ISSN 2522-9680
УДК 615.322.61.57.014
4'2023

Фітотерапія Часопис

Науково-практичне фахове видання

Електронна сторінка журналу –
phytotherapy.vernadskyjournals.in.ua

Видавничий дім «Гельветика» 2023

ISSN 2522-9680 DOI: 10.33617

ЗМІСТ / CONTENTS

МЕДИЦИНА. ФАРМАЦІЯ
MEDICINE. PHARMACEUTICAL

МЕДИЦИНА. ФАРМАЦІЯ
MEDICINE. PHARMACEUTICAL

ФІЗИЧНА ТЕРАПІЯ. ЕРГОТЕРАПІЯ. ДИСКУСІЇ
PHISICAL THERAPY. ERGOTHERAPY. DISCUSSIONS

ФІЗИЧНА ТЕРАПІЯ. ЕРГОТЕРАПІЯ. ДИСКУСІЇ
PHISICAL THERAPY. ERGOTHERAPY. DISCUSSIONS

БІОЛОГІЯ. ФАРМАЦІЯ
BIOLOGICAL. PHARMACEUTICAL

БІОЛОГІЯ. ФАРМАЦІЯ
BIOLOGICAL. PHARMACEUTICAL

UDC 615.322035:615.89

Nadiya GORCHAKOVA
Ph.D. in Medicine, Professor, Professor of the Department of Pharmacology, O.O. Bogomolets National Medical University, Beresteyskyi ave., 34, Kyiv, Ukraine, 03057 (gorchakovan1941@gmail.com)
***ORCID:** 0000-0001-7311-7347*
***SCOPUS:** 7003895729*

Igor BELENICHEV
Ph.D. in Biology, Professor, Head of the Department of Pharmacology and Medical Formulation with Course of Normal Physiology, Zaporizhzhia State Medical and Pharmaceutical University, Stalevariv str., 31, Zaporizhzhia, Ukraine, 69035 (i.belenichev1914@gmail.com)
***ORCID:** 0000-0003-1273-5314*
***SCOPUS:** 6602434760*

Tatyana HARNYK
Ph.D. in Medicine, Professor, Professor of the Department of Physical Education, Sports and Human Health, V.I. Vernadskyi Tavria National University, John McCain str., 33, Kyiv, Ukraine, 01042 (phitotherapy.chasopys@gmail.com)
***ORCID:** 0000-0002-5280-0363*
***SCOPUS:** 6508229538*

Olena SHUMEYKO
Ph.D. in Medicine, Associate Professor of the Department of Pharmacology, O.O. Bogomolets National Medical University, Beresteyskyi ave., 34, Kyiv, Ukraine, 03057 (ashu28051972@gmail.com)
***ORCID:** 0000-0003-0655-0911*

Olena KLYMENKO
Ph.D. in Medicine, Associate Professor of the Department of Pharmacology, O.O. Bogomolets National Medical University, Beresteyskyi ave., 34, Kyiv, Ukraine, 03057 (klymenkoolena75@gmail.com)
***ORCID:** 0000-0002-2537-7029*

To cite this article: Gorchakova N., Belenichev I., Harnyk T., Shumeiko O., Klymenko O. (2023). Membranotropna diia fitopreparativ [Membranotropic action of Phytodrugs]. *Fitoterapiia. Chasopys – Phytotherapy. Journal,* 4, 11–16, doi: 10.32782/2522-9680-2023-4-11

MEMBRANOTROPIC EFFECT OF PHYTODRUGS

Actuality. *The article, based on its own research and literature sources, presents data on the effect of herbal medicines, primarily on ion channels. Membranotropic action is also associated with receptors, enzymes, signaling systems. At the same time, the works of recent years link the effect of herbal drugs specifically on ion channels, therefore the article primarily focuses on the effects of herbal drugs on ion channels, focusing on the role of ion channels, the difference in their structure, and the importance in the mechanism of action of herbal drugs. It is in the modern pharmacotherapy of neurological, cardiovascular and other diseases that herbal remedies are often included due to their ability to increase the effectiveness of traditional pharmacotherapy and low toxicity and cost.*

The purpose of the work – *the goal of the work is to show the membranotropic effect of herbal drugs based on their effect on ion channels.*

Material and methods. *Were performed an analysis of domestic and foreign literature and collected information from printed and online publications. Properties and types of potassium, calcium, and sodium channels are determined.*

Research results. *The effect of herbal drugs on these channels, the connection with their pharmacological properties is shown. The ability of herbal drugs to influence potassium, calcium, and sodium channels indicates the membranotropic effect of the drugs.*

Conclusions. *Thus, herbal drugs, as well as synthetic agents, can have a membranotropic effect, which explains their cardio and neurotropic effect. The membranotropic action of these agents is due mainly to the effect on potassium and calcium channels.*

Key words: *phytodrugs, potassium, calcium, sodium channels, membranotropic effect.*

Надія ГОРЧАКОВА
доктор медичних наук, професор, професор кафедри фармакології, Національний медичний університет імені О. О. Богомольця, просп. Берестейський, 34, м. Київ, Україна, 03057 (gorchakovan1941@gmail.com)
ORCID: *0000-0001-7311-7347*
SCOPUS: *7003895729*

Ігор БЄЛЕНІЧЕВ
доктор біологічних наук, професор, завідувач кафедри фармакології та медичної рецептури з курсом нормальної фізіології, Запорізький державний медико-фармацевтичний університет, вул. Сталеварів, 31, м. Запоріжжя, Україна, 69035 (i.belenichev1914@gmail.com)
ORCID: *0000-0003-1273-5314*
SCOPUS: *6602434760*

Тетяна ГАРНИК
доктор медичних наук, професор, професор загальновузівської кафедри фізичного виховання, спорту і здоров'я людини, Таврійський національний університет імені В. І. Вернадського, вул. Джона Маккейна, 33, м. Київ, Україна, 01042 (phitotherapy.chasopys@gmail.com)
ORCID: *0000-0002-5280-0363*
SCOPUS: *6508229538*

Олена ШУМЕЙКО
кандидат медичних наук, доцент кафедри фармакології, Національний медичний університет імені О. О. Богомольця, просп. Берестейський, 34, 03057, м. Київ, Україна (ashu28051972@gmail.com)
ORCID: *0000-0003-0655-0911*

Олена КЛИМЕНКО
кандидат медичних наук, доцент кафедри фармакології, Національний медичний університет імені О. О. Богомольця, просп. Берестейський, 34, м. Київ, Україна, 03057 (klymenkoolena75@gmail.com)
ORCID: *0000-0002-2537-7029*

Бібліографічний опис статті: Горчакова Н., Бєленічев І., Гарник Т., Шумейко О., Клименко О. (2023). Мембранотропна дія фітопрепаратів. *Фітотерапія. Часопис,* 4, 11–16, doi: 10.32782/2522-9680-2023-4-11

МЕМБРАНОТРОПНА ДІЯ ФІТОПРЕПАРАТІВ

Актуальність. *У статті на підставі власних досліджень і джерел літератури наведені дані щодо впливу лікарських засобів рослинного походження, насамперед на іонні канали. Мембранотропна дія також пов'язана з рецепторами, ферментами, сигнальними системами. Разом із тим роботи останніх років пов'язують вплив рослинних препаратів саме на іонні канали, тому першочергово у статті акцентується увага на дії фітопрепаратів передусім на іонні канали, різниці їх структури і значенні в механізмі дії фітопрепаратів. Саме сучасну фармакотерапію неврологічних, серцево-судинних та інших хвороб часто доповнюють фітозасобами завдяки їх здатності підвищувати ефективність традиційної фармакотерапії і малої токсичності та вартості.*

Мета роботи *– показати мембранотропну дію фітопрепаратів на підставі їх впливу на іонні канали.*

Методи дослідження. *Був проведений аналіз вітчизняної і зарубіжної літератури, відомості з друкованих та інтернет-видань. Визначені властивості й види калієвих, кальцієвих, натрієвих каналів.*

Результати дослідження. *Показано вплив фітопрепаратів на ці канали, зв'язок з їх фармакологічними властивостями. Можливості рослинних препаратів впливати на калієві, кальцієві, натрієві канали свідчать про мембранотропну дію препаратів.*

Висновки. *Фітопрепарати, як і синтетичні засоби, можуть володіти мембранотропним впливом, що пояснює їх кардіо- та нейротропну дію. Мембранотропна дія цих засобів обумовлена здебільшого впливом на калієві та кальцієві канали.*

Ключові слова: *фітопрепарати, калієві, кальцієві, натрієві канали, мембранотропна дія.*

Aktuality. The membranotropic action of the drugs largely underlies their specific activity, neurotropic, cardiotropic and other types of action. during its implementation of a specific effect, attention was paid to the role of ion channels of messenger enzymes and certain signaling systems that started the reaction (Vislobokov et al., 2010).

Study purpose. Membranotropic activity is associated with thiolde components of the sulfide system and nitric oxide (Belenichev et al., 2020), revealing the

pharmacological properties of metabolitotropic drugs, which include phytoremedies (Belenichev et al., 2020).

Research materials and methods. Analyzing the effect of most herbal drugs, attention was paid to their significant effect on potassium channels. Potassium cations have a transmembrane gradient value, most of these ion channels are potential-dependent, although there are also potential-independent forms, a certain part of potassium channels are calcium-dependent and ATP-dependent (Mamchur et al., 2016).

Research results and discussion. Potassium channels, like sodium and calcium channels, are transmembrane proteins that selectively pass potassium ions, moving along an electrochemical gradient at a certain speed. Potassium channels have 4 alpha subunits and specialized formation segments:

– a pore filled with water and permeable to potassium;

– a selectivity filter that allows only potassium;

– the permeation mechanism, which switches to the open and closed state in response to changes in the membrane potential or to ligand binding.

In the structure of the channel there are areas responsible for selectivity, opening of the channel. Knowing the structure of the channels allows you to find means that allow you to use potassium channels more efficiently. There are many existing codes for potassium channels, because potassium channels are also found in mitochondria. These channels have a main subunit with S5-S6 segments or their analogues, which indicate ion selectivity, interaction with drugs (Pogilova et al., 2016).

Separately, three types of potassium channels are distinguished:

– channels with six transmembrane segments and one pore that vary genetically. A family of calcium-dependent channels related to the genes KCNA (Shaker), KCNB (Shab), KCNC (Shaker), KCND (Shal), hERG with the human gene, Ca^{2+}-activated K^+ channels and depolarization-activated KCNQ channels;

– channels with two transmembrane fragments and one pore – K^+ channels of internal rectification, consisting of an alpha subunit with two transmembrane segments M1 and M2 and a transforming linker;

– canals with four segments and two pores.

The channel filter contains carboxyl atoms of amino acids and passes potassium ions, but does not pass sodium ions because the pore diameter is too wide for them to provide energetic hydration of sodium ions. The selectivity of potassium channels, wherever they are, are located similarly. It is the search for pharmacological agents that allows us to selectively find drugs that correct the work of potassium channels, relative potentials of dependent potassium channels linked to genes. This applies to channels with six transmembrane elements and one pore.

Potential-controlled K^+ channels are distinguished by their functions, among which the main group are channels of delayed (outgoing) rectification, inward rectification, Ca^{2+-} sensitive, K^+ ATP-sensitive, K^+ channels, Na^+ activated R^+ channels sensitive to changes in cell volume, K^+ channels of the type And receptor-controlled potassium channels.

Potassium channels with heavy intermediate and low conductance are distinguished. there are mechanosensitive channels that open upon mechanical stimulation (Cukkemane et al., 2011).

They are believed to consist of four subunits that are in a tegrammer. The outer mouth of the P-cycle and adjacent residues of the S5-S6 segments are the binding site for toxins and blockers of K^+ channels located near the pore and responsible for inactivation.

The antiarrhythmic activity of the liquid extract and tincture of hawthorn and dog nettle, along with other aspects of their effects, is known from herbal drugs. The antiarrhythmic activity of these agents is based on the blockade of potassium channels (Karomatov et al., 2017).

The medicinal properties of these herbal drugs were determined during the creation of the drug Kratal, which, in addition to extracts of hawthorn and dog nettle, included taurine – Kratal has antianginal, cardio- and neuroprotective effects (Gorchakova, 2001).

In Chinese medicine, there are a number of herbal drugs that can block potassium channels and have an antihypertensive effect. These include phytodrugs of red beetroot, hawthorn root, bitter gourd, viburnum berries, and calendula flowers. These herbal drugs not only lowered blood pressure but also improved arterial blood circulation (Cao et al., 2021). Chinese herbal drugs, which have cardiotonic effects and some antiarrhythmic effects due to their effects on potassium channels, were tested for cardiotoxicity by their effects on Herg receptors. These drugs had no cardiotoxicity by affecting the Herg gene (Choi et al., 2019).

Ferulin plant oil has a vasodilatory effect due to the blockade of potassium channels, which was demonstrated in experiments on isolated rabbit aorta (Esmaeili et al., 2020).

When studying the effect on ATP-dependent potassium channels, there are now reports about herbal remedies that can have a hypoglycemic effect and that can be used in the complex treatment of diabetes. Among these plants, horsetail leaves, nettles, dandelions, blueberries, lingonberries, bean pods, almonds, hazelnuts, and others

are noted. drugs from these plants inhibit the absorption of glucose in the intestines, increase insulin reserves. Their mechanism of action is similar to the mechanism of action of sulfonamide derivatives and is associated with the blockade of ATP-dependent potassium channels, i.e., it is implemented membranotropically (Al Kury, 2023).

Many of these herbal drugs also have a beneficial effect on the digestive tract. Flavonoids have long been used in Chinese medicine to treat hypertension (Cao et al., 2021). The benefit of including flavonoids in the complex treatment of hypertension has been proven by clinical and clinical studies.

The inclusion of phytodrugs in the treatment regimen for hypertension in the elderly was especially useful. Very often, these agents had a positive effect on the function of the kidneys, the digestive tract and the central nervous system. Some of these phytoremedies simultaneously blocked sodium channels, and sometimes calcium channels, which expands the indications for use in medical practice. Ferulin oil was obtained from ferula plants, which was predicted to have a vasodilating effect. The complex herbal drug with the conventional name ferulin, due to the blockade of potassium channels, has a vasodilating effect, which was confirmed in experiments on an isolated rat aorta (Esmaeili et al., 2020).

In order to check the possibility of cardiotoxicity of herbal remedies used in cardiology, experiments were conducted on kidney tissues of embryos in which the herg gene, which is associated with potassium channels, was identified. In these experiments, 52 herbal drugs were tested. The absence of cardiotoxicity in cardiac herbal drugs was established, because they did not affect the herg gene and did not change the permeability of potassium channels (Choi et al., 2019).

Medicinal products obtained from sage, vaginal mustard, and St. John's wort, from which medicines are prepared that affect Ca, K, Na channels and fast and slow current receptors (Huang et al., 2019). Extracts from hawthorn fruits, bitter gourd, and lettuce were compared for potassium channel blockade and blood pressure. It has been shown that in equivalent concentrations they can have a comparable antihypertensive effect (Jitendra Joshi & Ashok Shelke, 2021).

Phytodrugs in food affect both potassium channels and TRPV receptors, which regulate body weight and blood pressure. Later, a correlation with the effect on these channels of onion terminals and common wort is shown, which means the elimination of diseases that block potassium channels and explains the effect of herbal medicines in a new way (Herbrechter et al., 2020).

It is interesting to note that herbal drugs with a calming effect on the central nervous system can simultaneously block potassium channels and NMDA receptors, which is observed when using peony root, dog nettle, rosehip fruits, sage grass and fennel seeds (Lin & Hsieh, 2021).

The herbal remedy of cilantro fruit blocks potassium channels of the KCNQ family and has efficacy not only in hypertension but also in encephalopathy (Manville & Abbott, 2019).

A herbal drug from Sophora root can block potassium channels and simultaneously increase NO levels, which explains its value in the treatment of hypertension and coronary heart disease (Manville et al., 2019).

Fern drugs also increase NO and heat shock proteins by blocking potassium channels. In addition, during inflammation, the drug reduces tumor necrosis factor α and pro-inflammatory interleukins (Mao et al., 2019).

In recent years, considerable attention has been paid to fennel and ginger phytoremedies, which have a complex mechanism of action, including the blockade of potassium channels, the effect on the content of NO and ATP, which are prescribed for hypertension, diabetes, and convulsions (Redford & Abbott, 2022).

Special importance is attached to ATP-dependent potassium channels, because herbal drugs that act on these channels can be prescribed for diabetes. Their mechanism of action is similar to glimepiride and they can be prescribed together with it. The phytodrug berberine has a similar effect.

A randomized, placebo-controlled trial was conducted. One group of patients was given barberine, the other a placebo. Berberine is a glucose-dependent insulin agent for the treatment of diabetes, but does not cause hypoglycemia, although it is less sensitive to K-sensitive channels and membranes (Zhao et al., 2021).

In recent years, the transmembrane effect of plants has been associated with the effect on calcium channels. Calcium ions in nerve cells and in the myocardium play a significant role. They participate in the initiation of the action potential, regulate rhythmic activity, gene expression, and, as secondary messengers, participate in the regulation of intracellular biochemical processes, promote the release of neurotransmitters in presynaptic membranes. Potential-dependent Ca^{2+} channels identified in the membrane of cells with electrical excitability (cardiac muscle, smooth muscle, neurons, endocrine cells). Therefore, potential-dependent and Ca^{2-} dependent inactivation are distinguished, which depends on the calcium content during the depolarizing pulse. Calcium channels can be blocked by cationic drugs and plant compounds (Timmermann et al., 2001). They are well permeable to divalent and not monovalent cations.

The selective dimer of Ca^{2+} channels can contain two areas of communication with cations – external and

internal. Calmodulin can be in the structure of a calcium channel, a similar part of the structure of calcium channels is similar to sodium channels and has five protein subunits: α1, α2, δ, γ. It is the α1 subunit that carries more functions. Calcium channels are divided into low-threshold (LVA), in which channel activation develops above the resting potential, and high-threshold (HVA), when activation develops above the action potential (Pahlavan et al., 2018).

Hypobaric hypoxia is more common in climbers and high-altitude climbers and has the ability to impair cognitive function. Ginkgo Biloba is a herbal remedy used for various diseases. It improves cognitive functions, reduces stress and is widely used as a medicine. It is indicated for neurological disorders. At the same time, the functions of the hippocampus improve, which is confirmed by the study of molecular mechanisms and morphology.

Ginkgo biloba modulates the activity of calcium-activated potassium channels, reducing glutamate excitotoxicity and apoptosis of some synaptic pathways. The drug can affect the calcium conductivity of activated potassium channels, activates extracellular signals of the regulation of kinase II and CAMP bonds, sexuterpene lactones – leucosine and achinine, which establishes their leading role in the implementation of the antispasmodic effect of the extract (Arias-Durán et al., 2020).

Tryptophan plays a role in the permeability of calcium channels, the activity of AMP, the interaction of the activity of peptides. That is, tryptophan actively interacts even with negatively charged polysaccharide lipids and other membrane components. Thanks to it, membranotropic ones are determined peptides that play a role in bactericidal action (Khemaissa et al., 2022).

Conclusion. Thus, phytodrugs as well as synthetic agents, can have a membranotropic action, which explains their cardio and neurotropic action. The membranotropic action of these agents is due mainly to the effect on potassium and calcium channels.

REFERENCES

AL Kury, L.T. (2023). Modulatory effect of medicinal plants and their active constituents on ATP-sensitive potassium channels (KATP) in diabetes. *Pharmaceuticals*, *16* (4), 523. https://doi.org/10.3390/ph16040523.

Arias-Durán, L., Estrada-Soto, S., Hernández-Morales, M., Chávez-Silva, F., Navarrete-Vázquez, G., León-Rivera, I., Perea-Arango, I., Villalobos-Molina, R., & Ibarra-Barajas, M. (2020). Tracheal relaxation through calcium channel blockade of achillea millefolium hexanic extract and its main bioactive compounds. *Journal of Ethnopharmacology*, *253*, 112643. https://doi.org/10.1016/j.jep.2020.112643.

Belenichev, I.F., Chekman, I.S., Nagornaya, E.A., Gorbacheva, S.V., Gorchakova, N.A., & Buhtiyarova, N.V. (2020). *Tiol-disulfidnaya sistema: rol v endogennoy tsito- i organoprotektsii, puti farmakologicheskoy modulyatsii.* Kyiv: Yuston, 232 pp.

Cao, Y., Xie, L., Liu, K., Liang, Y., Dai, X., Wang, X., Lu, J., Zhang, X., & Li, X. (2021). The antihypertensive potential of flavonoids from Chinese Herbal Medicine: A Review. *Pharmacological Research*, *174*, 105919. https://doi.org/10.1016/j.phrs.2021.105919.

Choi, S., Kwon, O.-B., Lee, S., Seo, C.-S., & Shin, H.-K. (2019). Cardiac safety assessment of medicinal herbal formulas using herg-HEK 293 cell. *Journal of Korean Medicine*, *40* (2), 94–105. https://doi.org/10.13048/jkm.19020.

Cukkemane, A., Seifert, R., & Kaupp, U. B. (2011). Cooperative and uncooperative cyclic-nucleotide-gated ion channels. *Trends in Biochemical Sciences*, *36* (1), 55–64. https://doi.org/10.1016/j.tibs.2010.07.004.

Esmaeili, H., Esmailidehaj, M., Entezari Zarch, S., & Azizian, H. (2020). Role of the potassium channels in vasorelaxant effect of asafoetida essential oil. *Avicenna J Phytomed*, *10* (4), 407–416.

Gorchakova, N.A. (2001). Primenenie kratala v kompleksnoy terapii bolnyih ishemicheskoy boleznyu serdtsa i neyrotsirkulyatornoy distoniey. *Zdorove Zhenschinyi*, *2* (6), 94–96.

Herbrechter, R., Beltrán, L.R., Ziemba, P.M., Titt, S., Lashuk, K., Gottemeyer, A., Levermann, J., Hoffmann, K.M., Beltrán, M., Hatt, H., Störtkuhl, K.F., Werner, M., & Gisselmann, G. (2020). Effect of 158 herbal remedies on human TRPV1 and the two-pore domain potassium channels KCNK2, 3 and 9. *Journal of Traditional and Complementary Medicine*, *10* (5), 446–453. https://doi.org/10.1016/j. jtcme. 2020.04.005.

Huang, Y., Ma, S., Wang, Y., Yan, R., Wang, S., Liu, N., Chen, B., Chen, J., & Liu, L. (2019). The role of traditional Chinese herbal medicines and bioactive ingredients on ion channels: A brief review and prospect. *CNS & Neurological Disorders – Drug Targets*, *18* (4), 257–265. https://doi.org/10.2174/ 1871527317666181026165400.

Jitendra Joshi, N., & Ashok Shelke, S. (2021). Medicinal plants as calcium-channel blockers against hypertension. *International Journal of Pharmaceutical Sciences Review and Research*, *67* (1), 118–124. https://doi.org/10.47583/ijpsrr. 2021.v67i01.020.

Karomatov, I.D., Davlatova, M.S., & Amonov, M.K. (2017). Perspektivy primeneniya v kardiologicheskoy i obshchevrachebnoy praktike lekarstvennogo rasteniya boyaryshnik [Prospects for the use in the cardiological and general medical practice of the medicinal plant hawthorn]. Biologiya i integrativnaya meditsina. *Biologiya i Integrativnaya Meditsina*, (1), 251–276.

Khemaissa, S., Walrant, A., & Sagan, S. (2022). Tryptophan, more than just an interfacial amino acid in the membrane activity of cationic cell-penetrating and antimicrobial peptides. *Quarterly Reviews of Biophysics*, *55*. https://doi.org/10.1017/s0033583522000105.

Lin, C.-H., & Hsieh, C.-L. (2021). Chinese herbal medicine for treating epilepsy. *Frontiers in Neuroscience*, *15* (798), 195. https://doi.org/10.3389/fnins.2021.682821.

Mamchur, S.E., Khomenko, E.A., Bokhan, N.S., Romanova, M.P., & Yakubik, G.G. (2016). Acuracy of topical diagnosis of ventricular ectopic arrhythmias using non-invasive mapping. *Complex Issues of Cardiovascular Diseases*, (3), 75–80. https://doi.org/10.17802/2306-1278-2016-3-75-80 (in Russian).

Manville, R.W., & Abbott, G.W. (2019). Cilantro leaf harbors a potent potassium channel–activating anticonvulsant. *The FASEB Journal*, *33* (10), 11349–11363. https://doi.org/10.1096/fj.201900485r.

Manville, R.W., van der Horst, J., Redford, K.E., Katz, B.B., Jepps, T.A., & Abbott, G.W. (2019). KCNQ5 activation is a unifying molecular mechanism shared by genetically and culturally diverse botanical hypotensive folk medicines. *Proceedings of the National Academy of Sciences*, *116* (42), 21236–21245. https://doi.org/10.1073/pnas.1907511116.

Mao, T., Zhang, J., Qiao, Y., Liu, B., & Zhang, S. (2019). Uncovering synergistic mechanism of Chinese herbal medicine in the treatment of atrial fibrillation with obstructive sleep apnea hypopnea syndrome by Network Pharmacology. *Evidence-Based Complementary and Alternative Medicine*, *2019*, 1–13. https://doi.org/10.1155/2019/8691608.

Pahlavan, S., Tousi, M.S., Ayyari, M., Alirezalu, A., Ansari, H., Saric, T., & Baharvand, H. (2018). Effects of hawthorn (crataegus pentagyna) leaf extract on electrophysiologic properties of cardiomyocytes derived from human cardiac arrhythmia-specific induced pluripotent stem cells. *The FASEB Journal*, *32* (3), 1440–1451. https://doi.org/10.1096/fj.201700494rr.

Pogilova, E.V., Novikov, V.E., & Levchenkova, O.S. (2016). The mitochondrial ATP-dependent potassium channel and its pharmacological modulators. *Reviews on Clinical Pharmacology and Drug Therapy*, *14* (1), 29–36. https://doi.org/10.17816/rcf14129-36.

Redford, K.E., & Abbott, G.W. (2022). KCNQ potassium channels as targets of Botanical Folk Medicines. *Annual Review of Pharmacology and Toxicology*, *62* (1), 447–464. https://doi.org/10.1146/annurev-pharmtox-052120-104249.

Timmermann, D.B., Westenbroek, R.E., Schousboe, A., & Catterall, W.A. (2001). Distribution of high-voltage-activated calcium channels in cultured γ-aminobutyric acidergic neurons from mouse cerebral cortex. *Journal of Neuroscience Research*, *67* (1), 48–61. https://doi.org/10.1002/jnr.10074.

Vislobokov, I.A., Ipatov, D.Y., Galenko-Yaroshevskiy, A.P., & Shabanov, D.P. (2010). *Membranotropnoe deystvie farmakologicheskih sredstv*. Prosveschenie Yug. 528 pp.

Zhao, M.-M., Lu, J., Li, S., Wang, H., Cao, X., Li, Q., Shi, T.-T., Matsunaga, K., Chen, C., Huang, H., Izumi, T., & Yang, J.-K. (2021). Berberine is an insulin secretagogue targeting the KCNH6 potassium channel. *Nature Communications*, *12* (1). https://doi.org/10.1038/s41467-021-25952-2.

Стаття надійшла до редакції 27.11.2023
Стаття прийнята до друку 26.12.2023

The authors declare no conflict of interest.

Contribution of the authors:

Gorchakova N.O. – data collection and analysis, article writing, critical review, final approval of the article;
Belenichev I.F. – data collection and analysis, correction of the article, annotations, conclusions;
Harnyk T.P. – concept and design of the work, correction of the article, critical review;
Shumeiko O.V. – data collection and analysis, participation in writing the article;
Klymenko O.V. – data collection and analysis,participation in writing the article.

Email address for correspondence with the authors:
gorchakovan1941@gmail.com