DOI: 10.17816/KMJ2021-960

Medicines and life (to the 100th anniversary of Professor Irina Vitalievna Zaikonnikova)

R.S. Garayev, A.U. Ziganshin*

Kazan State Medical University, Kazan, Russia

Abstract

Irina Vitalevna Zaikonnikova is a well-known Soviet pharmacologist, headed the Department of Pharmacology of the Kazan State Medical Institute between 1968 and 1989. The topic of I.V. Zaikonnikova's Ph.D. thesis was "The influence of dikain on blood vessels and its relationship with adrenaline". In her dissertation, Irina Vitalievna found that dicaine dilates blood vessels in low concentrations and causes their constriction in high concentrations. The thesis was successfully defended in 1947. In the 50s of the last century in Kazan, for the first time in the Soviet Union, the study of the biological activity of organophosphorus compounds was begun. A large experimental material concerning the correlation between the biological activity and chemical structure of compounds was summarized in his doctoral dissertation "Pharmacological characteristics of a number of dialkylphosphinic acid esters", which I.V. Zaikonnikova defended in 1968. At the Department of Pharmacology, which she headed since 1968, a close-knit team was formed, united by a common interest — the search and development of new potential drugs. This major work resulted in the creation of cidiphos, glycifon, phosphabenzide, and dimephosphon — organophosphorus compounds of a new type, which mechanism of action is not associated with inhibition of the activity of acetylcholinesterase. In addition, drugs that did not belong to organophosphates were created — the daytime tranquilizer mebikar, a regeneration stimulator with the immunomodulatory effect of xymedon. At present, the Department of Pharmacology of Kazan State Medical University continues the scientific traditions of our outstanding predecessors.

Keywords: I.V. Zaikonnikova, Pharmacology, Department of Pharmacology, Kazan State Medical University.

For citation: Garayev R.S., Ziganshin A.U. Medicines and life (to the 100th anniversary of Professor Irina Vitalievna Zaikonnikova). *Kazan Medical Journal.* 2021; 102 (6): 960–963. DOI: 10.17816/KMJ2021-960.

Irina Vitalievna Zaikonnikova is a well-known Soviet pharmacologist and head of the Department of Pharmacology of the Kazan State Medical Institute from 1968 to 1989.

From childhood, Irina was surrounded by medicines, not because she was often sick, but because she was born in the family of the famous Kazan pharmacist Vitaly Dmitrievich Gorshunov, who headed several large pharmacies in Kazan. Her childhood games were associated with preparing medicines and treating dolls and plush toy animals.

After graduation, it was no coincidence that Irina Vitalievna entered the Kazan State Medical Institute (KSMI). Her student years at the university fell during difficult war times. The development of clinical disciplines often took place in hospitals. At this time, she helped treat wounded Soviet soldiers.

In 1944, after graduating from KSMI, I.V. Zaikonnikova was assigned to the graduate school at the Department of Pharmacology. It was headed by Associate Professor Maria Alexandrovna Aluf. Scientific research at the department was conducted in two directions: (1) the study of the mechanism of action of local anesthetics and their relationship with adrenaline and (2) the search for new herbal medicines and chemical synthesis.

The dissertation of I.V. Zaikonnikova was titled "The influence of dikain on blood vessels and its relationship with adrenaline." The local anesthetic properties of dicaine were well studied at that time; however, its effect on the vessels and combined use with adrenaline were unknown. To determine the effect of drugs on the vessels, the mechanism of their action directly on the vascular wall was examined. For this purpose, the perfusion in the vessels of a frog's foot was used according to the Levene method and the vessels of the isolated ear of the rabbit according to the Pisemsky method. I.V. Zaikonnikova also studied the effect of dicaine on the heart of the rabbit and the effect on the arterial pressure of the cat.

I.V. Zaikonnikova's dissertation research revealed that dicaine dilates blood vessels at low concentrations and causes narrowing at high con-

For correspondence: auziganshin@gmail.com Received 15.10.2021; accepted 29.10.2021; published 15.12.2021.

centrations. Dicaine and adrenaline were found to enhance their effects, similar to the relationship of novocaine with adrenaline. The dissertation was successfully defended in 1947. The results of I.V. Zaikonnikova's research were important for the successful use of dicaine in medical practice, and it replaced cocaine.

In the 1950s in Kazan, for the first time in the Soviet Union, the study of the biological activity of organic phosphorus (OP) compounds was started. These studies were conducted at the Institute of Organic and Physical Chemistry under the guidance of Academician A.E. Arbuzov and at the Department of Pharmacology of KSMI under the guidance of Associate Professor M.A. Aluf. The first compounds, mixed esters of alkylphosphinic acids, which were synthesized at the Kazan Institute of Chemical Technology under the direction of Alexander Ivanovich Razumov, were representatives of compounds with an anticholinesterase mechanism of action. The most active cholinesterase inhibitor was mixed ethyl, para-nitrophenyl ester of ethylphosphinic acid [1]. The result of the joint investigation of chemists and pharmacologists introduced into practical medicine the new drug armine, as an antiglaucoma agent (1954). Later, A.I. Razumov and O.A. Mukhacheva synthesized a new series of derivatives of dialkylphosphinic acid esters.

I.V. Zaikonnikova also analyzed large amounts of experimental materials concerning the dependence of the biological activity of compounds on their chemical structure, which gave rise to the creation of the original drug nibuphine. Nibuphine turned out to be less toxic than armine [2], which led to the development of the injectable form of nibuphine. Prior to this, FOS was applied only topically, mainly in the form of eye drops. Nibuphine proved to be an effective treatment for postoperative intestinal atony, and its use as a labor stimulant has been proven. The main pharmacological effects of nibuphine, in both experiment and clinic practice, were associated with its anticholinesterase action. Moreover, I.V. Zaikonnikova expressed the idea of the possibility of a direct stimulating effect of nibuphine on smooth muscle tone.

The results of I.V. Zaikonnikova's research were summarized in her doctoral thesis, "Pharmacological characteristics of a number of esters of dialkylphosphinic acids," which she successfully defended in 1968. During these years, the strategic direction of scientific research of the Department of Pharmacology was determined –"Research, study and implementation of new drugs" [3].

Contacts of pharmacologists with chemists have become wider. At the Institute of Organic and Physical Chemistry of the Kazan Scientific Center of the Russian Academy of Sciences, N.I. Rizpolozhensky synthesized diglycidyl esters of phosphonic and phosphoric acids, and its antitumor activity was established by I.A. Studentova. Based on the results of many years of research by the oncological group, created on the initiative of I.A. Studentova and I.V. Zaikonnikova, with the participation of the employees of the department and the central research laboratory of KSMI, cidiphos and glycifon, drugs for the treatment of cancer and precancerous skin diseases, were developed [4, 5]. I.V. Zaikonnikova devoted substantial energy to the introduction of these drugs in practical medicine, which lead to the organization of their production in the production association "Alga" (currently "Tatkhimfarmpreparaty" KPKhFO).

The neuro- and psychotropic properties of phosphorylacetic acid hydrazides, synthesized at the Kazan Institute of Chemical Technology R.I. Tarasova, were studied at the department led by G.F. Rzhevskaya. These studies formed the basis for the introduction of the new original tranquilizer phosphabenzide, which has an anti-alcohol effect [6]. Its production was established on the initiative of I.V. Zaikonnikova, thanks to her contacts at the Riga Pharmaceutical Association.

Together with I.A. Studentova, I.V. Zaikonnikova started the introduction of dimephosphone, an original drug with a wide spectrum of biological activity [7, 8]. It is important to emphasize that cidifos, glycifon, phosphabenzide, and dimephosphone are new types of FOS, and their mechanisms of action are not associated with the inhibition of acetylcholinesterase activity.

Studies of the employees of the Department of Pharmacology under I.V. Zaikonnikova aimed at exploring the biological activity of not only OP compounds. Thus, the daytime tranquilizer Mebicar is a derivative of bicyclic bisureas. It was synthesized at the ND Zelinsky Research Institute of Organic Chemistry, in Moscow. The psychotropic properties of Mebicar were studied at the department headed by I.E. Zimakova [9]. The drug was introduced into medical practice by I.V. Zaikonnikova and I.E. Zimakova and is currently produced at the Tatkhimfarmpreparaty KPKhFO.

Studies of the biological activity of several new pyrimidine derivatives synthesized by V.S. Reznik and employees at the A.E. Arbuzov Institute of Organic and Physical Chemistry, conducted at the Department of Pharmacology under the guidance of I.V. Zaikonnikova, culminated in the development and implementation of xymedon, a stimulator of the regenerative processes with an immunomodulatory effect [10, 11]. The drug is also currently produced at the Tatkhimfarmpreparaty KPKhFO.

Professor I.V. Zaikonnikova was widely known in the Soviet Union and beyond as a prominent scientist and talented organizer [12]. For the development of a dosage form of nucleases, developed by a team of employees of KSMI, she was awarded the State Prize of the Council of Ministers of the USSR. Irina Vitalievna received the high title of Honored Worker of the RSFSR, a medal named after the founder of Russian pharmacology N.P. Kravkov, for success in the development of pharmacology, numerous thanks, and diplomas.

At present, the Department of Pharmacology of Kazan State Medical University continues the scientific traditions established by our outstanding predecessors. Among them, of course, the brightest representative is Professor Irina Vitalievna Zaikonnikova, who devoted her life to the creation of new drugs to ensure the well-being of people.

Author contributions. R.S.G. was involved in the collection of information and preparation of the initial version. A.U.Z. contributed to the analysis, editing, and preparation of the final version.

Funding. The study had no external funding.

Conflict of interest. The authors declare no conflict of interest for the presented article.

REFERENCES

1. Aluf M.A. To the pharmacology of armin. *Farmakologiya i toksikologiya*. 1955; 18: 21–27. (In Russ.)

2. Afonskaya L.S., Zaikonnikova I.V., Rzhevskaya G.F., Studentsova I.A. To the mechanism of action of armin and nibufin. *Farmakologiya i toksikologiya*. 1963; 26: 184–189. (In Russ.)

3. Garayev R.S. The search for new organophosphorus drugs is the leading direction of scientific research of the Department of Pharmacology of KSMU. *Kazan Medical Journal*. 2008; 89: 585–590. (In Russ.)

4. Studentsova I.A., Garayev R.S. Toxicity and some biological effects of organophosphorus epoxides. *Eksperimental'naya i klinicheskaya farmakologiya*. 1996; 59: 31–33. (In Russ.)

5. Garaev R.S., Gilmutdinova V.R., Zalyalyutdinova L.N., Khasanov R.Sh. Long-term results of treatment of basal cell cancer with glitsifon ointment. *Kazan Medical Journal.* 2010; 91: 511–515. (In Russ.)

6. Semina I.I., Baychurina A.Z. Development of new potential drugs with psychotropic activity among phosphorylacetohydrazides and other phosphorylated carboxylic acids derivatives — priority area of kazan school of psychopharmacologists. *Kazan Medical Journal.* 2016; 97: 148–155. (In Russ.) DOI: 10.17750/KMJ2016-148.

7. Pikuza O.I., Zaikonnikova I.V., Studentsova I.A., Aleksandrova L.Ya. Experience of using dimephosphone in the complex therapy of pneumonia in newborns. *Pediatriya.* 1989; (3): 39–41. (In Russ.)

8. Ziganshina L.E., Studentsova I.A., Ziganshin A.U., Valeyeva I.Kh. The mechanism of action of dimephosphone. *Eksperimental'naya i klinicheskaya farmakologiya*. 1992; 55: 43–45. (In Russ.)

9. Kamburg R.A., Zaikonnikova I.V. Results of an experimental study and clinical use of the tranquilizer mebikar. *Farmakologiya i toksikologiya*. 1986; 49: 89–91. (In Russ.)

10. Tsibul'kin A.P., Slabnov Yu.D., Pozdeyev O.K., Cherepnev G.V., Garayev R.S., Ismayev Kh.I. Modeling the expression of key molecules of membranes of immunocompetent cells by pyrimidine derivatives: substantiation of the systemic nature of the immunopotentiating effect. *Immunologiya*. 1998; (4): 29–33. (In Russ.)

11. Cherepnev G.V., Garayev R.S., Tereshchenko V.Yu., Malyshev K.V. Immunomodulator Ximedon Reduces the Level of Induced DNA Damage in Bone Marrow and Peripheral Blood Cells: Possibilities of Immunogenetic Correction. *Eksperimental'naya i klinicheskaya farmakologiya.* 1999; 62: 31–35. (In Russ.)

12. Garayev R.S., Studentsova I.A. In memory of Irina Vitalievna Zaikonnikova. *Eksperimental'naya i klinicheskaya farmakologiya*. 1996; 59: 74. (In Russ.)