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Review Article

Lathraea squamaria L. (*Orobanchaceae*): A Review of its Botany, Phytochemistry, Traditional Uses and Pharmacology

Bokov DO[1,2,#,*], Barkalova VE[3,#], Suslikova MA[1], Sokhin DM[1], Kakhramanova SD[1,4], Rendyuk TD[1], Strelyaeva AV[1], Antsyshkina AM[1], Balobanova NP[1], Prostodusheva TV[1], Grikh VV[1], Krasnyuk II[1] (junior), Marakhova AI[5], Moiseev DV[6]

Bokov DO[1,2,#,*], Barkalova VE[3,#], Suslikova MA[1], Sokhin DM[1], Kakhramanova SD[1,4], Rendyuk TD[1], Strelyaeva AV[1], Antsyshkina AM[1], Balobanova NP[1], Prostodusheva TV[1], Grikh VV[1], Krasnyuk II[1] (junior), Marakhova AI[5], Moiseev DV[6]

[1]*Institute of Pharmacy, Sechenov First Moscow State Medical University, 8 Trubetskaya St., bldg. 2, Moscow, 119991, RUSSIAN FEDERATION.*
[2]*Laboratory of Food Chemistry, Federal Research Center of Nutrition, Biotechnology and Food Safety, 2/14 Ustyinsky pr., Moscow, 109240, RUSSIAN FEDERATION.*
[3]*Faculty of Pediatrics, Siberian State Medical University, 2 Moscow tract, 634050, Tomsk, RUSSIAN FEDERATION.*
[4]*Department of State Pharmacopoeia and pharmacopoeia analysis, Federal State Budgetary Institution "Scientific Centre for Expert Evaluation of Medicinal Products", 8/2 Petrovsky Boulevard, Moscow, 127051, RUSSIAN FEDERATION.*
[5]*Pharmaceutical chemistry and pharmacognosy chair, Peoples' Friendship University of Russia (RUDN University), 6, Miklukho-Maklaya Street, Moscow, 117198, RUSSIAN FEDERATION.*
[6]*Chair of Standardization of Medicines, Vitebsk State Medical University, 27, Frunze avenue, Vitebsk, 210062, BELARUS.*
[#]*Bokov DO, Barkalova V.E. contributed equally to this work.*

Correspondence
Bokov DO
Institute of Pharmacy, Sechenov First Moscow State Medical University, 8 Trubetskaya St., bldg. 2, Moscow, 119991; Laboratory of Food Chemistry, Federal Research Center of Nutrition, Biotechnology and Food Safety, 2/14 Ustyinsky pr., Moscow, 109240, RUSSIAN FEDERATION.
E-mail: fmmsu@mail.ru

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ABSTRACT
This paper presents the results of the review pharmacognostic study of common toothwort, a perennial plant, parasitizing on the roots of trees. Currently, in Russian traditional medicine, there is considerable experience in the use of common toothwort (*Lathraea squamaria* L.) herb and roots as antitumoral, biligenic, infertility-treatment and diuretic drugs. The chemical composition of *L. squamaria* has not been quite well determined. Phenylethanoid glycosides (acteoside, isoacteoside), iridoid glycosides (aucubin, and aucuboside ester, 6'-O-glucopyranosyl-aucubin, melampyroside, 6'-O-glucopyranosyl melampyroside), simple sugars, fatty acids, organic acids, β-sitosterol were identified. Further study of *L. squamaria* raw materials is a very promising field including implementation in official medicine.
Key words: *Lathraea squamaria, Orobanchaceae,* Common toothwort, Parasitic plants, Chemical compounds, Iridoids, Aucubin.

INTRODUCTION

There is a specific interest toward groups of parasitic floral forms in Russia and abroad from the viewpoint of medical use. The research of the parasitic plants from figwort (*Scrophulariaceae* Juss.) and broom rape family (*Orobanchaceae* Vent.) is conducted intensively as evidenced by the numerous messages of its significant pharmacological activity. During the research, the relation of the pharmacological potential of the semi-parasite plants to their external conditions and their way of life was established. For solving pharmacognostic and phytotherapeutic goals the studies of diagnostic features and characteristics of parasitic plants were conducted. Different structural features of their vegetative organs described. These data can be used for further botanic diagnosis of the parasites of Figwort and Broom rape families and their products. One of the famous plants of the root rape family is common toothwort (*Lathraea squamaria* L., Figure 1). Earlier this plant was in the figwort family.[1-5]

L. squamaria is used only in folk medicine. There is no pharmacopeial monograph in any pharmacopeia in the world. It is known that aqueous extract from the common toothworh raw material has antitumoral, biligenic and diuretic activities; it is also used for treating infertility in men and women, stimulation of cardiac, hepar and renal system function.[1,2] Poorly understood chemical composition and the lack of product normative documentation prevent common toothwort crude herbal drugs from being released on the Russian market. However, earlier mentioned positive pharmacological properties of the common toothwort determine the topicality and the necessity of further pharmacological research.

Thus the research aims to find out the literary documents of the chemical composition and pharmacological properties of the common toothwort (*Lathraea squamaria* L.).

MATERIALS AND METHODS

Different methods of articles analyzing were used for the accomplishment of our goals. For example, information analysis documental and systematic. Electronic sources were analyzed: Web of Science, Scopus, PubMed, E-Library, Cyberleninka, search engines (Google Scholar). Since there were few scientific literature sources for *L. squamaria*, we have analyzed all available sources.

RESULT AND DISCUSSION

L. squamaria botanical and pharmacognostic characteristic

The common toothwort, being a member of the broom rape family, lacks chlorophyll and exists solely by the means of the host plant (obligate holoparasite). A colorless stem with crimson red flowers is the primary morphological feature to recognize this plant in a spring Russian forest. The Russian name "Peter's cross" ("Petrov krest") appeared during the botanical morpholocal description of the plant; during the growth, the roots of *L. squamaria* form something that looks like crosses. The common toothwort belongs to *Lathraea* L. genus which also includes other species like purple toothwort (*L. clandestina* L.), rhodope toothwort (*L. rhodopea* Dingler), Japanese toothwort (*L. japonica* Miquel).

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Figure 1: The common toothwort in bloom stage.

The common toothwort can be defined as an achlorophyllous perennial according to botanical morphological characteristics. Common toothwort has a thick albescent ramulous rootstock with subopposite squames. Stems with spike-like inflorescences grow up to 30 cm. Irregular flowers located on the pedicel. The flowers consist of heather covering leaves situated in two rows that are almost the size of a calyx. The calyx is glandulous, bell-shaped, quadrilobate. The flower crown is heather, bilabiate, tubulous campanulate, it is bigger than the calyx. The flowers are usually red or crimson and grow in a cluster or a raceme. The fruit has a bivalved egg- or ball-like shape (Figure 2). The common toothwort blooms in spring (April-May).

The central part of the plant is a vastly ramulous rootstock that is located deep underground. In spring during vegetation white or pink tendrils, carrying stems, start to grow above the ground. Also, thin roots that grow from the rootstock when touching the roots of the host plant form a special type of thickening, a surculus (haustorium).[5-9]

The squams that cover the common toothwort stem are of particular interest to the scientists. Earlier this plant was considered carnivorous and the squams to be a trap for catching the insects. The scale has cavities with small slits; its walls are covered with glands that look like carnivorous plant glands, for example, sundew (*Drosera rotundifolia* L.). The thought that the common toothwort is a carnivorous plant was supported by the findings of dead insects in the scale cavities regardless of being digested by the plant or not. Currently, this illusion is dispelled, the cavities are considered to be an organ for evaporation of water transpired by the glands. The squams are a special structure of this plant for underground living.[10,11]

Above ground tendrils of *L. squamaria* usually, look clustered, almost always adjoined. They form thick round or oval distinctive vegetative tendrils, from which underground branches all aboveground flower-bearing stems grow. It was identified that the common toothwort reproduces with the help of seeds of its fruit. The seeds sprout up after they come in contact with the roots of a host plant. After that thick underground tendrils appear and form cross-like branches that embed themselves to the roots of the host plant. Then in spring, rutilant-white aboveground sprouts with scale-like pinkish leaves and crimson flowers emerge. Host plants parasitized by common toothwort are affected significantly; they are weakened and its producing capacity decreased. *L. squamaria* parasitizes on the roots of trees and shrubs such as hazel, alder, beech, and bird cherry. In the first years, the rootstock of the common toothwort develops underground and only then inflorescences appear. The vegetation of the common toothwort coincides with the sap flow of a host plant in spring (April-May). The inhabitation of the *L. squamaria* is broad-leaved forests of Europe, Caucasus, also temperate forests from Western Europe to Pakistan and India. It grows in shade; *L. squamaria* is the only member of its genus which grows on the Russian and CIS territories. During the soil analysis in Europe, where the common toothwort grows, the researchers found out that this species prefers moderately acidic or week-base soils with moderate to high moisture. Due to the common toothwort being a parasite the plants growing near its area of inhabitation also should be considered. So it was concluded that the common toothwort usually coexists with geophytes and hemicryptophytes which bloom before forming leaves. In central Europe and neighboring areas of West and East Europe, the common toothwort is usually seen in alluvial or oak and hornbeam forests, also in forests with a large number of marple, ash, teil, and ulmus.[13-19]

It was found that there are chromoplasts in the common toothwort tissues when the scales structure of the aboveground stems and underground roots were studied. As a part of the study, it was found that one can see in the composition a clearly disturbed group of plastins and vesicles in circumferential position, a one almost round object made of well-formed and concentric double plastines in the central position. Also, starch granules were found. They are absent in chromoplasts of the underground organs and the structure of chromoplasts is less developed. There are a lot of proteoplasts in the scale cells of the rootstock. Such proteoplasts are lacking in the aboveground organs. Similarly, chloroplasts were not found even in the protoplastic phase.[20,21]

L. squamaria has a wide system of underground stems covered with small tightly overlapping scale-like leaves (Figure 3). In early spring epigeal buds start to grow from the stems side by side. These buds appear aboveground at the same time as the flowers (Figure 4, on the left).[20,22]

The majority of the lower and middle flowers already have dead corollas by the end of April; only 4-6 upper flowers remain blooming. After a few weeks, the dead corollas and ovaries swell greatly as a result of the development of the ovules (the process takes almost the whole month). In the middle of May, the capsules start to open (Figure 4, on the right)[20]; the

Figure 2: The common toothwort at the place of growth.

Figure 3: A fragment of *L. squamaria* underground stem.

Figure 4: Bud bursting (left) and capsules with *L. squamaria* seeds.

seeds emerge as a result of the opening. The seeds are black and coarse, around 1 mm, they look to be connected by a short footstalk with fleshy center line.[7-9]

L. squamaria medicinal usage

The common toothwort is a poisonous plant. When eaten it causes poisoning, despite that the common toothwort is used in traditional medicine. Roots and herb are used as crude herbal drugs. They are harvested in spring, in April or May during the mass blooming. The whole plant is dug out by hand, the soil is cleaned off and it is dried up in shade or in a well-ventilated place.

In folk medicine, the crude herbal drug of the common toothwort is used for treating kidney diseases, liver conditions, various diseases of reproductive systems of men and women. For example, the disorder of uterus muscle tone, infertility, menstrual disorders, benign prostatic hyperplasia. In combination with other drug plants (hemlock – *Conium matulatum* L., wolfsbane – *Aconitum napellus* L., etc.) it is used as an antitumoral drug.[3]

Folk medicine recommends using infusion. To make the infusion it is needed to grind the *L. squamaria* crude herbal drug, put one teaspoon of the drug into a cup, pour 250 ml of boiling water and let the infusion stay for an hour, then filter it. It is advised to take half a cup two times a day. A decoction can be also made from the common toothwort. To prepare it is needed to pour over the grated roots 250 ml of water and put it on a boiling water bath for 20 min, then the decoction is filtered. It is recommended to take half a cup of the decoction twice a day for a month. A tincture from the common toothwort is preparing with 40% ethanol as extraction agent. It is recommended to take 15-20 drops of the tincture mixed with 50 ml of water twice a day half an hour before meals. In scientific sources little attention is paid to the study of chemical composition and pharmacological properties of the common toothwort, preclinical studies were not conducted. There is a hypothesis that crude herbal has cytostatic properties (i.e. an alkylating agent), so potentially it could be used for treating oncological diseases. The use of the common toothwort for curing liver, gal bladder diseases is based on the fact that there are compounds that have a choleretic effect in the common toothwort. The diuretic effect of the plant lends to be used for getting rid of edema.[3]

Dr. O.D. Barnaulov's research is quite promising; he studied the ways of using the common toothwort as a drug in phytotherapy. Dr. Barnaulov is a Ph.D., corresponding member of the Russian Academy of Natural Science, leading scientific worker of the Institute of Human Brain of Russian Academy of Sciences, experimental and clinical phytotherapy group supervisor. In research, he pointed out the cases of the positive influence of herbal teas (mixture herbal products) on his patients. Men with multiple sclerosis and other neurotic disorders, who complained about a decrease in fertility, took part in the experiment. The herbal tea consisted of a small amount of the adaptogen plants, that was compensated by their combination. The author notes that the herbal tea effects not only to reverse symptoms of a neurotic disease apart from moderate sensory impairment but also increase libido, sexual vigor and erectile function. In the article published by Barnaulov, there were three medical records of the patients, which took part in the experiment. The first patient came to the clinic in 2003 when he was 29 years old. He had numbness in his limbs, diplopy, multiple sclerosis, and sexual vigor dysfunction with other symptoms of different nature. The patient was a typical asthenic, prone to depressions, try to hide his disease, he was very skeptical about phytotherapy.[23]

For treating this patient an individual mix of herbs (herbal tea) containing aboveground parts (garden parsley*, garden lovage*, bur beggar-ticks*, knotgrass*, Saint-John's-wort*, common motherwort, crisped-leaved mint*, common balm*, creeping thyme*, common self-heal, common winter cress*, European verbena*, wild strawberry*), leaves (red raspberry, drooping birch, goat willow, garden sage*, common plantain*, fireweed), fruits (cinnamon rose*, blood-red hawthorn*), flowers (wild chamomile, meadowsweet, pot marigold, forest anthriscus) and roots (setwell*) were gathered. The whole common toothwort*, carnation*, anise tree* and common nutmeg* were used. The author states that this herbal tea was aimed to control symptoms of the above-mentioned illnesses, to increase libido and sexual vigor of the patient. Plants mentioned in the mix with a "*" have a positive gonadotrophic effect. The majority of the plans also have antialterant, antidestructive, cerebroprotective, desensitizing, antioxidant, stress-limitative and anti-inflammatory pharmacological effects, notable to people with multiple sclerosis; the combination of these properties is commonly found in these plants. The same properties are observed for their mixture; it was proved by clinical supervision and high performance of phytotherapy.[23]

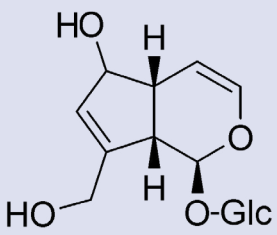
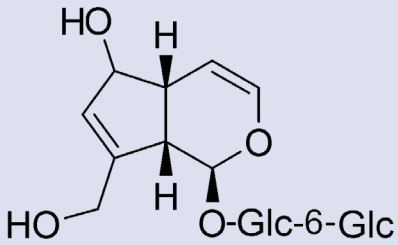
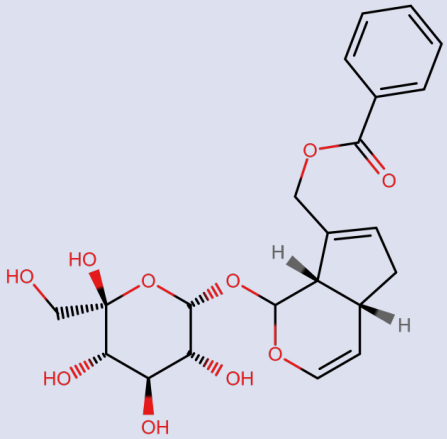
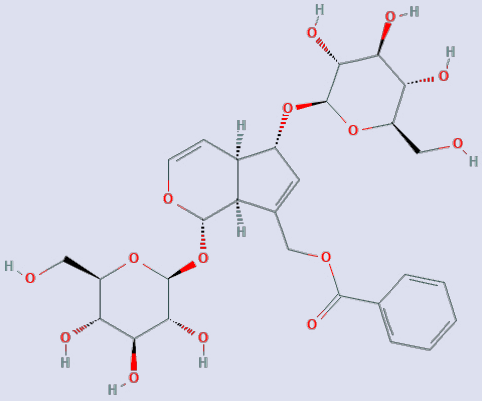
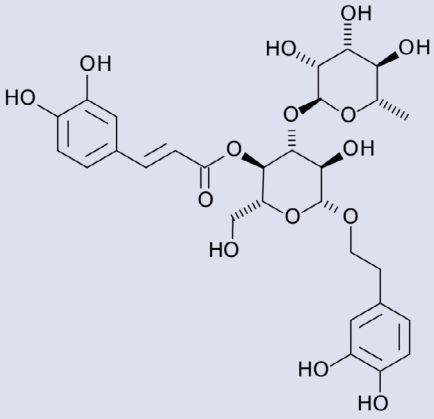
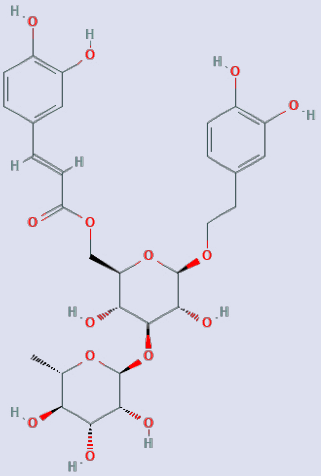
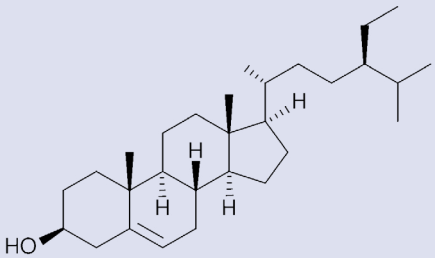
During the study, the patient has completed the courses of supporting phytotherapy in 7 years. During this time symptoms of all the illnesses disappeared, there was only one flare-up with a moderate sensory disorder. The decrease of sexual vigor stopped in 3 months after starting the treatment. The second patient was an example of a severe medical case. The patient was diagnosed with multiple sclerosis. According to medical history, the patient had symptoms that occurred a long time ago under stress. During the 11 years, he continuously took poly component herb tincture. For treating patient 2 different herbal teas were used including the tea containing fruits (common dill, anise*, fennel*, coriander, garden carrot*, cinnamon rose*), aboveground parts (crisped-leaved mint*, common balm*, creeping thyme*, spicate lavender*, common origanum). The whole common toothwort* and carnation* were used. Synergistic plants were prescribed to get the desired antidestructive, immunocorrecting, antifatigue, antistress effects. A significant amount of plants with a positive gonadotrophic effect were included in herbal tea. As a result of treatment, improvement became apparent; the patient stopped complaining of sexual vigor dysfunction, sometimes complained of constitutional weakness.[23]

L. squamaria phytochemical studies

Earlier, researches paid little attention to the phytochemistry of *L. squamaria*. Researchers from University of Veterinary and Pharmaceutical Sciences (Czech Republic) studied the chemical composition of this plant. Two isomeric phenylethanoid glycosides, acteoside and isoacteoside were isolated and identified; they were never described in this plant before. Besides, benzoic acid was discovered for the first time, the presence of iridoid glycoside aucubine in all studied parts of the plant was confirmed (Table 1).[24]

Also, iridoids were isolated from *L. squamaria*. Researches B. Grabias, S. Ofterdinger-Daegel, L. Świątek, A. Kurowska identified a new iridoid disaccharide, 6'-O- glucopyranosyl-melampyroside, among other

Table 1: The chemical composition of *L. squamaria*.

Iridoids	
	
Aucubin	6'-O-glucopyranosyl-aucubin
	
Melampyroside	6'-O-glucopyranosyl melampyroside
Phenylethanoid glycosides	
	
Acteoside (Verbascoside)	Isoacteoside
Steroid alcohols	
	
β-sitosterol	

known glycosides aucubine, melampyroside and 6′-O-glucopyranosyl-aucubin from the seeds of *L. squamaria*. The structure of above-mentioned chemical compounds was discovered with the help of spectrum data with 1H-NMR, 13C-NMR methods, desorption chemical ionization mass spectrometry (DCI-MS). Also, β-sitosterol was educed, six fatty acids (oleic, linolenic, linoleic, palmitic, stearic, myristic) were found in seed oil (Table 1).[25]

L. Swiatek и L. Dombrowicz educed aucuboside and D-mannitol, and found glucose, fructose and aucuboside ester. After hydrolysis 6 phenolic acids were identified. Also, the researches consider glycosides of aucubine group as elements of chemotaxonomic significance.[26]

The endogenous levels of abscisic acid in parasitic phanerogams of *Arceuthobium oxycedri* (DC) Bieb., *Cassytha filiformis* L., *Lathraea squamaria* L., *Melampyrum pratense* L., *Orobanche hederae* Duby. and *Viscum album* L. were studied. All in all, abscisic acid value was high in parasitic plants, that strip their hosts of the substances carried by phloem or xylem and lower in plants striping the hosts of their juices just from xylems. In studied parasites (for example, *O. hederae*, *L. squamaria* и *M. pretense*) the highest value of the abscisic acid is contained in the places of absorbing, especially in inflorescences. It is assumed that the high value of abscisic acid is associated with plant tissue, which suggests a high need for substances carried by the phloem. A possible role of abscisic acid in such tissues is discussed.[27]

CONCLUSION

The common toothwort is a perennial plant, which parasitizes on the roots of trees, usually hazel, alder, beech and bird cherry. The chemical composition of the common toothwort is underexplored very well. There is information that the common toothwort contains iridoids, phenylethanoid glycosides, organic acids, monosaccharides, fatty acids. The more thorough research of the bioactive substances was not conducted, so additional research of quantitative and especially qualitative profile is needed. There are no pharmacopeial monographs on *L. squamaria* in all the world's pharmacopeias. This plant is only used in traditional medicine for treating infertility, for example. Aqueous extract of the common toothwort raw material has antitumoral, biligenic and diuretic activities. It also stimulates cardiac, hepar and renal system functions.

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CONFLICTS OF INTEREST

None.

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GRAPHICAL ABSTRACT

ABOUT AUTHORS

- **Bokov Dmitry Olegovich**: Candidate of Pharmaceutical Sciences (Ph.D.), Institute of Pharmacy, Sechenov University; Laboratory of Food Chemistry, Federal Research Center of Nutrition, Biotechnology and Food Safety.
- **Barkalova Valentina Evgenievna**: Student, Faculty of Pediatrics, Siberian State Medical University.
- **Suslikova Maria Alekseevna**: Student, Institute of Pharmacy, Sechenov University.
- **Sokhin Dmitry Mikhailovich**: Student, Institute of Pharmacy, Sechenov University.
- **Kakhramanova Sabina Dzheykhunovna:** PhD student, Department of State Pharmacopoeia and pharmacopoeia analysis, Federal State Budgetary Institution "Scientific Centre for Expert Evaluation of Medicinal Products"; Institute of Pharmacy, Sechenov University.
- **Rendyuk Tamara Danilovna**: Candidate of Pharmaceutical Sciences (Ph.D.), Associate Professor, Associate Professor, Institute of Pharmacy, Sechenov University.
- **Strelyaeva Angelina Vadimovna**: Doctor of Pharmaceutical Sciences, Associate Professor, Professor, Institute of Pharmacy, Sechenov University.
- **Antsyshkina Alla Mikhailovna:** Candidate of Pharmaceutical Sciences (Ph.D.), Associate Professor, Associate Professor, Institute of Pharmacy, Sechenov University.
- **Balobanova Natalya Petrovna:** Candidate of Pharmaceutical Sciences (Ph.D.), Associate Professor, Associate Professor, Institute of Pharmacy, Sechenov University.
- **Prostodusheva Tatyana Vladimirovna:** Candidate of Pharmaceutical Sciences (Ph.D.), Associate Professor, Associate Professor, Institute of Pharmacy, Sechenov University.
- **Grikh Victoria Vladimirovna:** Candidate of Pharmaceutical Sciences (Ph.D.), Associate Professor, Institute of Pharmacy, Sechenov University.

- **Krasnyuk Ivan Ivanovich (junior):** Doctor of Pharmaceutical Sciences, Professor, Head of Department of Analytical, Physical and Colloid Chemistry, Institute of Pharmacy, Sechenov University.
- **Marakhova Anna Igorevna**: Doctor of Pharmaceutical Sciences, Professor, Head of Institute of Biochemical Technology and Nanotechnology, Peoples' friendship university of Russia (RUDN University).
- **Moiseev Dmitry Vladimirovich:** Doctor of Pharmaceutical Sciences, Associate Professor, Head of the Chair of Standardization of Medicines, Vitebsk State Medical University.

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