

ANNOTATION

of dissertation work on the topic: "**Development of a technology for a novel medicinal product based on *Xanthium strumarium* L. (common cocklebur) native to Kazakhstan and its standardization**" for the degree of Doctor of Philosophy (PhD) in the educational program 8D07201 - "Technology of Pharmaceutical Production"

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Relevance of the research topic. The relevance of the research problem addressed in this dissertation lies in its focus on providing the population of the Republic of Kazakhstan with high-quality, effective, and affordable domestically produced medicinal products, which represents an important priority of the pharmaceutical industry.

In accordance with the Address of the Head of State to the people of Kazakhstan "Kazakhstan in New Conditions: Time for Action", the National Development Plan of the Republic of Kazakhstan until 2025, the Order 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 Decree of the Government of the Republic of Kazakhstan "On the Concept for the Development of the Manufacturing Industry for 2023–2029", the importance of developing domestic medicinal products based on medicinal plants growing in the territory of Kazakhstan is increasing.

This also includes the development of a pharmaceutical cluster through enhancing the competitiveness of domestic products and promoting them to international markets.

In this regard, the search for approaches enabling more comprehensive utilization of wild-growing and cultivated plant resources and the creation of original phytomedicines based on them is highly relevant.

Plants of the *Asteraceae* Dumort. family are of significant scientific interest due to the presence of biologically active compounds in their chemical composition, which provide a wide spectrum of pharmacological activity. One such plant is common cocklebur (*Xanthium strumarium* L.). Currently, about 25 species of this genus are known, and the plant is widely used in folk medicine in many countries as medicinal raw material.

Common cocklebur grows as a weed throughout the world, except for the Far North regions. Its native areas include Europe, Asia, and North America, from where it spread to Africa, Australia, South America, India, China, Indonesia, and Malaysia. Two species of cocklebur are found in Kazakhstan. The most widespread, especially in southern regions, are common cocklebur or glandular cocklebur (*Xanthium strumarium* L.) and spiny cocklebur (*Xanthium spinosum* L.).

The chemical composition of *Xanthium strumarium* L. includes numerous classes of compounds such as mono- and sesquiterpenoids, di- and triterpenoids,

steroids, phenylpropanoids, coumarins, flavonoids, higher fatty acids, vitamins, nitrogen-containing compounds, and tannins. The most characteristic substances with antioxidant and anti-inflammatory activity are alkaloids, polyphenols, terpenoids, and flavonoids.

Due to the high content of vitamin C and iodine, the studied plant species are used in folk medicine to stop bleeding and treat colds and thyroid diseases. The presence of sufficient amounts of the phenylpropanoid ursolic acid and the sesquiterpenoid caryophyllene exerts an inhibitory effect on the growth and spread of various types of cancer.

Treatment of periodontal diseases is carried out using application dosage forms such as tampons, ointments, and solutions applied to medicinal carriers. However, due to uneven contact with mucous membranes and rapid reduction of drug concentration at the site of application, these dosage forms are often ineffective. Considering these shortcomings, the development of dental films appears promising to improve contact at the site of inflammation.

In this context, the development of new medicinal products from *Xanthium strumarium* L. raw material growing in Kazakhstan to expand the range of dental products is promising and scientifically justified for the pharmaceutical industry of the Republic of Kazakhstan.

The purpose of scientific research. To develop a technology for obtaining a substance and a dental film based on *Xanthium strumarium* L. raw material and to perform their standardization.

Objectives of study:

1. To conduct a pharmacognostic study of *Xanthium strumarium* L. herb.
2. To establish optimal extraction parameters for obtaining a thick extract of common cocklebur under ultrasonic activation conditions.
3. To perform pharmacological activity screening and select promising samples of thick extract of *Xanthium strumarium* L. for the development of a new medicinal product.
4. To develop the composition and technology of a finished dosage form based on the thick extract of *Xanthium strumarium* L.

Research methods: Pharmacopoeial, pharmacological, and biological methods.

Objects of study:

1. A sample of common cocklebur raw material collected during the fruiting phase in the vicinity of Baskunchi village, Panfilov district, Almaty region. Collection period: August–September 2022. Coordinates: 44°20'26" N, 80°22'56" E.
2. A sample of common cocklebur raw material collected in Agadyr settlement, Shet district, Karaganda region. Collection period: August–September 2022. Coordinates: 48°24'49" N, 72°83'75" E.

Subject of study: resource data, biomorphological features, diagnostic characteristics, and quantitative indicators of *Xanthium strumarium* L. herb raw material; thick extract obtained using ultrasonic exposure; chemical composition and

biological activity of the thick extract; biological activity of dental films prepared based on *Xanthium strumarium* L.; development of regulatory documentation; and compilation of final materials determining the theoretical and practical significance of the dissertation.

The main provisions for defense:

- Results of pharmacognostic analysis of *Xanthium strumarium* L. raw material growing in Kazakhstan and draft regulatory documentation;
- Method for obtaining thick extract from *Xanthium strumarium* L. raw material using ultrasonic exposure and results of its component analysis;
- Results of selecting an effective thick extract sample based on pharmacological activity screening (antimicrobial, anti-inflammatory, and antioxidant);
- Development of a medicinal product composition in the form of dental films based on plant extract with therapeutic effect;
- Results of pharmacological activity studies of the developed dental film.

Scientific novelty of the research

- For the first time, a pharmacognostic analysis and quality assessment of *Xanthium strumarium* L. medicinal plant raw material growing in Kazakhstan were conducted, and draft regulatory documentation was developed;
- For the first time, raw material reserves of *Xanthium strumarium* L. herb in Kazakhstan were assessed;
- For the first time, a method for obtaining *Xanthium strumarium* L. extracts using ultrasound was developed;
- For the first time, antimicrobial, anti-inflammatory, and antioxidant activity of thick extracts obtained by ultrasonic method was studied;
- For the first time, a new medicinal product in the form of a dental film based on thick extract of *Xanthium strumarium* L. was developed;
- For the first time, quality control methods, shelf life, and storage conditions of the developed medicinal product were established.

The scientific novelty is confirmed by a utility model patent of the Republic of Kazakhstan No. 9875 dated 15.08.2025 entitled “Use of *Xanthium strumarium* L. (common cocklebur) as an antimicrobial agent.”

Practical significance of the obtain results

As a result of the conducted studies, raw material reserves of *Xanthium strumarium* L. herb in Kazakhstan were determined.

A technology for harvesting plant raw materials of *Xanthium strumarium* L. has been developed, along with quality specifications and draft regulatory documentation. Using ultrasonic treatment, an extract based on *Xanthium strumarium* L. was obtained, and its chemical composition was determined and standardized. A dental film was developed based on the thick extract of common cocklebur (*Xanthium strumarium* L.). Acute toxicity studies established the absence of toxic properties in the thick extract; it was also evaluated for anti-inflammatory, antioxidant, and antimicrobial activities. Based on the research results, laboratory regulations and draft regulatory documentation were developed for the *Xanthium*

strumarium L. herb, the thick extract substance obtained by the ultrasonic method, and the films based on the cocklebur extract. The technological process for obtaining extracts of *Xanthium strumarium* L. via the ultrasonic method has been integrated into the educational programs of the School of Pharmacy at the NJSC "Karaganda Medical University," the Faculty of Biology and Geography at the NJSC "Karaganda Buketov University," and the Department of Pharmacognosy and Botany at Bashkir State Medical University.

Personal contribution of a doctoral student

All experimental results in the dissertation were obtained by the author, demonstrating their personal contribution to pharmaceutical production technology. The author investigated the anatomical and morphological traits of *Xanthium strumarium* L., created and analyzed ultrasonic extracts using ethanol and water via HPLC-MS, and developed extraction methods. Samples were screened for antimicrobial, anti-inflammatory, and antioxidant activity. Laboratory standards for the substance and dosage form were established, and results were statistically processed.

Conclusions

The dissertation is devoted to the development of a technology for a new medicinal product with antimicrobial, anti-inflammatory, and antioxidant activity based on *Xanthium strumarium* L.

1. The study of the distribution of raw material resources and the assessment of their utilization potential demonstrated that *Xanthium strumarium* L. herb is a renewable source of plant raw material for the production of medicinal products. Due to the polymorphism of the species, a pharmacognostic study of *Xanthium strumarium* L. herb collected in the territory of Kazakhstan was conducted, and diagnostic anatomical and morphological characteristics were established. The diagnostic features of common cocklebur raw material include the shape and structure of epidermal cells of leaves and fruits, petioles, roots, and seeds; the localization of essential oil glands and trichomes; the anatomical structure of leaves, stems, petioles, and roots in cross-section; and the shape of vascular bundles. The established numerical quality indicators of *Xanthium strumarium* L. plant raw material were included in the draft regulatory documentation.

2. For the first time, a technology for obtaining a thick extract of *Xanthium strumarium* L. was developed, and its quality parameters were investigated. A relatively maximum extract yield was achieved by double extraction of air-dried raw material with 70% ethanol under ultrasonic irradiation at a frequency of 40 kHz for 30 minutes. The main components of the extract were identified as monoterpenes (camphor 5.66%, borneol 3.39%, 1,8-cineole 2.27%, α -terpineol 1.95%, nerol 1.40%), the sesquiterpene lactone caryophyllene, xanthotoxin, flavonoids (hyperoside 6.5 mg/g, quercetin 2.98 mg/g), and phenolic compounds (gallic acid 7.23 mg/g, caffeic acid 1.40 mg/g, chlorogenic acid 4.21 mg/g, p-coumaric acid 6.38 mg/g, and rosmarinic acid 1.21 mg/g). A laboratory production protocol for the thick extract of *Xanthium strumarium* L. raw material was developed. The shelf life of the thick extract of common cocklebur was determined to be 24 months. Screening of the biological activity of *Xanthium strumarium* L. extracts obtained by different

methods revealed that the thick extract obtained by extraction with 70% ethanol under ultrasonic cavitation exhibited pronounced antimicrobial, anti-inflammatory, and antioxidant activity.

3. For the first time, an optimal composition of dental phytofilms was developed:

- the composition of active and excipient substances for the preparation of dental films was selected;
- a rational formulation and manufacturing technology of dental films were experimentally substantiated; formulation No. 7 was identified as a homogeneous, smooth, yellow-colored film with a specific odor. The pH of the aqueous solution of the film ranged from 5.5 to 6.8, which corresponds to acceptable physical and technological parameters;
- the physicochemical and biopharmaceutical properties of the obtained films were determined. The quality assessment of dental phytofilms was carried out according to the following criteria: organoleptic properties, pH value, quantitative content of ascorbic acid, dissolution and retention time, elasticity, adhesion, and moisture absorption;
- a method for the quantitative determination of active substances in dental films using HPLC was developed, enabling quality control during phytofilm production and ensuring the safety of the finished dosage form;
- a laboratory production protocol and quality specification for dental films were developed.

4. A feasibility study was developed for the production of an antimicrobial, anti-inflammatory, and antioxidant medicinal product based on the thick extract of *Xanthium strumarium* L.

Approbation of the results of the dissertation

The results and main provisions of the scientific research were presented at the following scientific events:

1. IX International Scientific Conference of Young Scientists and Students “Prospects for the Development of Biology, Medicine, and Pharmacy” (Kazakhstan, Karaganda, 2022);
 2. XV International Scientific and Practical Conference “Current Issues of Ecology” (Kazakhstan, Karaganda, 2023);
 3. International Scientific Conference “Actual Problems of the Chemistry of Natural Compounds” (Tashkent, Uzbekistan, 2023);
 4. XX Scientific and Practical Conference of Young Scientists and Students with International Participation “Intellectual Technologies in Medical Education and Science: Innovative Approaches” (Tajikistan, 2025);
 5. International Biomedical Forum: Research and Innovations (Kazakhstan, Karaganda, April 17–18, 2025).
- A certificate of participation was obtained for this conference.

Publications

The main results are reflected in 10 publications, including 1 patent, 2 national journals, 2 Scopus-indexed journals, and 5 conference proceedings.

Scope and structure of the dissertation

The dissertation comprises 149 pages, including 45 tables, 38 figures, 159 references, and 18 appendices. It consists of seven sections: introduction, literature review, materials and methods, experimental studies, and conclusion.