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COMPUTER RECOGNITION OF CHEMICAL SUBSTANCES BASED ON THEIR ELECTROPHYSIOLOGICAL CHARACTERISTICS

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The objective of this review was to analyze the results of electrophysiological studies of some biologically active chemicals in order to determine relationships between their chemical structures and effects that they produce. It was proposed to use these relationships to improve the logical module of biotechnical expert system that works using a module principle based on object-oriented and regression analysis. The data of electrophysiological studies of glutamatergic receptor antagonists, phenol- and indole-derivatives, purified from the spiders' venoms of *Arthropodae* species were analyzed in this work. Some characteristics of receptor blocking by these toxins have been used to demonstrate empirical relationships between the chemical structures of antagonists and their electrophysiological effects. Possibilities to apply such relationships for monitoring of harmful environmental pollutants, phenol- and indole derivatives, as well as for developing new methods of their qualitative and quantitative analysis are discussed.

Key words: toxins, receptor antagonists, transmembrane electric current, biological expert systems, electronic informational systems, bioinformatics.

Devices with automatic recognition of different objects are very actual in contemporary world [1]. Among them there are the large group of biotechnical information systems (IS) and devices for such tasks solution [1–12]. In our publication our developed electronic expert system (ExpS) was described for the registration and identification of the toxic organic substances, for example, in polluted environment with anthropogenic pollution: industrial, agricultural, military, due to the disasters and so on [11]. Here the continuation of these works is suggested. The works done were devoted to further perfection of logical unit of this biotechnical expert IS. In computer sciences the expert systems were studied usually together with knowledge bases as models of experts' behavior in a certain field of knowledge using the procedures of logical conclusion and decision making [1]. Knowledge bases, consequently, were seen as a set of facts and rules of logical conclusion in the chosen subject area of activity.

The suggested expert system obtains input signals with characteristics of different chemical substances and its logical unit solves the task of these substances identification (Fig. 1) [11]. This information expert system is aimed at distinguishing and identifying chemicals in contact with the detectors of this system that was patented [7, 11]. The architecture of this device was developed, the framework of the information expert system was created, and

its logic module identifies chemicals using the developed algorithm. The base of such algorithm may be formed by the following groups of methods: 1) statistical analyses [1, 2]; 2) methods of cluster analyses [1, 4]; 3) artificial neuronal network methods [1, 3]; 4) images processing [1, 5] and analyses as well as 5) substances identification using established qualitative empirical dependencies including ones based on the use of regression analyses methods. Such methods are successful likewise for biological objects analyses despite all the difficulties — their complexity, necessity of preliminary statistic processing of results, etc.

If necessary, the logic unit algorithm can be changed (or modified) without changing the system framework. From the point of view of software development, a software module was developed basing on approaches of object-oriented analysis. In the present work, it is proposed to pick up the last way as the basis of the logic module algorithm — using the empirical dependencies registered by Klyuchko O. As a demonstration of the developed method, the article presents its application to a number of active chemical agents.

Indeed, this is an attractive solution — to find a rule, a regularity which helps to "make a bridge" between "structure" and its "function", to find co-relations between characteristics of input signals in ExpS and chemical structures that have to be identified. Studying the experience of different chemicals electrophysiological investigations we had found a set of substances that may be suitable for such tasks solutions [13–107]. There are the experiments of electrophysiological investigations of some *Arthropodae* toxins. Indeed, some of these studied toxins had known chemical structures. Besides they have revealed electrophysiological activity, for

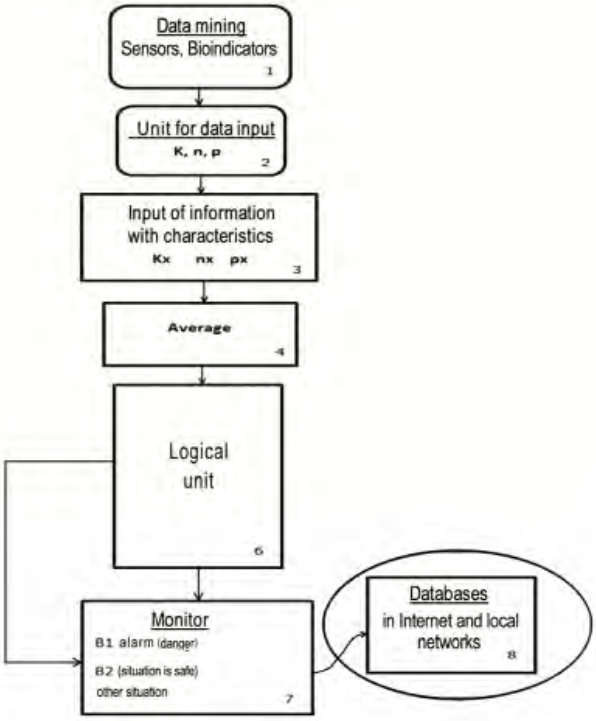


Fig. 1. **Biotechnical expert system**
Above: an algorithm of functioning of the expert system with the logical unit, the output data recording and the work of linked alarm subsystem. Below: interface for operator communication with expert analytic system; view of monitor screen (comments and instructions were written in Ukrainian for domestic use of device) [11]

example the toxins from the spiders *Nephila clavata* (JSTX-3 and others) and *Argiope lobata* (AR, ARN-1, ARN-2 and others) are known as antagonists of glutamate channel-receptor complexes (gCRC, CRC) in cell membranes. Chemical structures of these toxins are known: JSTX-3, AR are phenol derivatives, and ARN-1, ARN-2 are indole derivatives (Fig. 2) [33, 55–67]. The reactions of gCRC blocking by these toxins can be well studied using sodium salt of kainic acid (KK) that is agonist of gCRC causing non-inactivated transmembrane electric currents (KK-activated electric currents), so, the kinetic characteristics of blocking (modifying) effect can be studied well.

Electrophysiological effects of all studied toxins can be registered successfully on these non-inactivated KK-currents as exponential dependencies and they have well registered numerical characteristics. So, these substances have a set of their peculiarities that makes them attractive for the studying and our tasks solution.

Logical module: finding of empirical dependencies "effect" — "structure". In recent decades in neurophysiology, some researchers studed the influence of various chemical agents including organic compounds (derivatives of phenols and indoles) on transmembrane electrical chemo-activated currents. Huge amount of experimental results have been accumulated in this direction [13–107]. Among them there are the classic monographs by Prof. Kostyuk P. G. [68], Kryshtal O. A. [68], Magura I. S. [73], Skock V. I. [91], other researchers [13–67, 69–72, 74–107]. This huge experimental material allows us to make a number of generalizations that we will try to carry out basing on the results of the author's researches with colleagues [17, 48–67].

This enables us to solve the inverse problem, namely, the possibility to determine the approximate chemical structure of organic compound acting on the chemosensitive currents from the measured numerical characteristics of the currents *(*the "effect" — "structure" dependence study). And herein lies the difference from the direct problem — under the action of chemical compound with the known structure on the ionic currents the obtained effect is investigated (study of dependence "structure" — "effect"*).*

To find to find the inverse problem solution, we studied the characteristics of chemosensitive transmembrane ionic currents depending on the influence on them of phenols and indoles derivatives with known structure, namely the toxins of some *Arthropodae* species.

Empirical dependencies "effect" — "structure" were studied on the basis registered experimental data and their processing using the methods of regression analyses, other types of analyses. Empirical diagrams were done and they characterized such dependencies. In such a way the new methods of qualitative and quantitative analyses were developed [61–64].

Some of these works were described below. We suggested: 1) brief review of some known methods of qualitative and quantitative analyses for phenol and its derivatives identification [108–111]; 2) the review of investigations of toxins from *N. clavata* (JSTX-3 and others) and *A. lobata* (AR, ARN-1, ARN-2 and others); 3) results of these toxins studying that demonstrate the regularities between their "structure" and "function" [61–64]; and 4) conclusions — how to use these regularities for the perfection of logic unit in our biotechnical expert system. The author's results with inventions of new methods of qualitative and quantitative anaysis were supported by patents [46–57], as well as original biotechnical expert system [50]. Concerning the item of this article it is necessary to mention that in our previous publications we had written briefly about contemporary computer information systems [1–12] with expert subsystems [11], as well as about mathematic tools used for expert systems' construction [1–6]: methods of artificial neural networks [1, 3], methods of cluster analyses [1, 4], methods of images processing [1, 5]. Additional necessary data both experimental and theoretical were used for the work in [112–140].

Some methods of qualitative and quantitative analyses for phenol and its derivatives identification. A number of such methods for phenol and its derivatives identification is suggested in this sub-chapter.

A. Method of quantitative determination of mezaton, other phenol compounds was invented in Ukraine [108]. This method was applied for quantitative analyses of phenol compounds [108] in pharmacology with the use of diazole salts, as highly sensitive analytical color agents, by analyzing the optical characteristics of electronic absorption spectra, methods of spectrophotometric determination of medicinal substances.

B. Method for preparing phenolic compounds and their identification was protected by USA patent [109] A method for preparing a phenolic compound has been invented. The method includes providing a lignin depolymerization product, and hydrogenating the lignin depolymerization product under iron oxide and hydrogen gas to prepare a phenolic compound. The prepared phenolic compound is a crude phenolic composition including phenol, methylphenol, dimethylphenol or a combination thereof. The methods of gas chromatography — mass spectroscopy (GC-MS) were used for quantitative determination of phenol compounds.

C. Another USA patent for industry "Clear tobacco aroma oil, a process for obtaining it from a tobacco extract, and its use" is in [110]. Ther method of qualitative analyses of phenolic compounds is known. The invention relates to a process for obtaining aromatic materials from a tobacco extract (primary extract) obtainable by means of solvents, by mixing this tobacco extract with an adsorbent, treating the mixture obtained with CO_2 in a pressure extraction vessel under extraction conditions (secondary extraction) and isolating a clear tobacco aroma oil in a downstream separating vessel. The invention also relates to a new tobacco aroma oil which is free of resins, waxes and polyphenols and has a considerably reduced nicotine content. The invention further relates to the use of the obtainable tobacco aroma oil for aromatizing tobacco or tobacco products. To determine the compounds of phenol (nicotine) in the formed mixtures, spectrophotometric methods were used.

D. Method for phenol determining in aqueous media was invented in Russia. There is a method for determining of phenol in aqueous media [111]. This invention relates to the determination and sanitary-and-epidemiological control of the content of phenol in drinking, natural and sewage waters, as well as in atmospheric rainfalls. The method includes chemical modification of phenol in 2,4,6-threebromophenol, and further extraction concentration of 2,4,6-threebromophenol and subsequent gas chromatographic detection, and before chemical modification from the aqueous sample the humus acids on aluminum oxide are removed in the presence of cuprum sulfate in quantities of 0.05–0.25% of the weight of the water sample. The invention relates to the analytical chemistry of organic compounds (concentration and determination).

The disadvantages of all these above described methods are that they all can not be applied to such compounds of phenol whose chemical structure is destroyed at significant deviations from living conditions (temperature, pH, humidity, etc.), for example, to study the phenol compounds in living organisms. Our methods had no these disadvantages, they are grounded and described below, and they were protected by patents of Ukraine [61–64]. As chemical substances for logical module programming in our biotechnical expert system following substances (toxins) were used: JSTX-3 (from *N. cavata* venom) and AR, ARN-1, ARN-2 (from *A. lobata* venom).

The reason of used toxic organic substances selection. For logic module programming in developed expert system we needed in substances with physical (or biophysical) properties that depend on chemical structures or organic molecules detected by the sensor of this system. Taking the neuronal membrane as the element of sensor we registered transmembrane electric currents at input of this system. The sensitivity of glutamate CRC (gCRC) with kainat (KK) as agonist gave a bright possibility to register the kinetic and other characteristics of toxins blocking action at the stationary KK-activated currents. Than it gave a possibility to calculate further all other parameters, to find the relations and regularities between them necessary for logic unit functioning. This scheme suggests following advantages.

1. Electric currents — responces in described biophysical system are well combined, fit into the electrical circuit of the electronic recording system, which is important for the normal its functioning.

2. Kainat (KK) as gCRC agonist gives a bright possibility to register toxins' blocking (or modificatory) kinetics and other biophysical characteristics well at the stationary KK-activated currents.

3. Studied *Arthropodae* toxins are organic substances with relatively small molecular weight (in comparison with snakes' and some other toxins); they have known chemical structure; they all are phenol or indole derivatives with polyamine radicals (substituents) — linear or branched.

4. Main mechanisms of their interaction with the molecules of membrane CRC have

been already studied; they all have irreversible or sightly reversible type of the action.

5. Due to 2, 3, 4 it is possible to reveal satisfactory co-relation between obtained experimental data (and related calculated characteristics) and molecular structures of studied substances.

6. Finally, basing on the abovelisted, we tried to find the regularities between "chemical structures" and their "effects" necessary for our logical module good functioning.

So, below in the next sub-chapters there is a review of the studies of electrophysiological properties as well as chemical structures of JSTX-3, AR, ARN-1, ARN-2 [13–107].

Basic studies of blocking effects of Atrhropodae venoms and toxins. In the next few sub-chapters we would like to concentrate our attention on toxins and venoms of two spider species — *N. clavata* and *A. lobata*, they become known due to the properties of their venoms as antagonists of glutamatergic synapses, they were used successfully for electrophysiological experiments, for investigations of membrane structures from the late 1980th. In our previous publications we had written already about different Arthropods' venoms and toxins [17, 46, 49, 50, 51, 58–67]. Let's observe so important electrophysiological properties of *N. clavata* and *A. lobata* products in details. In present publication we would like to give more information on experimental studies of glutamate receptors antagonists from *Araneidae*, namely spider species *N. clavata* and *A. lobata*; these spiders are known as good producers of venoms and toxins for laboratory practice. Further we would like to compare some electrophysiological properties for the pairs: venom from *N. clavata* (JSTX-V) with toxin JSTX-3, and venom from *A. lobata* (AR-V) with toxin argiopin (AR). It is known that the studying of different natural toxins for the purposes of neurophysiologic investigations were demonstrated in details in classic monographs by professors Kostyuk P. G., Krishtal O. A., Magura I. S., Skock V. I., and others [68, 73, 91]. Later these investigations were continued by representatives of their scientific schools in collaboration with foreign colleagues [17, 46]. For today the results of the studying of some toxins from *Arthropodae* (including *Araneidae* toxins) as well as other similar phenol and indole derivatives were applied in agriculture [16, 20, 29, 59], and in methods of ecological monitoring of environment [38–57]. Because of importance of results of *Arthropodae* venoms and toxins studying and their applications [31–47, 70–107] in our review below the data from fundamental works of different authors who studied such venoms and toxins were given. In some of these works the results of arthropods' toxins chemical structures studying have been described [32, 33, 38, 45, 47, 50].

A. Basic studies of blocking effects of Nephila clavata venom and its active components — toxins of JSTX family. The first studies of the actions of *N. clavata* venom and obtained from it active component — toxin JSTX were done in Japan on 1982. For today glutamate receptors antagonists from *N. clavata* — venom and its elements — toxins from JSTX family — are seen as excellent tools for laboratory investigations in the whole world; these toxins include fragment of 2,4-dihydroxyphenyl acetic acid (DHPA) or its derivative binded with asparagin (DHPA-Asp) [50, 51]. But at the beginning, in early 1980-th, the chemists and biochemists obtained from *N. clavata* venom only one active toxic fraction that was called JSTX; later few such electrophysiologically active toxic fractions were subdivided from this venom [51]. The first experiments with the use of microelectrodes have demonstrated that JSTX-3 blocks specifically glutamatergic synapses in lobster muscles [40, 41], stellate squid ganglia [42–44, 88], and in the central nervous system (CNS) of mammals [42, 43, 88]. In all these experiments toxins of JSTX family blocked both excitatory postsynaptic potentials (EPSP) and potentials caused by ionophoretic application of glutamate (Glu) without the influence on inhibitory potentials (IPSP). The rest potential of presynaptic membrane remained constant until and after the action of toxin. The washing of JSTX even for a long time did not caused the EPSP restoring, that means that the toxin in postsynaptic membrane binds irreversibly and strongly to the glutamate channel-receptor complex (CRC).

The results of experiments had demonstrated that JSTX acts on the post-synaptic membranes. Antidromic potentials of action, registered on the squid giant axon [42, 43, 88] were insensitive to JSTX.

In addition, JSTX did not act on presynaptic potentials in a giant squid synapse [42, 43, 88]. Intracellularly registered spikes in lobster neuromuscular terminals also were insensitive to JSTX [13, 40, 41] and antidromic action potentials registered on pyramidal neurons of the hippocampus [88]. The quantum composition of mediator released in neuromuscular lobster junction

and its change under the action of JSTX were studied. It was revealed that under the action of JSTX it was not changed [80, 81]. During the intracellular registration from the nerve terminals of neuromuscular lobster junction, the changes in the membrane potential were recorded under the action of glutamate. However, these responses also were insensitive to JSTX [80, 81]. Based on these studies, it was concluded that JSTX blocks the transmission in glutamatergic synapses being bonded to glutamate CRCs in the postsynaptic membrane.

Later it has been found that JSTX affects not only the glutamate receptors of the postsynaptic membrane, but also the mechanism of glutamate reuptake. Both JSTX and a fragment of its molecule DHPA-Asp inhibited both sodium dependent and sodium-independent binding of marked glutamate to synaptosomes in rat brain [84–86]. The inhibition and binding of glutamate of both types was practically complete and depended on toxin concentration.

Already in the early work a number of quantitative characteristics of JSTX blocking action were obtained. On the neuromuscular lobster junction it was shown [13, 42, 43] that this toxin blocked the EPSP irreversibly in concentration that exceeded 10^3 units/l. At lower concentrations it could be removed by washing. Within the limits of concentrations 10^{-4}–10^{-2} units/l this toxin acted in dose-dependent manner, and the degree of EPSP suppression was the greater, the higher its concentration was. The speed of blocking depended on the concentration of toxin. The constant rate of EPSP amplitude decrease was directly proportional to the concentration of toxin: the higher toxin concentration was, the faster EPSP was blocked. The process of EPSP amplitude reducing could be described by one exponent [88].

The results of all experiments were analyzed to determine whether JSTX blocks ion channels of glutamate CRC (1987) [80, 81]. The effective JSTX concentrations were found to be slightly lower than those for channel type blockers. The phase of EPSP decrease in lobster muscle was described by one exponent and it does not depend on JSTX. Other channel blockers affect the EPSP decreasing them, evidently changing the dipole moments of the groups in the channel. Unlike other channel blockers, the JSTX's action was potentially dependent. The dependence of the peak amplitudes of EPSP on the potential was linear and it was not changed under the influence of JSTX. Otherwise, the toxin did not affect the electromotive forces in the synapses. Finally, the irreversibility of toxin action is also considered by the authors as proof that JSTX is not an antagonist of the channel type

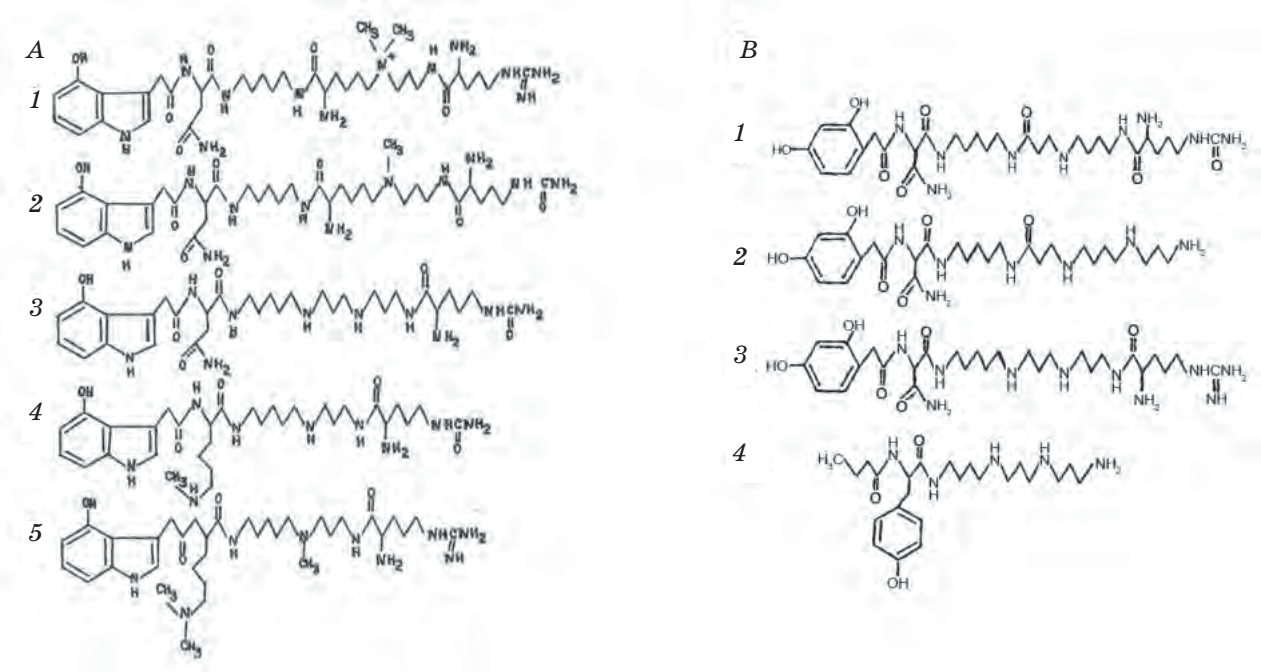


Fig. 2. **Chemical structures of some toxins from *Arthropodae* [33, 50, 51]:**
A — Family of toxins from *A. lobata* — argiopinines (ARN);
B — *1* — JSTX-3; *2* — NSTX-3; *3* — argiopin AR; *4* — PTX 433

[81]. In several publications the results of research of JSTX influence on the response of excitatory membranes were demostrated after the application of aspartate (Asp) and glutamate analogs — kainat (KK) and quisqualat (QL). The depolarization caused by aspartate in neuromuscular junction of the lobster was not sensitive to JSTX [13, 40–43].

Toxin JSTX did not block postsynaptic potentials caused by the application of aspartate in a giant squid synapse [42, 43]. He also did not affect the spikes caused by aspartate in the pyramidal neurons of hippocampus and neurons of brain cortex of guinea pig [42, 43, 88]. However, in some experiments on guinea pig hippocampal slices the same authors had shown that the depolarization of some pyramidal neurons caused by NMDA is reduced under the influence of JSTX-3, but lesser than that caused by glutamate [88].

Post-synaptic potentials caused by KK and QL in the neuromuscular lobster junction were blocked by JSTX [42, 43]. In squid giant synapse the depolarization caused by KK was blocked only partially [88]. In the pyramidal neurons of guinea pig hippocampus, the QL-receptors seemed to be more sensitive to JSTX than KK-receptors: smaller concentrations of toxin were required to block the responses induced by QL [88].

The results of experiments on various objects with blocking of glutamate receptors were very similar: irreversibility of JSTX action, blocking of responses to glutamate, but not aspartate, quantitative characteristics of blocking, and so on. Therefore, it was supposed that JSTX can be used as universal glutamate receptor "marker". In addition, it was concluded that there is a significant similarity of glutamate receptors in different phylogenetically distant objects: neuromuscular lobster junction [40–43] and some parts of guinea pig brain — hippocampus, olfactory bulb, *superior colliculus* [40–43, 88].

Therefore, JSTX was used to identify glutamatergic synapses. For example, until 1983 the question of whether glutamate performs a neuro-mediator function in giant synapses of star squid's ganglia remained open, because in previous experiments there were obtained contradictory data [42, 43]. The results of JSTX blocking role studying in this synapse were similar to those obtained in other sites where the role of glutamate as a neurotransmitter has already been proven [41–44, 88]. Here, the toxin also irreversibly and completely suppressed EPSP and miniature synaptic potentials, the rate of their blockage increased with toxin concentrations increasing, potentials caused by Glu and QL in post-synaptic membrane were completely blocked by JSTX, KK-activated potentials were blocked partially, Asp-activated potentials were not blocked at all. On the basis of this, the authors concluded that Glu in this synapse plays a mediator role by binding to a certain type of receptors [42–44].

However, further experiments have shown that the assertion that JSTX is a "universal marker" for glutamate receptors is not fully true. For example, in the presynaptic membrane of the lobster muscle were found the glutamate receptors that do not interact with JSTX [79]. Both Glu and QL-induced potentials in the membrane of presynaptic terminals were blocked by this toxin. Even more complicated case was registered in experiments on the membrane of the rod retina of the dogfish (shark eye) [89]. After the ionophoretic applications on these cells of glutamate, kainat and aspartate, the membranes were depolarized. The authors attempted, with the help of JSTX, to divide the population of studied receptors into types, but the toxin blocked the responses to all of these substances. The results of studies of chemoactivated single channels in the membranes of these cells can explain the reason of this failure. It has been shown that on this object all agonists interact with the same receptor molecule by opening only one ion channel [89].

The influences of glutamate receptors antagonists from *N. clavata* were studied also in Bogomolets Institute of Physiology of the National Academy of Sciences of Ukraine in scientific group of Prof. Krishtal O.O., Prof. Akaike N. (Japan) and young collaborators Drs. Tsyndrenko A., Kiskin N., Klyuchko O. using voltage-clamp technique in mode of holding potential at hippocampal membrane approximately at the mentioned period of these antagonists studying [17, 46, 50, 51]. Some of the results of these studying are presented on Figs. 3–9, and in the Table [17, 46, 55–67]. On Fig. 3, the blocking activity of the toxin JSTX-3 which is the main active element of the venom JSTX-V is presented.

B. Investigation of venom of spider Argiope lobata and toxins isolated from it. Usmanov and his co-authors published a paper devoted to the action of venom from spider *A. lobata* on glutamatergic and cholinergic synapses (1983) [101]. As elements of the venom, some factors have been identified that could

block postsynaptic processes in the nerve-muscle preparations of locusts and frogs. The venom was applied using ionophoresis, and synaptic potentials were recorded using glass microelectrodes. The venom influenced on the post-synaptic membrane, 75 μg/ml of the venom reduced the amplitude of the miniature potentials of terminal plate and the potentials of terminal plate up to their complete disappearance.

In these locust preparations the venom also reduced effectively the amplitude of both EPSP and miniature EPSP, and also blocked irreversibly the appearance of glutamate potentials after the application of mediator, and it was impossible to remove it by "washing" even with prolonged perfusion of the preparation with normal physiological solution. Potentials caused by application of acetylcholine at the same preparation were blocked by the venom, but in this case, the responses were restored after washing. Six months later, this group of authors tried to obtain the cockroach glutamate receptors using this venom [95, 96]. From the venom *A. lobata* there was isolated the fraction that blocks glutamatergic synapses.

The ligand fraction was bound to the affinity column, and it was incubated with membrane fragments of cockroaches containing glutamate receptors. The properties of the total protein fraction removed from the sorbent were studied using the technique of bilayer phospholipid membranes (BLM). The injection of protein fraction into the experimental block by itself caused a slight increase in BLM conductivity. The conductivity for sodium ions increased by two orders and depended on the mediator's concentration followed by glutamate adding. In presence of 10^{-4} M calcium ions, glutamate could increase conductivity to three orders. The complex of these proteins on BLM was inactive followed by neurotoxins adding.

Similar experiments on the isolation of glutamate receptors from neuromuscular crab synapses were carried out on 1985 [93, 94]. Characteristics of this protein on BLM did not differ from those described above [95, 96]. In addition, it has been shown that in the absence of glutamate, the increase in conductivity of BLM caused concanavalin A, wich prevents desensitization of glutamate receptor. Glutamate-induced BLM conductivity was blocked effectively by diethyl ether of glutamic acid, a glutamate receptor blocker [17, 46]. And, finally, an activity of single channels of glutamate complex receptor-ionophore in-built in BLM, was registered. The disadvantage of these works, however, is the use as ligand of "active fraction" of the venom during the isolation of rough mixture of toxins. In subsequent years, the composition of venoms and properties of the components isolated from them were investigated.

It was found that the protein — peptide fraction of the venom consists of several components — toxins, acting on signal transmission in glutamatergic synapses. The main active component of *A. lobata* venom was called argiopin [33, 72]. According to the Tashmukhamedov's works [95, 96] polypeptides with a molecular weight of 6–7 kDa are responsible for the activity of *A. lobata* venom. Subsequently, these data were related to argiopin with 636 kDa molecular weight [33]. Argiopin blocked effectively the glutamatergic transmission in locust neuromuscular preparations [95, 96], larvae of meat fly, frog muscle [72], frog spinal cord [14].

The blocking properties of argiopin were the same for all preparations. They were studied using intracellular microelectrodes from the region of synaptic contact under the voltage-camp conditions on the membrane [32, 90]. Like JSTX, argiopin acted on a post-synaptic membrane, but its action was reversible [14, 33, 72]. The decrease of registered postsynaptic currents was exponential and was approximated by two exponents [72]. The blocking action of argiopin depended on potential. In muscles of frog and fly larvae, it decreased strongly the amplitudes of excitatory postsynaptic currents near the resting potential and decreased them worse in case of hyperperpolarization [72]. On Fig. 4 the blocking activity of the toxin argiopin, the main active element from this venom is shown. In our experiments both, venom AR-V and argiopin, acted in reversible manner on glutamate receptors in hippocampal membranes but the rates of their reversible effects were different.

On locust neuromuscular preparations it was found that the venom *A. lobata* blocked not only glutamate, but also cholinoreceptors. Cholinoreceptors were blocked by the fraction of venom, which did not contain argiopin [101]. Contrary, according to other researchers, the active fraction of the venom influenced the transmission, both in glutamatergic and in cholinergic synapses, although in the latter — its effect was 40–70 times weaker [72] and argiopin blocked both glutamate and cholinergic receptors as well.

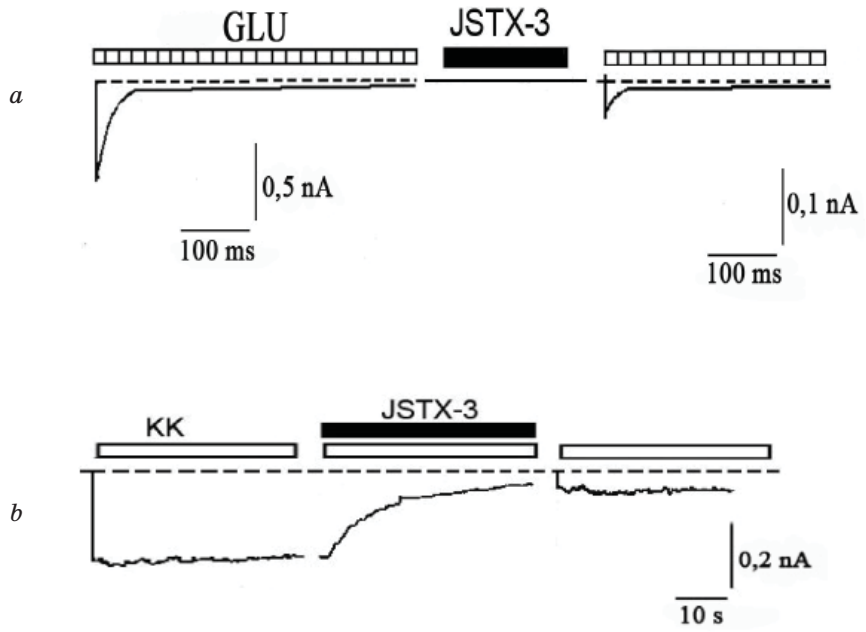


Fig. 3. **Blocking of chemo-activated transmembrane electrical currents by toxin JSTX-3:**
a — glutamate-activated; *b* — kainat-activated ionic currents. After the receiving of the control response to KK, toxin JSTX-3 was applied against the background of KK-activated current. Concentrations Glu and KK were 1 mmol/l; JSTX-3 was 10^{-4} mol/l; V_{hold} is — 50 mV.
Records *a* and *b* were done on different neurons [61, 62]

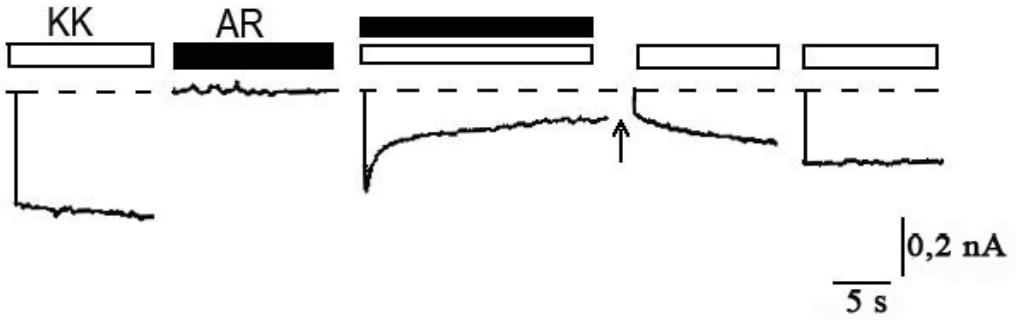


Fig. 4. **Argiopine causes blockage of the open state of kainat- activated ion channels**
After receiving of control response, the neuron was maintained in AR during 3 min, than on background of AR -KK was added. Concentrations: KK 1 mmol/l, AR 1.6×10^{-2} mol/l, V_{hold} — 100 mV.
Toxin removing by "washing" lasted 15 s [63]

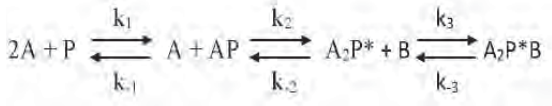
According to the results of experiments, the rate constants of argiopin binding to the open channel and the dissociation of this complex for glutamate and cholinergic synapses were calculated. Under the normal conditions, they differed 36 times due to the fact that the rate of argiopin binding with the glutamate receptor in activated state was 5.3 times higher, and its dissociation was 7.4 times lower than with cholinoreceptor [72].

In synapses of the frog spinal cord, argiopine did not interact with NMDA receptors. Argiopin suppressed the depolarization of motor neurones caused by glutamate, and did not affect depolarization caused by aspartate [14].

Argiopin acted mainly on the opening of ion channels activated by glutamate [72]. But due to the fact that the ability of argiopin to reduce excitatry postsynaptic currents was more pronounced near the resting potential, it was concluded that arginipin also binded to closed channel. The calculated values of the dissociation constants (K_d) of argiopin for the open and closed channels practically coincided respectively [72]:

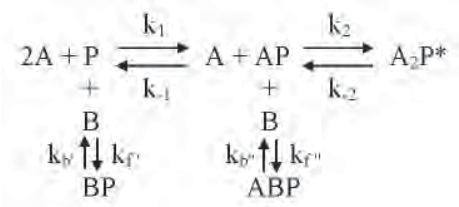
$(6.7\pm1.5)\times10^{-7}$ M and $(4.4\pm1.4)\times10^{-7}$ M.

The effect of argiopin on the kinetics of activation of glutamate-activated channels was demonstrated by analyzing the fluctuations in the membrane conductivity under the action of glutamate. The energy spectrum of these fluctuations was approximated by two Lorentz functions under the action of argiopin and by one Lorentz functions in control [72]. K_d value for argiopin in these experiments was 8 times lower than other one during the analyses of excitatory postsynaptic currents; perhaps, the toxin was more effective at application of glutamate than with its normal secretion. The set of received data allowed authors to describe the process of blocking from the point of view of model of consequent blocking of open channels:



where A is the activating molecule of mediator; P, P^* is the receptor corresponding to the closed and open states of channel; B is molecule-blocker, K_1–K_3 and K_{-1}–K_{-3} are the rate constants of corresponding reactions.

To describe the process of argiopin blocking of the closed channel, another scheme was proposed. According to it the antagonist can interact with P in a state of the rest or with inactivated (AR) receptor, which prevents further activation and transition to the state P^* [72].



In addition to argiopin, a number of other substances were isolated from the venom *A. lobata*. Grishin and his co-authors isolated at least three different compounds with similar biological activity from *A. lobata*. They all were able to block glutamatergic synapses. They all belong to family of toxins with homologous chemical structures [50, 51]. Like argiopin, they acted on glutamate receptors of the post-synaptic membrane, but the effectiveness of their action was different for various toxins [32].

It has been shown that the venom *A. lobata* contains at least two components differing in their effect on the binding of marked [^{3}H]-L-glutamate to locusts muscle membranes. One — with molecular weight of less than 5 kDa — suppresses effectively the synaptic potentials, but does not affect binding of [^{3}H]-L-glutamate, and thus does not interact with the glutamate-binding site of receptor. Another one, with molecular weight more than 5 kDa, interacts with the site of glutamate binding, suppressing competitively both mediator binding and synaptic potentials [101–104].

In addition to glutamate receptor antagonists, *A. lobata* venom contained high molecular weight components of presynaptic action. The activities of these components were aimed on the process of mediator release due to excitation and caused a decrease in quantum composition of mediator, but the rate of spontaneous mediator release was constant [71, 72].

Characteristics of *A. lobata* venom are determined by the sum of characteristics of all these components and combining 2 effects: 1) the presynaptic effect — is suppression of mediator release stimulus due to the excitation and 2) post-synaptic effect, the most important component of which is the ability to block the opening of postsynaptic ion channels [71, 72]. In the experiments of some authors the properties of integral venom (AR-V) differ from the properties of its main component (argiopin). Thus, some authors demonstrated that argiopin blocked glutamate receptor in reversible manner [72]. The action of integral venom in different experiments was less reversible [72], or irreversible [95, 96, 101].

C. Investigations of venoms and toxins of N. clavata and A. lobata in Ukraine. The influences of glutamate receptors antagonists from *N. clavata and A. lobata* were studied also in Bogomolets Institute of Physiology the National Academy of Sciences of Ukraine in scientific group under the supervision of Prof. Krishtal O.O. by his collaborators Drs. Tsyndrenko A., Kiskin N., Klyuchko O. The experiments were done using voltage-clamp technique in mode of holding potential at hippocampal membranes [50, 51]. IThe author analyzed some *Araneidae* toxins with the following known chemical structures: JSTX-3, AR are derivatives of DHPA-Asp, and ARN-1, ARN-2 are derivatives of indole-acetat-asparagin. Some of the obtained experimental results are presented on Figs. 3–9 and in the Table.

Among all of these substances JSTX-3 has the simplest structure: the chain of its polyamine is the shortest one, there is no

branching. In AR molecule the chain is slightly longer and 2 chemically active amino-groups are linked with it. ARN-1 and ARN-2 have the same length of polyamines, and amino groups are linked with them. The characteristic feature of ARN-1 is cationic group presence that is able to dissociate easily. This group contains pentavalent nitrogen in its polyamine chain. These substances can be arranged in a line depending on the length of their polyamine chains:

JSTX-3<AR<ARN-1=ARN-2.

The action of all studied toxins on the glutamate receptor was characterized by the number of similar characteristics. They all blocked GLU, KK, and QL (quisqualate)-activated currents in the membranes of rat hippocampal neurons in varying degrees and they all were able to be removed ("washed") to different degrees by normal Ringer solution (Fig. 7).

They did not act on electrically excitable membranes, glycine- and GABA-activated currents in membranes of these neurons. Their blocking effect depended on the membrane holding potential — it become less visible with depolarization of the membrane. All these substances could block the open glutamate channel-receptor complex (gCRC). It is natural to assume that all these toxins' properties are due to the common for all toxins fragments of their molecules, namely the phenolic or indole group, linked with asparagine.

Figs. 8, 9 demonstrate other experimental data on the development of new methods for qualitative analyses: the characteristics of transmembrane electrical currents, by which various substances can be identified according to dose-effect dependencies. K_d values were different for the toxin JSTX-3 and for the venom JSTX-V, from which this toxin was obtained. Together with JSTX-3 this venom containes other toxins and substances that caused registered shift [50–51]. K_d values for studied venoms and toxins were presented in the Table below.

Our experiments did not show significant differences in properties of toxins — phenol or indole-derivatives. There is only a little insignificant difference: the dissociation of AR derivatives is going a little bit slower (Table) [64].

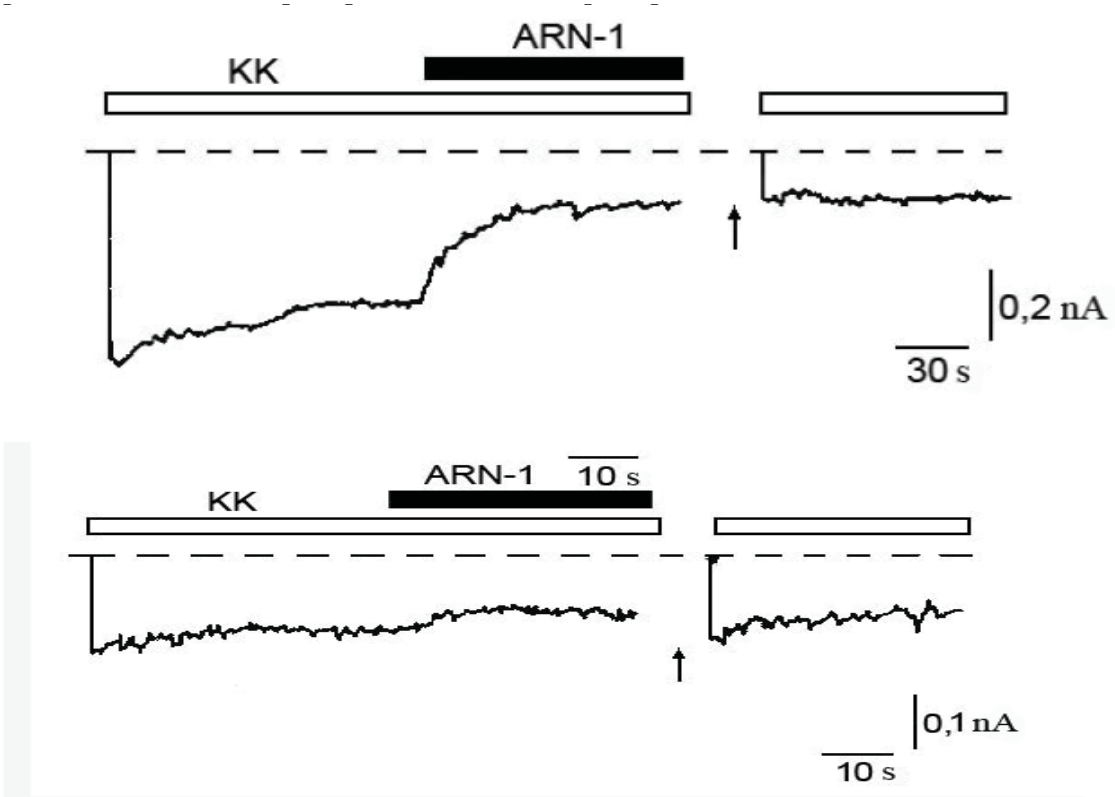


Fig. 5. **Irreversible blocking of KK-activated currents by argiopinin1(ARN-1) [61–64]**

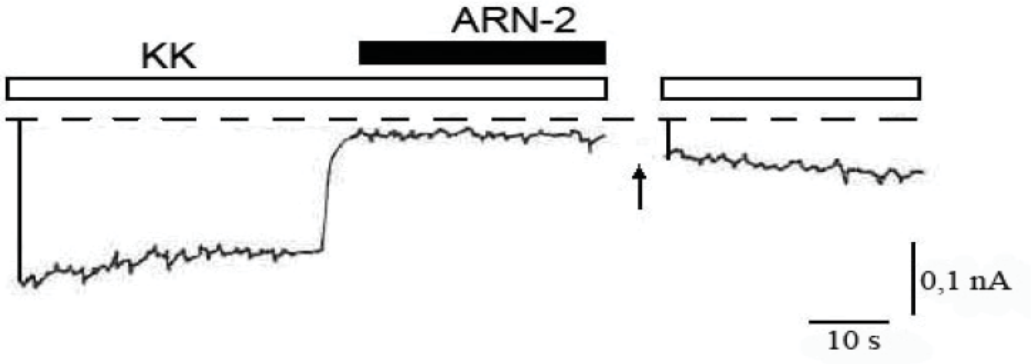


Fig. 6. **Irreversible blocking of KK-activated currents by argiopinin 2 (ARN-2) [61–64]**

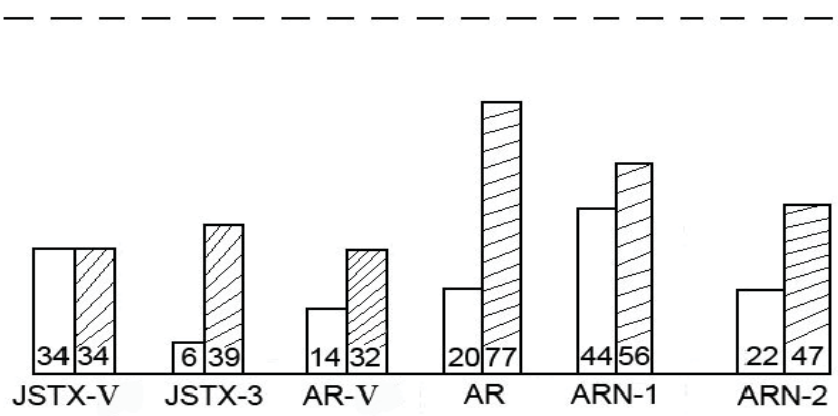


Fig. 7. **The degree of blocking of kainat-activated currents by various antagonists (white columns) and the degree of recovery of currents' amplitudes after the antagonists removing in Ringer's solution (shaded columns)**
The values are given in percent of the amplitude of control response, the value of which was taken for 100% (top straight dotted line). Diagram was done for 6 different antagonists of glutamate CRC [61–64]

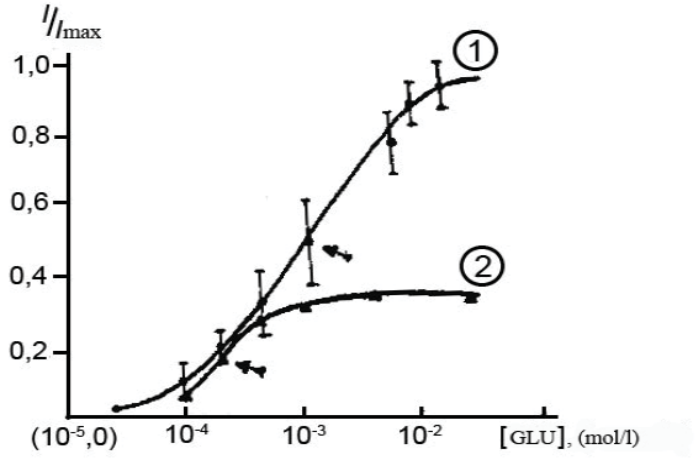


Fig. 8. **Dose-effect dependence of the glutamate-activated currents in the control (*1*) and during the action on the cell of 5×10^{-5} units/μl JSTX-V**
The currents' values at the points of peaks were normalized to the maximum. The curves represent a single-binding isotherm with $K_d = 1.1\times10^{-3}$ mol/l (1) and $K_d = 2.35\times10^{-4}$ mol/l (2) [61–63]

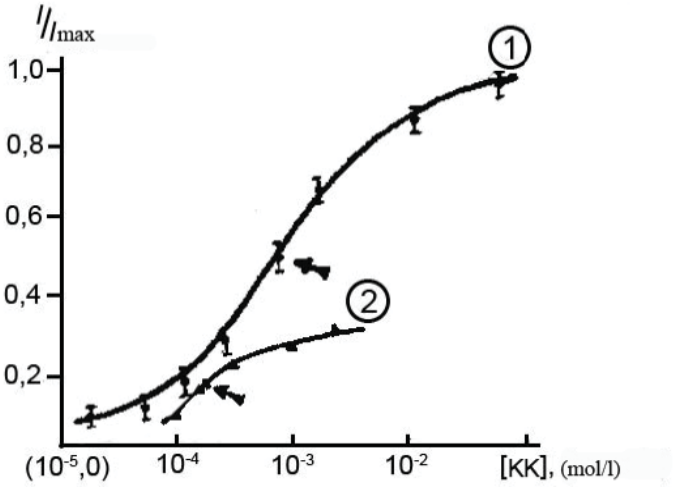


Fig. 9. **Dose-effect dependence of the KK-activated currents in the control (*1*) and during the action on the cell of 10^{-5} mol/l AR (*2*)**
Both curves are single-bonded isotherms with dissociation constants $K_d = 5.0\times10^{-4}$ mol/l (*1*) and $K_d = 2.4\times10^{-4}$ mol/l (*2*) [61–63]

Kinetic characteristics of KK-activated ionic currents blocking
Comparative analysis of the properties of various *Araneidae* toxins as result of their chemical structure

Antagonist	Constant rate of blocking (direct reaction)		Velocity of electrical current amplitude recovering
	K_1	K_2	I
JSTX-V	4.4×10^3 μl/(un.s)	–	0
JSTX-3	2.1×10^3 l/(mol.s)	–	1.3×10^{-2} s^{-1}
AR	1.6×10^3 l/(mol.s)	0.85×10^4 l/(mol.s)	4.9×10^{-2} s^{-1}
ARN-1	3.3×10^3 l/(mol.s)	1.6×10^4 l/(mol.s)	7.9×10^{-2} s^{-1}
ARN-2	2.9×10^3 l/(mol.s)	0.59×10^4 l/(mol.s)	3.1×10^{-2} s^{-1}

However, the direct constant rates of reactions between toxins and AR derivatives didn't get the significant differences. Such characteristics of toxins — phenol and indole derivatives — permitted to make conclusions.

Firstly on the basis of gCRC blocking mechanism by toxins, it should be the reaction of the interaction of toxin aromatic groups with membrane. This conclusion coincides with the Japanese authors opinion [86]. Secondly, this reaction should be common to indole and phenolic groups, so, the membrane should not "distinguish" them. And, finally, probably exactly these groups (or in connection with asparagine) determine the blocking effect of gCRC and its main features (potential-dependence, and others).

Toxins influence on activated and non-activated receptor. The main difference in the effect of toxins is that JSTX-3 interacts with the gCRC, regardless of whether it is in the activated state or inactivated. The main mechanism of action of AR, ARN-1, ARN-2 is the blocking of GLU- and KK-activating channels in the open state [33, 38].

What may cause the difference in the effects of toxins? The only structural difference between JSTX-3 and others studied toxins is simpler structure of its molecule. Perhaps slightly more complex structure of toxin molecule of *A. lobata* (lengthening of

polyamine chain, presence of amino-groups branched off the main chain) increases the selectivity of their interaction with gCRC so, that they lose their ability to bind with gCRC conformations corresponding to inactivated state. Thus, more simple JSTX-3 molecule, probably less "legible" and "does not distinguish between" receptor conformations corresponded to activated and inactivated state. In both cases, ion currents are blocked almost completely. In future it would be nice in similar experiments to study even more simple fragments of molecules: DHPA and DHPA-Asp, that also block gCRC [86] and the selectivity of which is not known well. Such ideas [86] stimulated the discovery of new methods of qualitative and quantitative analyses based on the registered differences in electrophysiological effects of toxins with known structure. So we tried to find regularities in effects of toxins with unknown structures.

An interesting regularity is that the removing of toxins AR and JSTX-3 from membrane (their "washing") was the same in Ringer's solutions, both in the presence of agonists (GLU, KK), and without them. According to our preliminary data, for the "washing" of some argiopines in solutions, contrary, the presence of agonists (GLU, KK) was necessary. For these substances, activation of the gCRC improved both the formation and dissociation of toxin-receptor complex. In compliance with the literature, there is known another toxin with similar property — gCRC antagonist: δ-phylantototoxin [18]. However, a significant difference in its molecule structure (instead of DHPA or DHPA-Asp it has oxyphenol) and not so much data on this issue allow to make any conclusions about the relationship of properties with the structure of its molecule.

According to some authors, the necessary condition for AR removing by "washing" was the presence of an agonist in washing solutions [18, 38]. This contradicts our data. However, this effect is easy to explain taking into account that in these works the roughly purified AR preparations were used, and this effect might be caused be the mixtures of argiopinins.

A. *The degree of blocking of KK-activating currents*. Any of studied toxins blocked chemoactivated currents completely even at high concentrations (10^{-4} mol/l). JSTX-3 decreased the amplitudes of KK-activated currents the most effectively — up to 6% of the initial value. The effectiveness of KK-activating currents depression decreased from left to right in the line of toxins:

JSTX-3 > AR > ARN-2 > ARN-1.

As one can see, the degree of blocking of currents by toxins can depend on the length of their polyamine: the shorter the toxin the more effectively it closes the ion channel. However, this statement should be reinforced by studies of other analogs with different lengths of polyamine chains.

B. *Irreversibility of toxins' effects*. For analogues of JSTX-3 with different lengths of polyamine chain, it has been found that elongation of polyamine chain is accompanied by the formation of more stable toxin-receptor complex [36, 38]. However, in our experiments, the most pronounced reversed action had AR, although its length is slightly longer than that of JSTX-3, Perhaps this is due to the fact that two amino groups are coupled with AR polyamine chain, which are easy to react, and the length of the polyamine appears to be functionally less important? To answer this question, let's analyze how molecular structure is linked the degree of "washing" of other *A. lobata* toxins. In our experiments there were registered that among *A. lobata* toxins AR has peculiar characteristics: all its analogues were "washed" much worse, regardless of their structure. However, during studying of the properties of AR analogues separately, it also appeared that it was easier to remove the substances with longer fragment of polyamine. This was true within groups of argiopinins 1-5 and pseudo-arhiopinins 1-3 (own in print data, as well as the data given in [17, 46]). Thus, our conclusion is completely opposite to other one one that was made by other authors for JSTX-3 analogues earlier. For AR analogues the longer is the toxin molecule the better it is washed off. The argiopinin 1 was the exception because it acted practically irreversibly. However, unlike other toxins, its polyamine includes easily dissociated cationic group containing pentavalent nitrogen. This group is likely to contribute to the formation of a more stable toxin-receptor complex.

C. *Kinetic characteristics of blocking effects of the toxins*. Basing on the results of calculations of the values of binding constant rates and the rates of "washing" of toxins (given in the Table), as well as basing on the preliminary data obtained during the argiopins 1-5 and pseudo-argiopinins 1-3 studies, the following conclusion can be made. When lengthening the chain of polyamine, the value of the first binding constant rate of toxins

with gCRC increases, and the rate of toxin "washing" respectively. Otherwise, the longer toxin molecule is, the faster it binds to the receptor and faster breaks the links with gCRC when dissociating. This rule is not true for the molecules having long side chains, namely ARN-4, whose binding constant is higher than expected, and this is exclusion. Perhaps this regularity should be transformed as follows: the longer and the branched molecule of the toxin is the sooner it binds and faster breaks the links with the gCRC.

Some regularities in biophyscal effects of JSTX-3, AR, ARN-1, ARN-2. Basing on the observed data following regularities between these molecules "chemical structures" and their "effects" can be presented.

A. The presence of phenol- or indole acetate-fragments in the toxin molecules is the "key" phenomena of the interaction of the toxin with gCRC. So the reaction of interaction of aromatic groups with the membrane groups should lie at the heart of the blocking mechanism. These fragments define the basic and common for all properties of these antagonists (potential-dependence of blocking, and others).

B. The length and structure of polyamine determine the individual differences in toxins' properties. Thus, with the complication of polyamine structure, the selectivity of toxins action increases and the toxins don't bind more with gCRC in inactivated state. Shortening of polyamines' chains leads to the effect that the toxin more "tightly closes" the ion channel, and the degree of blocking increases. At the same time, the shorter the molecule of the toxin, the worse it is "washed" off. And, finally, the longer and branched the molecule of the toxin, the faster the reaction of formation toxin-receptor complex is going, and the sooner this complex dissociates.

C. Among all the tested toxins, JSTX-3 really has unique characteristics. Having the simplest structure it causes maximal hysiological effect. This observation coincides with the data from the literature [28]. Among all known for today glutamate receptor antagonists, JSTX-3 has an optimal structure in terms of physiological effect. Toxin AR is distinguished by its properties among *A. lobata* toxins (the highest degree of "washing" and others). We can assume that these particular features in the process of evolution have selected the toxins JSTX-3 and AR as the main active components of the *Araneidae* venoms among the large families of other toxins — antagonists of glutamate receptors.

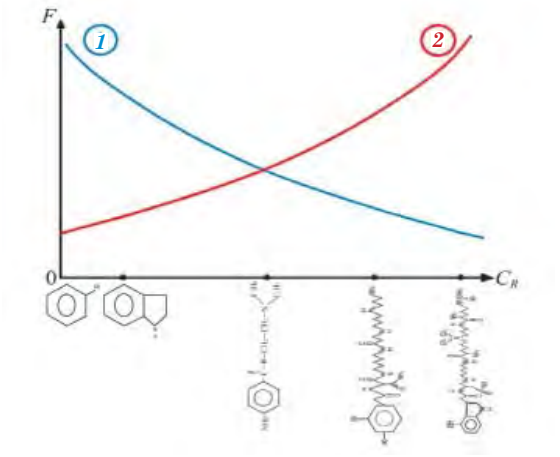


Fig. 10. **The qualitative regularities of the damaging toxic effect of studied substances [61–64]**

Empiric qualitative dependence demonstrates that with elongation and complication of polyamine:
1 — Toxin (Tx) molecules close the ion channel less densely;
– ability to depress the amplitudes of ion currents by Tx decreases;
– Tx molecules loss the ability to bind with gCRC in inactivated state.
2 — reversibility of Tx action increases;
– complexes Tx-gCRC are forming better;
– complexes Tx-gCRC are dissociating better;,
– Tx molecules can be better removed by "washing" in normal Ringer solution;
– selectivity of Tx action increases (Tx molecules loss the ability to bind with gCRC in inactivated state)

D. All toxins, studied in this work, were received both from the natural sources — venoms as well as ones that were synthesized in laboratory conditions. The effect of synthetic analogues was completely identical to the action of natural toxins. This confirms again the correctness of the decoded toxins' structures and the identity of the synthetic toxins with the corresponding natural analogs.

Above said can be illustrated by the simple qualitative graph (Fig. 10). Axis OX means the chemical structures (phenol or indole derivatives). Their structure complication is going from the left to right. Axis OY — qualitative representation of the the following effects described above. Circles 1 and 2 mean the effects: 1 — decrease with chemical structure complication, and 2 — increase with chemical structure complication [61–64].

Further development of this task suppose also further complication of molecular structures with the registration

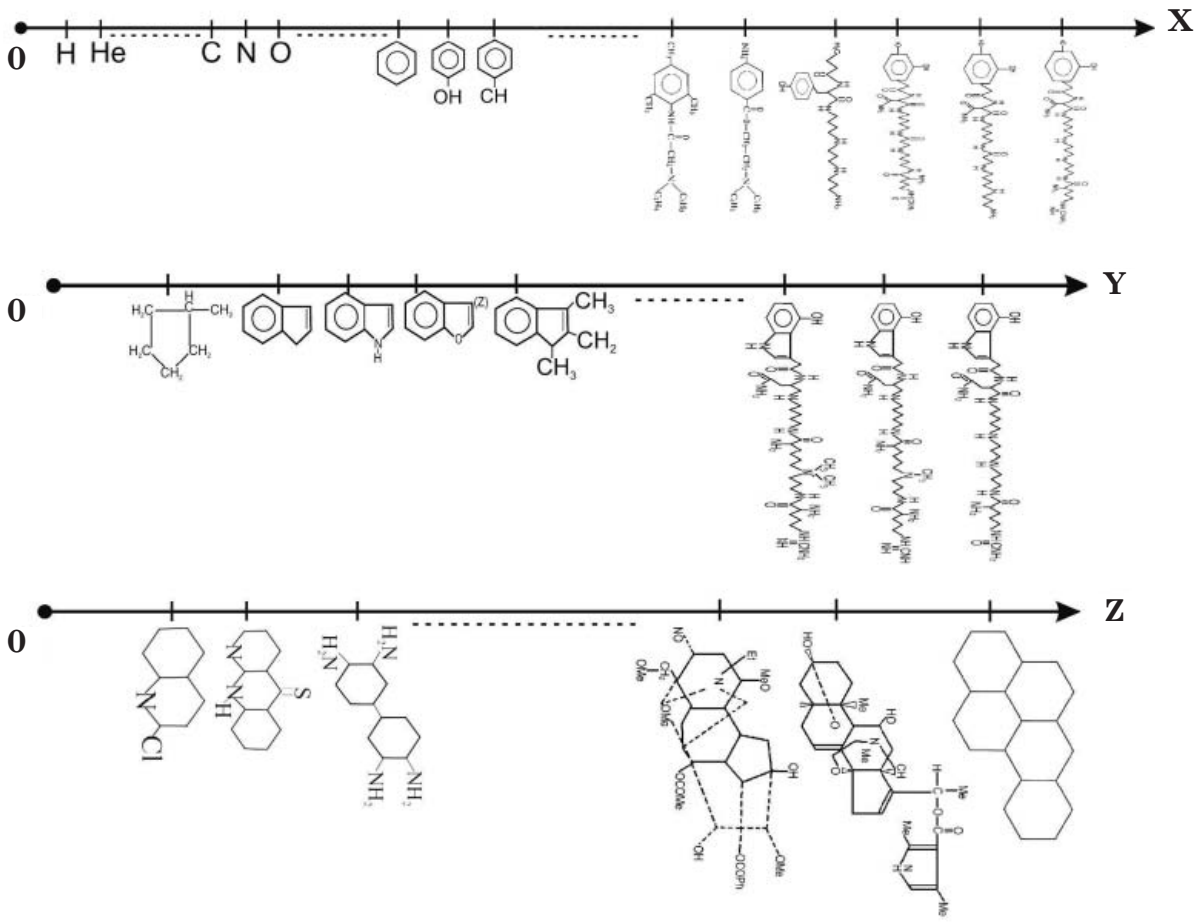


Fig. 11. **Observed and analyzed chemical substances that influence the living organisms [63]**

There are harmful, toxic substances — derivatives of phenol, indole, etc., combined with radicals of different length and complexity. In terms of the chemical structure, all of the compounds are represented by molecules with a «head» formed by cyclic compounds (phenol, indole, or polycyclic structures) that is coupled to polyamine (s) radical (s) of varying length and complexity.

Axis *X*: phenol and its derivatives with polyamine radicals of varying length and complexity. Length and complexity of chemical structure of radicals increase from the left to right, accordingly, their biophysical properties are gradually changed;

Axis *Y*: indole and its derivatives with polyamine radicals of varying length and complexity. Length and complexity of chemical structure of radicals also increase from the left to right, their biophysical properties are gradually changed;

Axis *Z*: some hydrocarbons that have several cycles in their composition and affect the biophysical processes in living organisms (and, consequently, their physiological effects including the expressed harmful and toxic effects). The chemical structure of these substances is complicated from the left to right, their biophysical properties also varying gradually.

of relative biophysical effects for perfection of possibilities of the qualitative and quantitative analyses of organic structures. For example, in computer databases all studied chemical substances can be arranged according to their complication along to hypothetical axes (Fig. 11). The axes CR on Fig. 10 could be substituted by any of the axes from Fig. 11 (*OX*, *OY* or *OZ*). In this case when somebody plots toxin blocking characteristics along the axes F (Fig. 10) theoretically it is possible to find related chemical structure along the axes CR. Having united all together the axis F, OX, OY, OZ, a virtual space "structure"-"function" that had been laid in a base of the novel methods of substances' computer analysis was formed. If necessary, it is possible to use other axis where other groups of substances are ordered in the framework of this model.

Today we have no enough standardized information for the construction of such computer expert system for qualitative and quantitative analyses, but with time with further databases completing this idea may be realized.

Thus, in this publication it was demonstrated further development of electronic expert system logical module, a powerful tool in contemporary biotechnology that also can be used as analytical system for quantitative and qualitative analyzis of organic chemical substances, derivatives of phenol and indole with polyamine radicals (substituents) — linear or branched. Fundamental observation of the results of some *Arthropodae* toxins and venoms studies was done to determine the regularities in chemical structures and electrophysiological properties they have.

The results from numerical literature sources of electrophysiological investigations (including own ones) were presented: analyses of chemosensitive transmembrane electric currents obtained in voltage-clamp mode under the influence of phenol and indole-derivatives from two spider species. They are known as antagonists of glutamatergic receptors and were used successfully for investigations of membrane structures. In such a way JSTX-3 (from *N. clavata* venom) and AR, ARN-1, ARN-2 (from *A. lobata* venom) were studied. These substances were selected due to their relatively small molecular weights and known chemical structures.

All described above gave us a possibility to find the regularities between "chemical structures" and "effects" of these substances influence necessary for our logical module. Also this gave us potential opportunity to solve the inverse problem to traditional one. Previously the direct problem was solved in such a way: under the action of chemical compound with known structure on the ionic currents, the researchers investigated obtained effect (study of dependence "structure" — "effect"). And now the possibility of inverse problem solution was suggested — to determine the approximate chemical structure of organic compounds through their effects on chemosensitive currents from the measured numerical characteristics of electrical responces (the "effect" — "structure" dependence study). On the base of experimental data in our work we tried to solve inverse problem: knowing electrical reaction of cell membrane on the influence of unknown substance to decipher its structure — structure of acting molecule.

We would like to emphasize the practical value of these data. Empirical dependencies "effect" — "structure" were found on the basis of the registered experimental data, their processing using the methods of regression analyses, other types of analyses. Empirical diagrams were constructed, which characterized such dependencies. In such a way the new methods of qualitative and quantitative analyses were developed and patented [61–64].

These regularities may be laid in base of logical module functioning. The observed chemical substances — toxins JSTX-3, AR, ARN-1, ARN-2 and other from this family were really good for such purpose. Obtained regularities have been described and used for further development of logical module in biotechnical expert system for automatic identification of organic substances.

Logical unit programmed on the base of such data, found regularities may be really useful for identification of organic environment pollutants in industrial regions, places of accidents, and etc. Among such pollutants there are many organic substances (including derivatives of phenol or indole); their identification, studies and analyses are really difficult for today [137]. Our developed methods show a way to qualitative and quantitative analyses conducting not only in stationary laboratory conditions but also for mobile methods of organic pollutants revealing and identification in environment.

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КОМП'ЮТЕРНЕ РОЗПІЗНАВАННЯ ХІМІЧНИХ РЕЧОВИН НА ОСНОВІ ЇХНІХ ЕЛЕКТРОФІЗІОЛОГІЧНИХ ХАРАКТЕРИСТИК

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Метою огляду був аналіз результатів електрофізіологічних досліджень деяких біологічно активних хімічних речовин для визначення закономірностей між їхньою структурою та ефектами, які вони спричиняють. Запропоновано також використовувати ці закономірності для вдосконалення логічного модуля біотехнічної експертної системи, яка працює з використанням модульного принципу на основі об'єктно-орієнтованого та регресійного аналізу. В роботі проаналізовано дані електрофізіологічних досліджень антагоністів глутаматергічних рецепторів: фенол- та індолпохідних, отриманих з отрут павуків видів *Arthropodae*. Деякі характеристики блокування рецепторів цими токсинами було використано для демонстрації емпіричних закономірностей між хімічними структурами антагоністів та їх електрофізіологічними ефектами. Обговорено можливість практичного застосування подібних закономірностей для моніторингу шкідливих забруднювальних речовин навколишнього середовища — фенол- та індолпохідних, а також розроблення нових методів їх якісного та кількісного аналізу.

Ключові слова: токсини, антагоністи рецепторів, трансмембранний електричний струм, біологічні експертні системи, електронні інформаційні системи, біоінформатика.

КОМПЬЮТЕРНОЕ РАСПОЗНАВАНИЕ ХИМИЧЕСКИХ ВЕЩЕСТВ НА ОСНОВАНИИ ИХ ЭЛЕКТРОФИЗИОЛОГИЧЕСКИХ ХАРАКТЕРИСТИК

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Целью обзора был анализ результатов электрофизиологических исследований некоторых биологически активных химических веществ для определения закономерностей между их химической структурой и эффектами, которые они оказывают. Предлагается также использовать эти закономерности для совершенствования логического модуля биотехнической экспертной системы, работающей с использованием модульного принципа на основе объектно-ориентированного и регрессионного анализа. В работе проанализированы данные электрофизиологических исследований антагонистов глутаматэргических рецепторов: фенол- и индолпроизводных, полученных из ядов пауков видов *Arthropodae*. Некоторые характеристики блокирования рецепторов данными токсинами были использованы для демонстрации эмпирических закономерностей между химическими структурами антагонистов и их электрофизиологическими эффектами. Обсуждается возможность практического использования подобных закономерностей для мониторинга вредных загрязняющих веществ окружающей среды — фенол- и индолпроизводных, а также разработки новых методов их качественного и количественного анализа.

Ключевые слова: токсины, антагонисты рецепторов, трансмембранный электрический ток, биологические экспертные системы, электронные информационные системы, биоинформатика.