

ANNOTATION

of dissertation work of **Kozykeyeva Raushan Aidarbekovna** on the topic of «**Standardization and perspectives in development of production technology of new phytopreparations on the base of the herb *Agrimonia asiatica***» submitted for the degree of philosophy doctor (PhD) in the specialty 6D110400 – «Pharmacy»

Relevance of the research topic

Creation of the herbal medical facilities is one of the basic directions for the pharmaceutical industry development, owing to the comparative safety and treatment effect, moreover prices available for the population.

The relevance of the selected topic consists in the necessity of using effective support measures of domestic manufacturers, who direct their investment programs on the spreading of safety drugs in the treatment of social significant diseases and correspond of Government program of healthcare development in Republic of Kazakhstan on the 2020-2025 years. Question of import substitution is important in the sphere of drug supplying. Thorough and full-scale research of the poorly studied species of the drug plants need for rational decision of the task for drug development on the base of it.

Thus, effective using of domestic plant raw material for systematic decrease of import addiction of Republic of Kazakhstan from foreign drugs is actually at the time. Asian agrimonia (*Agrimonia asiatica* Juz.), which are growing in the foothills of Kaskasu and Tolebi region, present enough raw material bases. It is the source of biological active substances. Asian agrimony grass widespread using in the folk medicine in the cases of inflammatory processes in the organism.

Purpose of research: Pharmacognostical study of the healing plant *Agrimonia asiatica* Juz., and pharmaceutical creation of phytosubstances on the base of it.

Tasks of research:

- to conduct the pharmacognostical study of the aerial part (grass) of *Agrimonia asiatica* Juz;
- to study optimal technology of extract receiving from the grass of *Agrimonia asiatica* Juz;
- to define indicators and norms of the quality, term of dry extracts good storage of the raw material of *Agrimonia asiatica* Juz;
- to conduct non-clinical studies of acute, sub-acute toxic, antioxidant and anti-inflammatory activity of extract from *Agrimonia asiatica* Juz;
- to create the drugs and conduct technic-economical basement for drug production from the phyto substance from *Agrimonia asiatica* Juz.

Objects of research: *Agrimonia asiatica* Juz herb, dry extract, lozenges «Agrimol».

Research methods: pharmacognostical and pharmacotechnical, physical and physical-chemical, pharmaceutical and biological, pharmacopoeia methods.

Scientific novelty of received results

At the first time:

- conducted full pharmacognostical studying of the agrimony herb (*Agrimonia asiatica* Juz.), which is growing in the south part of Kazakhstan;
- studied acute, sub-acute toxic, antioxidant, chelating and anti-inflammatory activity of phyto substance from *Agrimonia asiatica* and defined the safety of it. Novelty confirmed with patent on invention №33804 «Way of plant remedy receiving with antioxidant and chelating activity», registered in the Government inventions register of Republic of Kazakhstan in 09.01.2018;
- conducted researches on technology creation of tablets «Agrimol» on the base of phyto substances *Agrimonia asiatica* Juz.

Basic provisions of dissertation research, submitted for defense:

- results of healing plant preparation, standardization and studying of grass *Agrimonia Asiatica* Juz. stability correspond with the RK SP demands;
- results of dry extract production from the grass *Agrimonia asiatica* Juz., quality evaluation of dry extract from the herbal raw material *Agrimonia asiatica* Juz., results of non-clinical studying of acute, sub-acute toxic, and antioxidant and anti-inflammatory activity of *Agrimonia asiatica* Juz. extract.
- results of pharmaceutical development of tablets from the grass extract of *Agrimonia asiatica* Juz.

Practical significance of research

- On the base of received results recommended phyto substance *Agrimonia asiatica* Juz. in the quality of the treatment source.
- Quality specification on the raw material *Agrimonia asiatica* Juz. and dry extract *Agrimonia asiatica* Juz. was developed.
- Technology of experience-industry production of tablets was implemented in the production act of LP «VIVA PHARM», Almaty state, Republic of Kazakhstan

Private contribution. Kozykeyeva R.A. conducted scientific research own.

Work approbation. Basic results, received in the path of dissertation research performance reported in the following materials and works of scientific-practical conferences: Annual International Conference of “Modern Molecular-Biochemical Markers in Clinical and Experimental Medicine”, in the article collection in the journal «Biological Markers in Fundamental and Clinical Medicine» (Prague, Czech Republic, 2017); «Actual aspects of experimental and clinical pharmacy: from the molecule to the medicine, conducted in the framework of the third International conference (in Pyatigorsk, Russia, November 16-17, 2017); VI Russian conference «Belikov readings», (Pyatigorsk, Russia, 2018); International conference, dedicated to memory of professor R.Dilbarkhanov (Almaty, Kazakhstan, July 16, 2019); «Science and education in the modern world: challenges of XXI century, III International conference (Nur-Sultan, Kazakhstan, July 10-12th 2019); International scientific-practical conference «University days – 2019; Pediatrics of XXI century. Modern challenges and trends», dedicated to 130 years of S.D. Asfendiyarov (Almaty, Kazakhstan, December 5-6 2019, internet-conference «Ways of science development in modern crisis conditions», 1st International Scientific and Practical Internet Conference, May 28-29, 2020. – Dnepr, 2020.

Information about publications

From the results of conducted scientific work, in the frameworks of dissertation work publicized 12 scientific works;

- article in the international journal – 1;
- articles in the journals, recommended from CCSES MES RK - 4;
- materials (in the thesis and articles) in International conferences (Kazakhstan, Czech Republic, Russia, Ukraine) – 1;
- author certification.

Structure and volume of dissertation

Dissertation written on 151 pages of computer text and consists of introduction, literature review and 5 chapters, dedicated to materials and methods of research, basic part, which included 4 sections, with results of research and conclusions, and list of 101 used sources. Dissertation work contains 53 tables, 53 pictures, 3 diagrams, 16 formulas and attachments from A to Ы (Russian alphabet).

Conclusion. In results of research, in the framework of doing dissertation work, can be done following conclusions:

1) Conducted pharmacognostic study of aerial part of asian agrimony, were indicated following macroscopic features:

- leaves of agrimony asiatica unpaired, feathery and complex. Leaflets are elliptic with coarse-toothed edge. Leaves are green in the top; in the down part – grey and green, interrupted feathery. They are slightly pubescent in the top and velvety pubescent with mix of little glands.

Indicated following microscopic features of the plant *Agrimonia asiatica* Juz.:

- top leave epidermis characterizes with powerful tortuosity of the cells, in the time low epidermis has the cells with right walls, anomocytic type of stomata. Filaments are simple in appearance of unicellular outgrowth.

In the herb of asian agrimony indicated polysaccharides, phenolic compounds, saponins, tanning substances, flavanoids, carbon acids. According to the conclusion of studying of ethereal oil, got from grass of asian agrimony, basic ingredients were β -selinen (36,4%), α -panasinsen (21,7%), palmitic acid (7,8%), 1,2-nonadien (6,2%), nonanal (4,2%), hermaceren A (2,5%) and β -huayen (2,4%). Quantitative content sums of flavanoid indicated in terms of quercetin (9%) and sum of polysaccharides (20%) in the herb of asian agrimony.

2) In the path of development of optimal technology of extract receiving from the grass *Agrimonia asiatica* Juz. has reached following results:

- extract from the grass of asian agrimony received from percolation; and sublimated drying used for preparation of dry extract. Yield of extract was 4,4%. Received product has brown color and characteristic smell, easy dissolves in the water and ethanol.

Isolation of individual compounds was performed by column chromatography. Five basic compounds were excreted, which were indicated as: 3-O-kaempferol-2,3-di-O-acetyl-4-O-(cis-p-coumaroyl)-6-O-(trans-p-coumaroyl)- β -Dglucosopyranoside), kaempferol-3-glycoside, quercetin-3-O- α -arabinofuronosyl- β -D-galactosopyranoside, catechin and sucrose by the method of NMR spectroscopy. Quantitative content of

catechin and astragalín was indicated in percent relationship as 1,73% и 0,227% by the method HPLC.

3) Standardization of dry extract from the raw material of *Agrimonia asiatica* Juz. performed. According to it, indicated following quality specifications of dry extract from the raw material of *Agrimonia asiatica* Juz.: description, identification, loss of weight by the drying, heavy metals, microbiological clean and quantitative indication. All quality indicators correspond to requirements. Extract stability was long term studied in the temperature $25\pm 2^{\circ}\text{C}$ and relative wet $60\pm 5\%$.

4) Evaluation of acute, sub-acute toxic of dry extract from *Agrimonia asiatica* Juz. was indicated. Indicated, that dry extract of *Agrimonia asiatica* Juz. refers to grade 4, low toxic substances. Antioxidant and anti-inflammatory activity of dry extract from *Agrimonia asiatica* Juz. indicated.

5) Pharmaceutical development of lozenges with dry extract of asian agrimony conducted. Rational composition, optimal technology of receiving tablets was done, relatively indicated saving period of tablets owing to the long-term research method in conditions of temperature 25 ± 2 and humidity $60\pm 5\%$ for 2 years. Technical and economical basement of tablets production with extract of asian agrimony were studied.

Evaluation of completeness of assigned tasks decision. All assigned tasks for final goal done.

- Conducted pharmacognostic, pharmaceutical-technological research and standardization of healing herb *Agrimonia asiatica* Juz.

- Developed optimal technology of delivering extract from the grass *Agrimonia asiatica* Juz.

- Developed pharmacopeia criteria of quality and conducted standardization of dry extract from the raw material of *Agrimonia asiatica* Juz.

- Conducted non-clinical research of acute, sub-acute toxic and antioxidant, anti-inflammatory activity of extract *Agrimonia asiatica* Juz.

- Developed way and production technology of healing drug and conducted technical-economical basement for production medicine from the extract from *Agrimonia asiatica* Juz.

Development of recommendations and initial data on a specific using of results.

- received invention act for lozenges production from the dry extract of asian agrimony;

- methods of study and block-scheme divided on the fraction and may be used in the path of scientific practice in the studying process.

Evaluation of technical-economical effectiveness of invention and scientific level of dissertation work reflect in following results:

- developed the scheme of isolation biological active substances from the plant of asian agrimony. One new compound 3-O-kaempferol-2,3-di-O-acetyl-4-O-(cis-p-coumaroyl)-6-O-(trans-p-coumaroyl)- β -D-glucosopyranoside) indicated for *Agrimonia asiatica* Juz.

- studied acute, sub-acute toxic, antioxidant and anti-inflammatory activity of phytosubstance *Agrimonia asiatica* and indicated its safety. Novelty confirmed by the invention patent RK;

- research of technology development of tablet «Agrimol» conducted on the base of phytosubstance of *Agrimonia asiatica* Juz.