

ANNOTATION

of the dissertation work on the topic «**Theoretical and experimental substantiation of the creation and standardization of a cosmetic product with antioxidant activity**» for the degree of Doctor of Philosophy (PhD) on specialty 8D10102 – «Pharmacy»
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Relevance of the research topic.

Strengthening the health of the population is a priority within the framework of the national project "High-quality and affordable healthcare for every citizen "Healthy Nation". Increasing the pace of the domestic pharmaceutical industry, including the perfumery and cosmetics industry, remains an urgent problem, since import dependence, expressed by the share of domestic production of cosmetic products, is 93.3%. Thus, the domestic production of perfumes and cosmetics, according to the Agency for Statistics of the Republic of Kazakhstan, is less than 10% of total consumption. In recent years, the demand for cosmetic products containing components of natural origin has been rapidly increasing. At the same time, cosmetic products should not only have a quick effect (softening, moisturizing), in the case of decorative cosmetics (giving a certain color, tone and masking skin imperfections), but also have an attractive appearance, and also contain substances with various functional properties (antioxidant activity, stimulation of collagen synthesis, etc.).

The production of a full cycle of perfumery and cosmetic products, carried out in accordance with the requirements of good GACP and GMP practices, will ensure the consistency and uniformity of product quality.

In recent years, the Republic of Kazakhstan has seen the active formation and development of such a field of activity as cosmetology. Aesthetic medicine centers providing cosmetology services have formed a solid cluster of small and medium-sized businesses. The increase in consumption of such products by the population should develop the domestic market, which includes both an increase in turnover and an expansion of the product range. At the same time, there is a tendency to develop original formulations of perfumery and cosmetic products using local vegetable raw materials, due to the introduction of achievements of modern pharmaceutical science and new production technologies.

To create original perfumery and cosmetic products, plants, including those growing on the territory of Kazakhstan, for example, a plant of the species *Ceratocarpus arenarius* L. from the Chenopodiaceae family, are a promising source of biologically active substances. Many plants from the Chenopodiaceae family show antioxidant activity, have anti-inflammatory, antimicrobial effects.

This work is devoted to the study of the properties of the widespread but little-studied plant *Ceratocarpus arenarius* L., the antioxidant properties of plant raw materials, and the development of drugs with antioxidant activity. In the future, the creation of methodological approaches to the development of a cosmetic product with antioxidant activity for the prevention of premature skin aging.

Anti-age is a medical field designed to improve the quality of life and prolong youth. The relevance of the research topic lies in the search for active ingredients of natural origin and the improvement of the technology for obtaining a cosmetic product with antioxidant activity.

Purpose of the dissertation research:

Ceratocarpus arenarius L. development and standardization of a therapeutic and cosmetological agent with an antioxidant effect based on a pharmaceutical substance from plant raw materials

Objectives of the research:

-conducting pharmacognostic analysis and standardization of plant raw materials *Ceratocarpus arenarius* L.;

- obtaining extracts from plant raw materials *Ceratocarpus arenarius* L. and comparative study of antioxidant activity;

-pharmacological research and standardization of *Ceratocarpus arenarius* L. extract;

- development of the optimal composition and technology of the cream from *Ceratocarpus arenarius* L. extract;

- determination of the antioxidant activity and locally irritating effect of the cream with *Ceratocarpus arenarius* L. extract.;

- standardization and determination of the stability of a cream based on *Ceratocarpus arenarius* L. extract.

Objects of research: raw materials *Ceratocarpus arenarius* L., thick extract, antioxidant cream.

Methods of research: pharmacopoeial and non-pharmacopoeial methods (physical, physico-chemical, pharmacognostic, pharmaceutical-technological, pharmacological, biological, information-analytical and statistical).

Subject of study: the distribution area of medicinal plant raw materials *Ceratocarpus arenarius* L., determination of pharmacognostic features; development of optimal technology for obtaining extracts and its standardization; determination of antioxidant activity and pharmacological action of an extract from *Ceratocarpus arenarius* L.; development of technology for obtaining an antioxidant cream based on a thick extract of *Ceratocarpus arenarius* L. and its standardization.;

Scientific novelty:

For the first time in Kazakhstan:

- pharmacognostic analysis and standardization of the little-studied medicinal plant raw materials *Ceratocarpus arenarius* L. was carried out;

- extracts from medicinal plant raw materials *Ceratocarpus arenarius* L. were obtained by vortex and ultrasonic extraction methods;

- the chemical composition of the extracts was determined by modern physico-chemical methods (TLC, GC-MS, HPLC) and antioxidant activity, cytotoxicity, preclinical effects were studied. The extract obtained by ultrasonic extraction, which showed high antioxidant activity, was optimal.

The scientific novelty of the study was confirmed by the patent for the invention of the RSE "National Institute of Intellectual Property" dated 06/09/2023,

registration number No.36158 "Method for obtaining an extract from medicinal plant raw materials of *Ceratocarpus arenarius* L. with antioxidant activity".

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

- Results of pharmacognostic research of medicinal plant raw materials *Ceratocarpus arenarius* L.;
- Results of technology for obtaining extracts from plant raw materials *Ceratocarpus arenarius* L.;
- results of antioxidant, cytotoxic activity and non-clinical studies of extracts from plant raw materials *Ceratocarpus arenarius* L.;
- composition and technology of preparation of cream obtained on the basis of a thick extract of *Ceratocarpus arenarius* L.

Practical significance of the research:

- the technology of collecting and harvesting plant raw materials *Ceratocarpus arenarius* L. was proposed. Identification certificate No.01-09/305 was received from at the Institute of Botany and Phytointroduction of the Science Committee of the Ministry of Education and Science of the Republic of Kazakhstan (Appendix A);
- a regulatory document project has been developed for an antioxidant cream from *Ceratocarpus arenarius* L. extract at NPP Antigen LLP (Appendix B);
- the optimal technology for obtaining an antioxidant cream from *Ceratocarpus arenarius* L. extract has been introduced in NPP Antigen LLP (Appendix D);
- a method for obtaining a thick extract by ultrasonic extraction methods from plant raw materials *Ceratocarpus arenarius* L. implemented at the Department of Pharmaceutical Technology of the non-profit joint-stock company "KazNMU named after S. D. Asfendiyarov" (Appendix D);

Author's personal contribution.

On the topic of the dissertation work, the dissertation conducted an independent review and analysis of domestic and foreign literature, carried out practical work on all the tasks set. This is confirmed by the results of studies obtained in laboratory and production conditions using modern equipment and literature.

The reliability and validity of the research results is confirmed by the focus on solving the actual problem of the work performed, the implementation of regulatory documents in a modern research center and projects.

Conclusions:

1. A pharmacognostic analysis was performed on the plant raw materials of *Ceratocarpus arenarius* L. :
 - leaves, stem, root were identified by anatomical and morphological features;
 - according to the results of quantitative analysis, flavonoids (3.7%), alkaloids (1.11%), saponins (1.53%), coumarins (0.08%), organic acids (2.18%), polysaccharides (2.18%), ascorbic acid (0.20%) were determined; according to the mineral composition - 4 macronutrients (Ca, Mg, Na, K), 4 trace elements (Mn, Cu, Zn, Fe) and 1 conditional trace element (N); 20 amino acids and 8 fatty acids have been identified;

-pharmacopoeial numerical indicators of raw materials were determined (humidity - 6.8%, total ash -5.9%, organic additives - 0.5%, mineral additives - 0.025%, insoluble ash in hydrochloric acid - 0.28%) and pharmaceutical and technological parameters;

-quality indicators have been determined and a quality specification for *Ceratocarpus arenarius* L. has been developed.. The results of a long-term study of the stability of medicinal raw materials *Ceratocarpus arenarius* L. at a temperature of $(25 \pm 2) ^\circ \text{C}$ and relative humidity $(60 \pm 5)\%$ allowed us to set its shelf life at 24 months.

2. An optimal technology has been developed for the production of extracts from *Ceratocarpus arenarius* L. by vortex and ultrasonic extraction methods in order to isolate natural antioxidants from raw materials:

- the component composition of the extracts was studied by GC-MS method;

-the antioxidant activity of the extracts was comparatively evaluated by DPPH and FRAP methods. The thick extract obtained by ultrasonic extraction methods has the greatest ability to inhibit the DPPH radical and reduce the Fe^{3+} iron ion to the Fe^{2+} iron ion. Validation for the DPPH analysis method was performed;

- flavonoid compounds of the thick extract were studied by TLC and HPLC methods. As a result, the content of catechin belonging to the flavonoid class was 3.08%

- the assessment of acute, subacute toxicity and cytotoxic activity of the thick extract was carried out;

- a specification of the quality of a thick extract obtained by ultrasonic extraction has been developed: description, identification of catechin, mass consumption during drying, heavy metals, microbiological purity, quantitative determination of catechin, packaging, transportation, storage, shelf life, main pharmacological effects. In three series at a temperature of $(25 \pm 2) ^\circ \text{C}$ and $(60 \pm 5)\%$ relative humidity, the shelf life is set for 2 years during long-term tests;

3. The composition and technology of an antioxidant cream with a thick extract of *Ceratocarpus arenarius* L. has been developed.:

- the optimal composition and technology for producing the cream has been selected, which includes: a thick extract of *Ceratocarpus arenarius* L. obtained by ultrasonic extraction (2.0), base - mineral oil

(8.0), emulsifier – stearic acid (1.0), Twin 80 (1.0), glycerin monostearate (2.0), thickener-cetearyl alcohol (1.0), triethanolamine – (0.5), glycerin (2.0), solvent - purified water (up to 100). A quality specification of a cream with 2% thick extract of *Ceratocarpus arenarius* L. has been developed.

- the antioxidant activity of the cream and the local irritant effect have been studied;

- a quality specification of a cream based on a thick extract of *Ceratocarpus arenarius* L. has been developed.. The evaluation of the physico-chemical parameters of the cream was carried out: determination of the type of cream, washability, hydrogen index, dispersion analysis, colloidal and thermal stability, rheological properties. Long-term stability test at temperature $(25 \pm 2) ^\circ \text{C}$ and

relative humidity (60 ± 5)% pH, the microbiological purity of the cream are within acceptable limits. The shelf life of the cream is 18 months

Approbation of the results of the dissertation:

The main results of the dissertation research were published and reported in the materials of: The International Scientific and Practical Conference dedicated to the memory of Professor R. Dilbarkhanov "Formation and prospects for the development of the scientific school of pharmacy: succession of generations" (Almaty, 2020, 2021), the IV international scientific and practical conference, "The current state of the pharmaceutical industry: Problems and prospects" (Tashkent, Uzbekistan, 2023), "Asfen.forum, New Generation-2023" I International Forum (Almaty, 2023).

Publications:

The results of the dissertation research have been published in 8 scientific papers, including:

- article in Scopus journal, included in the international database - 1;
- in publications recommended by the Ministry of Education and Science of the Republic of Kazakhstan, the Committee for Control in the Field of Education and Science - 3;
- abstracts and articles in the materials of the international scientific and practical conference -3;
- patent for invention -1.

Scope and structure of the dissertation:

The dissertation work includes 166 pages of machine text, 56 tables, 56 figures, 231 domestic and foreign literature, as well as appendices. The work consists of an introduction, a literary review, materials and methods, 4 sections of the experimental part, conclusions by sections and conclusions.