochroleuca* L. extracts by high-performance liquid chromatography, it was found that the ethyl acetate fraction contained catechin (0.51 % in microwave and ultrasonic extraction) and naringin (1.27 % in microwave extraction, 1.30 % in ultrasonic extraction) in the highest concentration.

During the long-term (24 months) study of the shelf life of *Scabiosa ochroleuca* L. extracts, their quantitative and qualitative indicators, microbiological purity were within the limits of the norm. No significant changes were observed in the monitored research parameters. The results obtained allow us to determine the shelf life of 2 years at a temperature of 25±2 °C and a relative humidity of 60±5 %.

A technological scheme for obtaining thick extracts by maceration using ultrasound and microwave activation has been developed. At all stages of production, additives and materials, intermediates, packaging materials, instructions for use, boxes, and labels were monitored for compliance with the requirements of regulatory documents.

A full-scale validation of the technological process for obtaining extracts from *Scabiosa ochroleuca* L. raw materials confirmed the stability and repeatability of the

process, as well as the successful transfer of technology to the scale of the pilot production series of the pharmaceutical enterprise LLP "PLP "ZHANAFARM.".

A feasibility study was conducted to confirm the possibility of producing extracts of *Scabiosa ochroleuca* L. on an industrial scale. The minimum estimated price for 10,000 vials: for ultrasonic extraction – 10,308,792 tenge. The minimum estimated price for a bottle is 1030 tenge, and for microwave extraction – 10,755,900 tenge. The minimum estimated price per bottle was 1,075 tenge. The return on investment is 1 year and 9 months.

The study of acute, chronic toxicity, and allergenic properties of the extract of the pale yellow scabious herb was conducted in the vivarium of B.A. Atchabarov Institute of Fundamental and Applied Research. As a result of the study, it was found that when an extract from the pale yellow scabious herb (*Scabiosa ochroleuca* L.) was injected into the root of the tongue of outbred white mice using a special syringe at a dose of 500, 2000, and 5000 mg/kg, no death of animals was recorded, motor activity, dyspeptic manifestations were not noted, they did not lose weight, and all reflexes have been saved. When observing the skin reaction, no reaction and pronounced erythema were observed. During the study, laboratory mice were constantly monitored. Their activity, uniform, shiny hair growth, and even care of trimmed sides are noted. The permissible dose of *Scabiosa ochroleuca* L. extract, applied topically, did not cause skin irritation. The results of macroscopic visual and histological microscopic studies of the internal organs of laboratory animals have shown that the studied extract does not cause general pathological and specific destructive changes in animal organs and tissues.

The results of studies conducted on sterile white mice showed that the extract from the herb *Scabiosa ochroleuca* L. It has no toxic effect on the animal body and is not harmful. LD_{50} was calculated using the Kerber method. According to the classification of Hodge and Sterner and K.K. Sidorov, LD_{50} >5000 mg/kg belongs to practically non-toxic drugs, class 5 compounds.

The cytotoxic activity of *Scabiosa ochroleuca* L. extracts on the *Artemia Salina* L. (*Branchiopoda Crustacea*) test object was studied using a technique based on determining the difference between the test sample and dead Artemia larvae in water purified from toxic substances (control). As a result of the conducted research, it was found that extracts of the herb *Scabiosa ochroleuca* L. concentrations of 10, 5, and 1 mg/ml did not have a significant cytotoxic effect on Artemia salina larvae in all samples.

The total amount of antioxidants in *Scabiosa ochroleuca* L. extracts was determined by the amperometric method. As a result, the largest amounts of water-soluble antioxidants were obtained for ultrasonic and microwave extraction (190.64 mg/100 g and 239.78 mg/100 g, respectively), and the largest amounts of fat-soluble antioxidants were obtained for ultrasonic extraction (30.42 mg/100 g) and microwave extraction (33.79 mg/100 g).

Studies have shown that extracts of *Scabiosa ochroleuca* L exhibit significant antiradical activity, which is confirmed by the generally accepted DPPH method. The extracts obtained by microwave and ultrasound methods showed moderate activity at concentrations of 0.1 and 0.25 mg/ml, higher than average activity at

concentrations of 0.5 mg/ml, and very high activity was observed at concentrations of 0.75 and 1 mg/ml. To further evaluate the antioxidant activity of the extracts, the FRAP method was used, which made it possible to compare the recovery potential of the extracts with ascorbic acid. The highest activity according to this method was shown by the microwave extract at a concentration of 1.0 mg/ml with a result of 1.7701, which is close to the standard value (1.7738). The ultrasound extract also showed a high result (1.7571), which allows it to be considered to have an activity comparable to ascorbic acid. The results obtained indicate the high biological activity of *Scabiosa ochroleuca* L. extracts, which opens up prospects for their further use in the development of effective medicines with antioxidant and antiradical properties.

The correlation coefficient of the antioxidant activity of the extracts was determined by the FRAP method. Thus, the results of the conducted studies allow us to conclude that ultrasonic and microwave alcohol extracts of *Scabiosa oshroleuca* L. have high antioxidant activity, whereas ultrasonic and microwave aqueous extracts of *Scabiosa oshroleuca* L. have low antioxidant activity. The correlation coefficient of the antioxidant activity of *Scabiosa ochroleuca* L. extracts was determined, and all extracts showed a linear relationship.

The research results showed that extracts of *Scabiosa ochroleuca* L. have bactericidal activity against Gram-positive microorganisms (*Staphylococcus aureus* ATCC 6538-P, *Staphylococcus haemophylus, Enterococcus hirae* ATCC 10541, *Streptococcus pneumonia* ATCC 660) and Gram-negative microorganisms (*Escherichia coli* ATCC 8739, *Klebsiella pneumoniae* ATCC 10031, *Pseudomonas aeruginosa* ATCC 9027, *Acinetobacter baumannii* ATCC 1790), as well as fungicidal activity against *Candida albicans* ATCC 10231, *Candida utilis*.

Scientific novelty of the study

For the first time, during the extraction and research of extracts from the herb *Scabiosa ochroleuca* L.*,* it was found that:

– Extracts were obtained from *Scabiosa ochroleuca* L. herb using microwave and ultrasound methods;

– The component composition of extracts obtained from *Scabiosa ochroleuca* L. herb using microwave and ultrasound methods was determined;

The safety and specific biological activities of extracts from *Scabiosa ochroleuca* L. herb have been determined.

The scientific novelty of the research was confirmed by the innovative patent for the invention No. 34786 “Method for obtaining an ultrasonic extract from the *Scabiosa ochroleuca* L. herb with antiradical activity” (Appendix A) and the patent for the utility model No. 6401 “Method for obtaining a microwave extract from the *Scabiosa ochroleuca* L. herb with antiradical activity” (Appendix B).

The practical significance of the work and implementation of research results into practice.

Laboratory regulations for the extract of *Scabiosa ochroleuca* L obtained by the method of ultrasonic extraction and the extract of *Scabiosa ochroleuca* L obtained by the method of microwave extraction, and the quality specification of the finished products have been developed (Appendix B, Appendix G, Appendix D,

Appendix E).

Innovative methods of obtaining extracts with full release of biologically active substances with microwave exposure have been introduced into production on the basis of PLP «ZHANAFARM» LLP» (Appendix ZH).

The results of scientific research on extracts from the medicinal plant Pale yellow scabious (*Scabiosa ochroleuca* L.) were introduced into the educational process of the Kazakh National Medical University, named after S.Zh. Asfendiyarov (Appendix I), Karaganda Medical University (Appendix K), and the «Bolashaq» Academy (Appendix L).

Personal contribution of the doctoral student

Research on the implementation of the set goals and objectives was carried out by the doctoral student herself, independently processed the obtained results, carried out work on publishing scientific articles and wrote the dissertation.

Conclusions

1.1 In 20%, 30%, 40%, 50%, 60%, and 70% water-alcohol extracts from the residue of carbon dioxide extraction of the herb *Scabiosa ochroleuca* L. ketones, pyrimidine derivatives, glucopyranosides, saturated carboxylic acids, saturated fatty acids, monosaccharides, phytosterols, and monosaccharides were determined. Among the water-alcohol extracts obtained, alcohol extracted at 70% proved to be the richest in the content of biologically active substances: 11 substances were identified in its composition.

1.2 In order to develop an optimal technology for obtaining extracts from the *Scabiosa ochroleuca* L. herb, the pharmacological and technological characteristics of the raw materials were determined, and their quantitative values were determined as well. The conditions and parameters of the extraction of the herb *Scabiosa ochroleuca* L. have been determined. Using ultrasonic activation: extractants – 70% alcohol, purified water, and sunflower oil; ultrasonic activation power – 40 kHz; extraction duration – 25 minutes. The conditions and parameters of the extraction of the herb *Scabiosa ochroleuca* L. have been determined by the method of microwave activation: extractants – 70% alcohol, purified water, and sunflower oil, microwave activation power – 360 W, extraction time – 3 minutes.

2.1 The main compounds identified during the study of the component composition of extracts from the *Scabiosa ochroleuca* L. herb: 43 compounds in ultrasonic alcohol extraction, including: L-lactic acid (27.98%), succindialdehyde (5.37%), 4H-pyran-4-one, 2,3-dihydro-3,5-dihydroxy-6-methyl- (3.69%), heptanic acid, 7-chloro-7-oxo, ethyl ether (16.33%), 9-oxabicyclo [3.3.1]nonan-2,6-diol (4.93%), quinic acid (16.20%); The microwave alcohol extract contained 46 compounds, including: L-lactic acid (25.15%), 1,2-cyclopentanedione (3.11%), tributyl phosphate (6.46%), heptanic acid, 7-chloro-7-oxo, ethyl ether (22.12%), 9-oxabicyclo [3.3.1]nonan-2,6-diol (3.08%), quinic acid (10.83%). Among the identified components in the extracts obtained by ultrasonic extraction, acids prevailed – 14.6%, ketones – 56%, phenols – 5%, aldehydes – 5.9%, terpenoids – 3.6% and esters – 18.3%. In turn, extracts obtained by microwave extraction contain 38% acids, 11.5% ketones, 4.8% phenols, no aldehydes, 5% terpenoids and 30.5% esters.

2.2 Extracts of *Scabiosa ochroleuca* L. were studied using high-performance liquid chromatography (HPLC) to determine the profile of flavonoid compounds. Naringin and catechin made the greatest contribution. 1.27% naringin and 0.051% catechin were found in microwave extracts, and 1.30% and 0.051%, respectively, were found in ultrasonic extracts.

3.1 A rational technology for obtaining extracts from raw materials of *Scabiosa ochroleuca* L. has been developed: a technological scheme of production is presented, and a description of the technological process is given.

A full-scale validation of the technological process for obtaining extracts from raw materials of *Scabiosa ochroleuca* L. confirmed the stability and repeatability of the process, as well as the successful transfer of technology to the production and pilot scale of the pharmaceutical enterprise LLP "PLP "ZHANAFARM".

3.2 As a result of the feasibility study for the production of extracts from raw materials of *Scabiosa ochroleuca* L. the cost of production, wholesale price, and profitability of the project were calculated, and a feasibility study was developed: the minimum estimated price for 10,000 bottles is 10,308,792 tenge. The minimum estimated price per bottle is 1030 tenge, and the payback period for production is 1 year and 9 months.

4.1 The quality indicators of concentrated extracts obtained from the Scabiosa ochroleuca L. herb and the criteria for their usefulness have been established. The quality specification of extracts from *Scabiosa ochroleuca* L. was developed based on the following indicators: description, identification, dry matter, weight loss during drying, heavy metals, microbiological purity, quantification, packaging, labeling, transportation, shelf life, and main pharmacological effects.

4.2 During the long-term study period (24 months), the shelf life of extracts from *Scabiosa ochroleuca* L. qualitative and quantitative indicators, microbiological purity were within the established standards. There were no significant changes in the controlled quality indicators. The obtained results allowed us to determine the shelf life of 24 months at a temperature of +15 °C - +25 °C and a relative humidity of 60±5 %.

5.1 Extracts of *Scabiosa ochroleuca* L. are recognized as safe and non-irritating. As a result of the study, no allergic reactions were detected on the skin area where an oil solution of *Scabiosa ochroleuca* L. herb extract was used.

Extracts of *Scabiosa ochroleuca* L. are recognized as safe and non-irritating. According to the classification of Hodge and Sterner and K.K. Sidorov, LD_{50}>5000 mg/kg allows it to be classified as practically non-toxic drugs, to class 5 compounds, and according to the danger of the extract, to class IV "Low-risk substances" (GOST 12.1.007-76 "Occupational Safety Standards System. Harmful substances").

Macroscopic visual and histological microscopic studies have shown that extracts from the *Scabiosa ochroleuca* L. herb do not cause general pathological and specific destructive changes in the organs and tissues of laboratory animals; therefore, the extracts studied confirm that they do not have a toxic effect on the bodies of experimental animals.

As a result of the conducted research, it was found that extracts of the *Scabiosa ochroleuca* L. herb in concentrations of 10, 5 and 1 mg/ml did not have a cytotoxic effect on the larvae of *Artemia salina* in all samples.

Extracts from the herb *Scabiosa ochroleuca* L. belong to the group of practically non-toxic medicines, therefore, the possibility of being recommended for clinical studies with the aim of presenting them as a substance for pharmaceutical production has been proven.

5.2 The total amount of antioxidants in extracts from *Scabiosa ochroleuca* L was determined by the amperometric method, as a result of which the highest values of the total content of water–soluble antioxidants and the highest values of the total content of fat-soluble antioxidants (mg/100 g) were typical for alcoholic microwave extracts - 239.78 mg/100 g and 33.79 mg/100 g, respectively.

The correlation coefficient of the antioxidant activity of the extracts was determined using the FRAP method, and it was proved that a linear relationship is observed in all extracts. The highest activity according to this method was shown by the microwave extract at a concentration of 1.0 mg/ml with a result of 1.7701, which is close to the standard value (1.7738). The ultrasound extract also showed a high result (1.7571), which allows it to be considered to have an activity comparable to ascorbic acid.

5.3 Studies have shown that extracts of *Scabiosa ochroleuca* L. exhibit significant antiradical activity, which is confirmed by the generally accepted DPPH method. The extracts obtained by microwave and ultrasound methods showed moderate activity at concentrations of 0.1 and 0.25 mg/ml, higher than average activity at concentrations of 0.5 mg/ml, and very high activity was observed at concentrations of 0.75 and 1 mg/ml.

5.4 As a result of the conducted studies, the bactericidal activity of *Scabiosa ochroleuca* L. extracts was determined against Gram-positive microorganisms (*Staphylococcus aureus* ATCC 6538-P, *Staphylococcus haemophylus, Enterococcus hirae* ATCC 10541*, Streptococcus pneumonia* ATCC 660) and Gram-negative microorganisms (*Escherichia coli* ATCC 8739, *Klebsiella pneumoniae* ATCC 10031, *Pseudomonas aeruginosa* ATCC 9027, *Acinetobacter baumannii* ATCC 1790), as well as fungicidal activity against *Candida albicans* ATCC 10231, *Candida utilis*.

Approbation of work

The main provisions of the dissertation work were outlined and published in the materials of international scientific conferences:

– “Prospects for the Development of Biology, Medicine and Pharmacy” (organized by the Foundation of the First President of the Republic of Kazakhstan
– Elbasy and the South Kazakhstan Medical Academy for Young Scientists and Students, Shymkent, 2018);
– “Pharmacy and the social policy of the state” (Dushanbe, 2019);
– “Global Science and Innovation 2020: Central Asia” (Nur-Sultan, 2020).
– Presented at the Department of Pharmaceutical Technology of the Kazakh National Medical University named after S.Zh. Asfendiyarov (Almaty, 2024), at the

Scientific Committee of the School of Pharmacy of the Kazakh National Medical University named after S.Zh. Asfendiyarov (Almaty, 2024).

Information about publications

Based on the results of the dissertation research, 13 scientific papers were published, including:

– Articles in international peer-reviewed scientific journals indexed in Scopus and Web of Science Core Collection databases – 2;

– Articles in journals recommended by the Committee for Quality Assurance in the Field of Education and Science of the Ministry of Science and Higher Education of the Republic of Kazakhstan - 6;

– Abstracts and articles at international scientific and practical conferences (Kazakhstan, Tajikistan) - 3;

– 1 patent for an invention and 1 patent for a utility model.

Thesis scope and structure

The dissertation is typed on 166 pages of typewritten text, contains 48 tables, 58 figures, a bibliography including 123 sources, as well as 11 appendices. The work consists of an introduction, a literature review, a section on research materials and methods, as well as four sections of individual studies, and conclusions.