ANNOTATION

of dissertation work by Zhumabekova Ainur Maratkyzy on the topic: «Comprehensive study of biologically active substances of certain representatives of the genus *Thymu*s L. and the prospects for their use in medicine », in candidacy for a degree of Doctor of Philosophy (PhD) in specialty 6D110400 – Pharmacy

Relevance of the research topic. Increasing demand for herbal medicines may lead to depletion of herbal medicinal products. This justifies the need to expand the raw material base of official medicinal plants at the expense of additional plant sources and their complex use.

Plants of the genus Thymus *(Thymus* L.) are of undoubted interest in terms of the development and implementation of original effective herbal remedies in practical health care. Plants of the genus Thyme are popular in traditional medicine of many countries and peoples as a valuable medicinal raw material. The State Pharmacopoeia of the Republic of Kazakhstan includes creeping thyme (*Thymus serpyllum* L.) and common thyme (*Thymus vulgaris* L.) as medicinal plants. In official medicine, these herbs are used as a medicinal plant material with antibacterial, astringent, anti-inflammatory, sedative, anticonvulsant, expectorant, antispasmodic, choleretic, analgesic, diuretic, wound healing and anthelmintic effect, used in the form of decoctions and infusions.

A possible reduction in stocks of medicinal plant raw materials creeping thyme and common thyme leads to the need to expand the raw material base of official medicinal plants through the use of endemic species of flora of Kazakhstan. On the territory of Central Kazakhstan, 15 species of plants of the genus Thyme grow, of which 5 species are endemic, including the common-leaved thyme (*Thymus crebrifolius* Klok.), Shaved thyme (*Thymus rasitatus* Klok.) And hermit thyme (*Thymus eremita* Klok.).

Common thyme, shaved thyme and hermit thyme are common in Central Kazakhstan. According to the results of a survey of raw materials on the territory of the Karaganda region, these plants have sufficient general operational reserves and possible volumes of annual harvests for use in pharmacy and medicine. However, the chemical composition and biological properties of these plant species have not been sufficiently studied.

Therefore, the study of the chemical composition of common-leaved thyme, shaved thyme and hermit thyme, the development of a method and technology for obtaining the amount of extractive substances and the study of its biological properties is an urgent and priority task.

The purpose of scientific research: comprehensive study of biologically active substances of common-leaved thyme, shaved thyme, hermit thyme, development of technology for their production and study of biological properties.

Research objectives:

1. Pharmacognostic study of common-leaved thyme (*Thymus crebrifolius*), that is, shaved (*Th. Rasitatus*) and the hermit (*Th. Eremita*).

2. To develop a method and technology for obtaining the sum of extractives of common-leaved thyme, shaved thyme and hermit thyme using ultrasound.

3. To conduct a study of the chemical composition of polyphenolic compounds of ultrasonic extracts of common thyme, shaved thyme and hermit thyme.

4. To study the biological properties of ultrasonic extracts of common-leaved thyme, shaved thyme and hermit thyme, to select samples with a pronounced biological effect for the development of effective domestic medicines.

5. To develop normative documents in the form of ND projects for medicinal plant raw materials and the substance of the ultrasonic extract of thyme parti-leaved, laboratory regulations for the preparation of the substance.

Research objects: plant raw materials: grass of common-leaved thyme (*Thymus crebrifolius* Klok.), *Thymus rasitatus* Klok. amounts of extractive substances: dry ultrasonic extracts of common-leaved thyme, shaved thyme and hermit thyme.

Subject of study: biomorphological features, diagnostic features, merchandising indicators and chemical composition of common-leaved thyme, shaved thyme and hermit thyme; method and technology for producing dry ultrasonic extract of common-leaved thyme, shaved thyme and hermit thyme; chemical composition and biological properties of dry ultrasonic extracts of common-leaved thyme, shaved thyme and hermit thyme; regulatory documentation for the substance of the ultrasonic extract of common thyme.

Research methods: To achieve this goal and solve problems, modern physicochemical methods of extraction and analysis were used: ultrasonic extraction, high-performance liquid chromatography (HPLC / UV, HPLC / MS), gas chromatography (GC / FID), gas chromatography-mass spectroscopy (GC / MS), ultraviolet (UV) spectrophotometry.

Scientific novelty of work:

– for the first time, a pharmacognostic study of endemic species of common-leaved thyme, shaved thyme and hermit thyme was carried out, external signs and microscopic characteristics were described, the results of merchandising analysis were presented, a comprehensive study of the content of various classes of biologically active substances and mineral elements was carried out;

– for the first time, ultrasonic extraction of plant raw materials was used to extract the amount of extractive substances from common-leaved thyme, shaved thyme and hermit thyme;

– for the first time, the study of flavonoids and phenolic acids of ultrasonic extracts of common thyme, shaved thyme and hermit thyme was carried out using HPLC-UV and HPLC-MS / MS;

– as a result of the conducted bioscreening, for the first time it was established that the ultrasonic extract of common-leaved thyme exhibits pronounced antimicrobial activity against 6 strains of gram-positive bacteria (two strains of Staphylococcus aureus, Staphylococcus epidermidis, Micrococcus luteus, Bacillus subtilus pneumonia, Streptococcus pyogenes), 2 strains of gram-negative

bacteria (Klebsiella pneumoniae, Proteus mirabilis), causes a growth retardation of 2 strains of Candida albicans, Candida krusi fungi, and has a pronounced bactericidal effect against Helicobacter pylori;

– for the first time, according to bioscreening data, it was revealed that an ultrasound extract of shaved thyme has a pronounced antimicrobial activity against 3 strains of gram-positive bacteria (Staphylococcus aureus, Staphylococcus epidermidis, Streptococcus pneumoniae, causes a growth retardation of cultures of Micrococcus luteus, Bacillus cereus 1 bacteria (Klebsiella pneumoniae), causes a growth retardation of the culture of the fungus Candida albicans, and has a pronounced bactericidal effect against Helicobacter pylori;

– for the first time it was found that the ultrasonic extract of hermit thyme exhibits pronounced antimicrobial activity against 1 strain of gram-negative bacteria (Klebsiella pneumoniae), causes growth retardation of 4 strains of gram-positive bacteria (Micrococcus luteus, Staphylococcus epidermidis, Staphylococcus aureus, B bactericidal action against Helicobacter pylori;

– for the first time it was found that the expectorant effect close to the reference drug "Bronchicum C" is shown by the ultrasonic extract of shaved thyme, the ultrasonic extract of the thyme is 1.5 times inferior to the comparison drug, and the ultrasonic extract of the hermit thyme has practically no expectorant activity;

– according to the results of an acute toxicity study in an in vivo experiment, it was established that the substance of the ultrasonic extract of thyme common-leaved belongs to the group "Practically non-toxic" (V class of toxicity);

– a technology has been developed for obtaining the substance of an ultrasonic extract of common-leaved thyme;

– a draft ND for medicinal plant raw materials “Thyme herb” was developed, regulatory documents for the substance of an ultrasonic extract of thyme, in the form of a draft ND and laboratory regulations for obtaining.

The practical significance of the work:

– according to the results of a comprehensive study of the content of various classes of biologically active substances, it was found that the herb of common-leaved thyme, herb of shaved thyme and herb of hermit thyme contain a significant amount of terpenoids, flavonoids, phenol carboxylic acids, tannins, triterpene compounds, water-soluble polysaccharides, pectin substances, amino acids and organic acids, the presence of which, in combination with the quantitative content of many important mineral elements, determine the prospects for their use in pharmacy and medicine;

– on the basis of the results of pharmacognostic research and commodity analysis of common-leaved thyme, an ND project for medicinal plant raw material "Thyme leafy herb" has been developed;

– taking into account the yield of ultrasonic extract and biological properties, as a promising substance for the development of domestic medicines of a wide spectrum of antimicrobial action, including *Helicobacter pylori*, an ultrasonic extract of thyme is recommended;

– the technology of ultrasonic extract of common-leaved thyme has been

developed and implemented;

– ND project for the substance ultrasonic extract of common thyme was developed;

– developed and approved laboratory regulations for the production of the substance of the ultrasonic extract of common thyme (JIP-005491-MK-05-21);

– on the basis of the Scientific Research Center of NJSC "MUK", the release of pilot batches of the substance of the ultrasonic extract of thyme common-leaved for pharmacological research was organized.

The main provisions for the defense:

– results of a pharmacognostic study of endemic species of common-leaved thyme (*Thymus crebrifolius* Klok.), Shaved thyme (*Th. Rasitatus* Klok.) And hermit thyme (*Th. Eremita* Klok.);

– method and technology for obtaining ultrasonic extracts of common-leaved thyme, shaved thyme and hermit thyme;

– results of the study of the qualitative and quantitative composition of polyphenolic compounds of ultrasonic extracts of common-leaved thyme, shaved thyme and hermit thyme;

– results of biological properties and acute toxicity of ultrasonic extracts of common-leaved thyme, shaved thyme and hermit thyme;

– regulatory documents for the substance of the ultrasonic extract of common thyme, in the form of ND project and laboratory regulations for obtaining; IDA project for medicinal herbal raw materials “Thyme leafy herb”.

Publications. Based on the dissertation materials, 1 patent of the Republic of Kazakhstan was obtained, the main provisions of the dissertation are reflected in the following publications:

- 4 articles in journals recommended by the Committee for Quality Assurance in Science and Higher Education of the Ministry of Science and Higher Education of the Republic of Kazakhstan;

- 1 article in an international scientific publication included in the Scopus Q3 database;

- 9 articles and abstracts in the collections of International conferences;

- 1 article in the Republican scientific journal.

CONCLUSIONS:

1. For the first time, a pharmacognostic study of common-leaved thyme (*Thymus crebrifolius* Klok.), Shaved thyme (*Th. Rasitatus* Klok.) And hermit thyme (*Th. Eremita* Klok.) was carried out. According to the results of a comprehensive study of the content of various classes of biologically active substances, it was found that the herb of common-leaved thyme, herb of shaved thyme and herb of hermit thyme contain a significant amount of terpenoids, flavonoids, phenol carboxylic acids, tannins, triterpene compounds, water-soluble polysaccharides, pectin substances, amino acids and organic acids , the presence of which, in combination with the quantitative content of many important mineral elements, determine the prospects for their use in pharmacy and medicine. On the basis of a pharmacognostic study and the results of a commodity analysis of

common-leaved thyme, an ND project for medicinal plant raw materials "Thyme-leaved herb" was developed.

2. A method and technology has been developed for obtaining the sum of extractives of common-leaved thyme, shaved thyme and hermit thyme using ultrasound. Ultrasonic extracts have been developed to study the chemical composition and biological properties.

3. For the first time, the study of flavonoids and phenolic acids of ultrasonic extracts of common thyme, shaved thyme and hermit thyme was carried out using HPLC-UV and HPLC-MS / MS. 12 phenolic compounds were identified and quantified in the ultrasonic extract of common-leaved thyme, four of them were phenolic acids, eight were flavonoids, 12 phenolic compounds were found in the ultrasonic extract of shaved thyme, five of them were phenolic acids, seven were flavonoids, 14 were identified in the ultrasonic extract of hermit thyme. phenolic compounds, five of them are phenolic acids, nine are flavonoids. The obtained ultrasonic extracts showed differences both in the qualitative composition of phenolic compounds and in the quantitative content of phenolic acids and flavonoids.

4. As a result of the bioscreening, it was found for the first time that the ultrasonic extract of common-leaved thyme exhibits pronounced antimicrobial activity against 6 strains of gram-positive bacteria (two strains of *Staphylococcus aureus, Staphylococcus epidermidis, Micrococcus luteus, Bacillus subtilus*), 2 strains of gram-negative bacteria (*Klebsiella pneumoniae, Proteus mirabilis*), causes a growth retardation of 2 strains of *Candida albicans, Candida krusi* fungi, and has a pronounced bactericidal effect against *Helicobacter pylori*. Ultrasonic extract of shaved thyme, has a pronounced antimicrobial activity against 3 strains of gram-positive bacteria (*Staphylococcus aureus, Staphylococcus epidermidis, Streptococcus pneumoniae,* causes growth retardation of cultures of *Micrococcus luteus, Bacillus cereus, Streptococcus pyogenes* bacteria), 1 growth of the culture of the fungus *Candida albicans*, and has a pronounced bactericidal effect against *Helicobacter pylori*. Ultrasonic extract of hermit thyme, exhibits a pronounced antimicrobial activity against 1 strain of gram-negative bacteria (*Klebsiella pneumoniae*), causes growth retardation of cultures of 4 strains of gram-positive bacteria (*Micrococcus luteus, Staphylococcus epidermidis, Staphylococcus aureus*).

5. Taking into account the yield of ultrasonic extract and biological properties, as a promising substance for the development of domestic medicines of a wide spectrum of antimicrobial action, including *Helicobacter pylori*, an ultrasonic extract of common thyme is recommended; according to the results of the study of acute toxicity in the experiment in vivo, it was found that the substance of the ultrasonic extract of thyme common leaf belongs to the group "Practically non-toxic" (V class of toxicity).

6. An ND project was developed and the substance of an ultrasonic extract of common thyme was standardized. Developed and approved laboratory regulations for the production of the substance of the ultrasonic extract of common thyme (LR-005491-MK-05-21). On the basis of the Scientific Research Center of NJSC "MUK", the release of experimental batches of the substance of the ultrasonic

extract of thyme of common-leaved thyme for pharmacological research has been organized.

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- 1 article in an international scientific publication included in the Scopus Q3 database;
- 9 articles and abstracts in the collections of International conferences;
- 1 article in the Republican scientific journal.

The structure and scope of the dissertation. The dissertation is presented on 123 pages of typewritten text, includes 31 figures and 39 tables; consists of introduction, 5 chapters, conclusion, list of references and applications. The list of references includes 150 literary sources.