ABSTRACT
of thesis for the scientific degree of Doctor of Philosophy (PhD)
speciality 6D070100 – «Biotechnology»

Kustova Tatyana Sergeevna

"Development of new complexes of herbal remedies for correction of complications of experimental diabetes"

General characteristics of the work.
The work is dedicated to the development of integrated herbal remedies on the basis of biologically active substances of plant, with wound-healing, antimicrobial and other properties for the prevention and treatment of trophic skin lesions typical for diabetes complications.

Urgency of the work.
In recent years there has been an increase in the number of newly registered drugs, but the search and development of domestic drugs remain relevant, among them there are promising drugs of plant. Under the analysis of the situation in the modern pharmaceutical market of Kazakhstan, there is the advantage in favor of expensive imported drugs, on the other hand - do not fully realize the potential use of plants growing on the territory of our Republic, which affects the efficiency of domestic drugs. Herbal remedies have several advantages, lack of side effects and low toxicity for the human body, and they may have a complex effect (antimicrobial, anti-inflammatory, antispasmodic, analgesic, anti-toxic and membrane stabilizing et al.).

Herbal remedies are used in a number of diseases caused by the depletion of endogenous antioxidant defenses, including hormonal and metabolic (exchange) changes caused by diabetes. For the treatment of various diabetic complications, can be used complex herbal medicines with a specific course of action. According to the data, the number of diabetics is growing steadily; the number of newly diagnosed cases is from 6 to 10% of the total number of diabetics, of which the vast majority suffer from type II diabetes (non-insulin dependent). The most significant complication of diabetes is sores (diabetic foot), which are characterized by a long, low intensity and a septic wound.

Thus, the development of efficient systems on the basis of biologically active substances of plant origin, with wound-healing, antimicrobial and other properties for the prevention and treatment of trophic skin lesions typical for diabetes complications, is an urgent task of modern science.

The purpose of research - the creation of new integrated herbal remedies from plants growing on the territory of the Republic of Kazakhstan, with antimicrobial, antioxidant and wound-healing activities.

Research tasks:
– Conduct the extraction of biologically active substances from plant material collected during field expeditions in Almaty and East Kazakhstan regions;
In vitro study of antioxidant, antimicrobial and wound healing activities of the extracts;

Select active extracts with no cytotoxic activity and develop herbal remedies on them;

Study the effect of herbal remedies on the morphometric and microbiological picture of the dynamics of a skin wound in experimental diabetes on rats;

Identification of the active compounds in the extracts, combined to create herbal remedies.

Objects of research: Plants were collected in the expeditionary trips to Almaty and East Kazakhstan regions. Plants belong to different families: Epilobium hirsutum (Onagraceae), Rumex confertus (Polygonaceae), Vexibia alopecuroides (L.) Jakovl. (Fabaceae), Polygonum undulatum Murr. (Polygonaceae), Rhodiola quadrifida (Pall.) Fisch. et Mey. (Crassulaceae), Atraphaxis laetevirens (Ledebe.) Jaub. Et Spach (Polygonaceae), Salvia deserta Schang (Lamiaceae).

Research methods: Microbiological, biochemical, cytological, culture, histological and morphometric techniques.

Scientific novelty of the work: The scientific novelty of the thesis is as follows:

For the first time carried out research work to find plant extracts with high antimicrobial, antioxidant and wound healing activities, based on two promising plants - Salvia deserta and Vexibia alopecuroides.

On the basis of comprehensive experimental study shows the effectiveness of pharmacological and prospects of using plant Salvia deserta Vexibia alopecuroides and the production of herbal remedies to treat "diabetic foot".

The conditions for release of biologically active complexes of the roots of Salvia deserta and Vexibia alopecuroides and their division into individual components using flash-chromatography.

From the roots’ extract of Vexibia alopecuroides allocated 9 individual substances belonging to the group of flavonoids from the roots’ extract of Salvia deserta allocated 4 substances belonging to the group of diterpenoids.

For the first time shows the total and individual antimicrobial activity for the 9 substances extracted from plants Vexibia alopecuroides (soforaflavon G, leahianon A, alopekuron A, alopekuron B, alopekuron C, alopekuron F, alopekuron D, soforaflavon I and glabrol) and taxodione, isolated from the roots of Salvia deserta.

On the basis of extracts from the roots of Salvia deserta and Vexibia alopecuroides develop new non-toxic compounds which reduced in 2 times the healing time of wounds in animals.

Correlation of the dissertation with the planned research projects: The thesis is carried out under the state program of fundamental research of the project "Complex research of extracts of biologically active substances from plants and
microalgae Kazakhstan to create a multicomponent preparation for correction of complications of diabetes», № state registration: 0113RK00350.

**The scientific and practical value of the work:**

The scientific and practical significance of the thesis is an experimental justification opportunities and perspectives of the extracts isolated from the roots of *Vexibia alopecuroides* and *Salvia deserta*, as wound healing and antimicrobial herbal remedies for external application on the background of streptozotocin-induced diabetes.

The results of the study of wound healing activity of the complex of herbal remedies on the basis of 2% of the roots’ extract of *Vexibia alopecuroides / Salvia deserta* and 5% Dimexidum, are a prerequisite for the creation of local herbal remedies for correction such complications of diabetes as "diabetic foot" and introducing *Vexibia alopecuroides* and *Salvia deserta* in the pharmacopoeia of Kazakhstan.

The results can be used in research practice in the educational process in teaching students on a specialty "Biotechnology", "Chemical technology of organic substances" and others.

**Statements submitted for defense:**

- The results of screening tests with the presence of antimicrobial, antioxidant and wound healing activity of the extract, confirming the final selection of raw materials for the development of medicines.
- Selecting conditions – isolation on individual substances of biologically active complexes and their separation scheme using flash chromatography.
- The results of the development of the original herbal remedies for the treatment of skin wounds in patients with diabetic foot, composed of extracts from the roots of *V. alopecuroides* and *S. deserta*.
- The results of pharmacological studies of herbal remedies developed their specific activity and possible side effects.

**The approbation of the thesis:** The main materials of the thesis were reported and discussed at the 8th and international scientific conferences and 2 conference republican values including:

- International Conference on Personalized Medicine and Global Health (2013, Astana, Kazakhstan);
- IX International Interdisciplinary Congress "Neuroscience for Medicine and Psychology" (2013, Sudak, Ukraine);
- 61st International Congress and Annual meeting of the Society for Medicinal Plant and Natural Product Research (2013, Muenster, Germany);
- European Biotechnology Congress 2014 (2014, Lecce, Italy);
- American Society of Pharmacognosy 2014 Annual Meeting (2014, Oxford, USA);
- 62nd International Congress and Annual Meeting of the Society for Medicinal Plant and Natural Product Research (2014, Guimaraes, Portugal);
- International Conference on Plant Biology and Biotechnology (2014, Almaty, Kazakhstan);
– 40th Congress of Federation of the European Biochemical Societies «The Biochemical Basis of Life» (2015, Berlin, Germany);
– XXII International Scientific conference of students, graduate students and young scientists name by Lomonosov - 2015, Section: "Biology" (2015, Moscow, Russia);
– 63rd International Congress and Annual Meeting of the Society for Medicinal and Natural Product Research (2015, Budapest, Hungary);

Publications:
On materials of thesis published 16 publications, including 4 articles in national scientific journals recommended by the Committee for Control of Education and Science; five theses in journals with non-zero impact factor; two articles in journals included in the database of Thomson Reuters.

Apply for a patent for utility model. State registration number 2015 / 0289.2. The name of a utility model: Drug extract *Vexibia alopecuroides* having wound healing and antimicrobial actions.

Volume and structure of the thesis: Dissertation is stated on 124 pages of computer text and consists of normative references, symbols and abbreviations, introduction, literature review, materials and methods, results and discussion, conclusions, list of references from 181 titles, contains 31 tables, 38 pictures and 15 applications.