MATHEMATICAL MODELING OF BIOCHEMICAL PROCESS

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A NEW SELECTIVE INHIBITOR OF THE Mg^{2+}, ATP-DEPENDENT SODIUM PUMP CALIX[4]AREN C-1130 AS A MODULATOR OF MYOMETRIAL CONTRACTION ENERGY

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It is known, that the functioning of non-electrogenic $2Na^+$-Ca^{2+}-exchange system, localized in the myometrium cells plasma membrane, is ensured by the energy of the transmembrane sodium gradient, created by the Mg^{2+}, ATP-dependent sodium pump. The aim of the study was to determine how the inhibitor of this pump calix[4]arene C-1130 affects the mechanokinetics and energy of myometrium contraction-relaxation. The experiments were conducted using female Wistar rats. The contractile activity of the longitudinal smooth muscles of the uterine horns was studied tensometrically. The method of determining the mechanical work A and power N at any time moment t of the of smooth muscle isotonic contraction-relaxation complete cycle was developed and tested in the tensometric experiments. Calix[4]arene C-1130 was dissolved in dimethylsulfoxide and introduced into the working solutions in a 10^{-5} M concentration. It was found that under calix[4]arene C-1130 treatment, the relative values of the mechanical work A were achieved at a time when the contraction-relaxation cycle under control conditions was practically completed, while the maximum values of power N were reached faster than in the control. These results indicate that calix[4]arene C-1130 was capable of inducing the increase in the maximal value of the smooth muscle mechanical work, promoting its relaxation without a considerable change in the contraction power. The developed methodology may be useful for the comparative study of the pharmacological drugs effect on the smooth muscles contractile activity in the "norm-pathology" format.

K e y w o r d s: calix[4]arene C-1130, myometrium smooth muscle, contractile activity, kinetics and energy parameters.

Smooth muscles play a fundamental role in ensuring the functioning of the internal organs and their systems – the urogenital (uterus, urinary tracts, and urinary bladder), vascular, gastrointestinal tract, excretory gland ducts, iris sphincter muscle, etc. [1, 2]. At present, there are relevant accumulated data regarding ion, molecular, membrane, and cellular mechanisms of conjugating excitation and contraction in case of smooth muscles at norm and in the pathological states [2-4]. It was reliably demonstrated that in the smooth muscles, the intracellular ions of calcium (Ca^{2+}) control the electro- and pharmacomechanical coupling [1, 4, 5], and there are elaborated notions of the biochemical mechanisms, regulating the concentration of these ions in smooth muscle cells [4, 6, 7]. The corresponding experimental data were mostly obtained using modern biophysical methods to investigate the intracellular calcium signalling: the methods of epifluorescence, laser confocal microscopy and laser

flow cytofluorimetry using Ca^{2+}-sensitive fluorescent probes (to study intracellular calcium transients), and a patch-clamp in the configuration of "a whole cell" (to register transmembrane Ca^{2+} currents), etc. [7-9].

It was proven that the control over intracellular calcium homeostasis and, thus, the energy of Ca^{2+}-dependent contraction of smooth muscles is exercised by the superposition of the functioning of membrane-bound energy-independent and energy-dependent Ca^{2+}-transporting systems. The former cover calcium channels of the plasma membrane and sarcoplasmic reticulum, and the latter – Mg^{2+}, ATP-dependent calcium pumps of the plasma membrane and sarcoplasmic reticulum, Na^+-Ca^{2+} – the plasma membrane exchanger, the calcium uniporter, and systems of Na^+/H^+-Ca^{2+} – the exchange of mitochondria [10-12].

It was found that changes in the concentration regulation for the ionized Ca in the myoplasm, related to the impairment in the functioning of Ca^{2+}-transporting systems, including Na^+-Ca^{2+}-exchanger of the plasma membrane, can lead to the occurrence of dangerous pathologies in the functioning of smooth muscles – the pathologies in the urogenital system (hypo- and hypertonicity of the uterus, inability to bear a fetus, miscarriages, spontaneous abortions, impairments in the functioning of the urinary bladder and urinary tracts, etc.), hypo- and hypertension; pathologies in the motility of the gastrointestinal tract, asthma [13-15].

Therefore, it is relevant to search for selective, affine effectors of no or low toxicity, capable of targeted modification of the activity of specific cation-transporting systems, including Ca^{2+}- and Na^+-transporting ones, and thus correcting Ca^{2+}-dependent contractile activity of smooth muscle cells when it is impaired. This search is promising for the development of new-generation medications – regulators of the contractile activity of smooth muscles in cases of the aforementioned pathological states.

In our previous experiments, conducted on myometrium tissue, we demonstrated [16] that a macrocyclic compound, calix[4]arene C-1130, is an efficient inhibitor (the inhibition coefficient $I_{0.5}$ < 100 nM) of Mg^{2+}, ATP-dependent sodium pump (Na^+,K^+-ATPase) of the plasma membrane; the method of laser confocal microscopy was used to demonstrate that the application of this calix[4]arene to smooth muscle cells induced an increase in the concentration of Ca ions in them. Taking into consideration that the functioning of the system of non-electrogenic $2Na^+$-Ca^{2+}-exchange, localized in the plasma membrane of myometrium cells [15, 17, 18], is ensured by the energy of the transmembrane sodium gradient, directed to myocytes, which is created by the Mg^{2+}, ATP-dependent sodium pump, it was reasonable to determine how the inhibitor of this pump, calix[4]arene C-1130, affects the mechanokinetics and energy of the "contraction-relaxation" of myometrium.

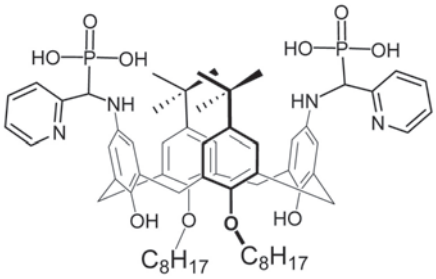
It should be highlighted that despite active use of the abovementioned precise experimental biophysical methods while studying Ca^{2+}-dependent mechanisms of "contraction-relaxation" of smooth muscles, still relevant are also classic physiological approaches, directed at investigating the mechanokinetics of the contractile process in these muscles with the involvement of the tensometric method on the level of intact muscle preparations *in vitro* in case of isotonic and isometric mode of registering the contractile process [19-21].

Previously, we developed a complex method of mechanokinetic analysis of "contraction-relaxation" of smooth muscles and tested it in experiments; this method allows determining a number of objective quantitative characteristics of this process [22]. This method can also be useful for strict interpretation of the experiment results while studying the effect of biologically active substances, pharmacological compounds, and physical-chemical factors on the dynamics of the complete contraction-relaxation cycle, and in the course of the quantitative characterization of the contractile process in case of a tensometric experiment in the "norm–pathology" format or to compare mechanokinetic characteristics of different smooth muscles [23-25].

Based on our previously developed method of mechanokinetic analysis for the contractile activity of the smooth muscles [22, 26], in this article, we aimed to suggest an approach to determining the energy characteristics of the isotonic muscle contraction of myometrium – work ΔA and power $N = d\Delta A/dt$ and to study the impact of the selective inhibitor of Mg^{2+}, ATP-dependent sodium pump, calix[4]arene C-1130, on these characteristics.

Materials and Methods

Synthesis of calix[4]arene C-1130. Calix[4]arene C-1130, (5,17-di(dihydroxyphosphoryl-2-pyridylmethyl)amino-11,23-di-tret-butyl-26,28-dihydroxy-25,27-dioctyloxycalix[4]arene) was obtained using the method recently described in [16].



Calix[4]arene C-1130

Tensometric studies. The experiments were conducted using female rats of the Wistar line (the animals were between 200 and 250 g in weight). All the manipulations with animals were done pursuant to the European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes and the Law of Ukraine "On Protection of Animals from Cruelty" (the Minutes of the Bioethics Committee of the Taras Shevchenko National University of Kyiv No. 8, dated December 26, 2024). The rats were euthanized by hypoxia, caused by carbon dioxide (CO_2).

The contractile activity of the longitudinal smooth muscles of the uterine horns was studied tensometrically in the isotonic mode using the average size preparations, 2×10 mm, with intact endometrium. The weight of the muscle preparation was 38 mg.

All the preparative procedures were conducted in the Krebs solution of the following composition (mM): NaCl – 120.4; KCl – 5.9; $NaHCO_3$ – 15.5; NaH_2PO_4 – 1.2; $MgCl_2$ – 1.2; $CaCl_2$ – 2.5; glucose – 11.5 (pH 7.4; pH was adjusted using concentrated NaOH and HCl solutions). The high-potassium solution (80 mM) was prepared by isotonic replacement of Na^+ ions with K^+ ions in the Krebs solution.

The preparations of smooth muscles were placed into the working chamber of the tensometric equipment with the flowing Krebs solution (the flow rate – 8 ml/min and thermostating at 37.5±0.3°C). The preparations were given a constant load of 10 mN and left for at least one hour until the occurrence of spontaneous contractions with constant amplitude and frequency.

Calix[4]arene C-1130 was preliminarily dissolved in dimethylsulfoxide (DMSO) and introduced into the working solutions in a concentration of 10^{-5} M (DMSO concentration was 0.1%); the control contractions were registered on the background of 0.1% DMSO. When preparing the stock solution of calix[4]arene C-1130, its aliquot was dissolved in DMSO to a concentration of 10^{-1} M and then its aliquots were added to normal and high-potassium Krebs solutions. The stock solution was stored for no more than 24 h at 4°C and in the absence of light.

Mechanokinetic analysis and evaluation of energy parameters of the muscle contraction. We have done the estimations in the sphere of kinetics and energetics of the isotonic muscle contraction, presented in this article, based on the mechanokinetic analysis of the smooth muscle contraction-relaxation process, previously developed by us [26].

Statistical analysis. The experimental data were analyzed in Origin 2018 and Microsoft Excel 2007. The validation analysis of the approximation of the charts by the linear function while using the mechanokinetic analysis was performed using Fisher's criterion; the determination coefficients (R^2) were 0.98-0.99 in all cases.

Results and Discussion

Theoretical part

The estimation of mechanokinetic parameters. The complete mechanokinetic curve in the mode of spontaneous or induced isotonic contraction (force f = const) reflects the change in the linear length of a muscle preparation Δl, depending on time t. Usually, this curve, which has a maximum – the contraction amplitude ΔL_{max} ($(d\Delta l/dt)_{\tau 0} = 0$ at the time moment τ_0, the coordinates of the maximum point – $[\Delta L_{max};\tau_0]$), is characterized by two inflexion points ($(d^2\Delta l/dt^2)_{\tau C,\tau R} = 0$): at the time moments $t = \tau_C$ (on the level of contraction phase, the coordinates of the inflexion point $[\Delta l_C;\tau_C]$) and at $t = \tau_R$ (on the level of relaxation phase, the coordinates of the inflexion point $[\Delta l_R;\tau_R]$). Usually, it is assumed that this curve is monotonous and does not contain fragments which complicate its quantitative description (oscillations, presence of intermediate plateau, etc.). According to these conditions, in case of spontaneous and induced isotonic responses of a smooth muscle strip, a complete mechanokinetic curve in the simplest case can be described by the equation (1):

$$\Delta l = Rt^n \cdot e^{-kt}, \quad (1)$$

where R, n, and k are mechanokinetic constants. Using equation (1), we get a formula for constant R:

$$R = \left(\frac{e}{\tau_0}\right)^n \Delta L_{max} = \left(\frac{ke}{n}\right)^n \cdot \Delta L_{max},$$

thus,

$$\tau_0 = \frac{\tau_C+\tau_R}{2} = \frac{n}{k},\ \tau_C = \frac{n-\sqrt{n}}{k},$$

$$\tau_R = \frac{n+\sqrt{n}}{k}. \quad (3)$$

According to equations (1) and (2) for time dependence, changes in the length of a muscle preparation Δl in the isotonic mode (f = const), we finally have a basic ratio (4) for the description of the mechanokinetics of the complete smooth muscle contraction-relaxation cycle:

$$\Delta l = \left(\frac{ke}{n}\right)^n \Delta L_{max} t^n e^{-kt}. \quad (4)$$

From equation (3), we see that characteristic constants n and k are determined only by the values of temporal parameters τ_0, τ_C and τ_R, namely:

$$n = \left[\frac{\tau_0}{(\tau_R-\tau_0)}\right]^2 = \left[\frac{\tau_0}{(\tau_0-\tau_C)}\right]^2;$$

$$k = \frac{\tau_0}{(\tau_R-\tau_0)^2} = \frac{\tau_0}{(\tau_0-\tau_C)^2}.$$

The characteristic constants n and k, which are a part of equation (4), can easily be estimated as a result of using a linearized isotonic mechanokinetic curve in case of a complete contraction-relaxation cycle. Indeed, if Δl_C – a change in the length of a muscle preparation on the level of the contraction phase proper at any time moment $t < \tau_0$, and Δl_R – a change in the length of a muscle preparation on the level of the relaxation phase proper at a time moment $t + \Delta t > \tau_0$ (Δt = const, which is arbitrarily set by the researcher in case of the analysis of the primary isotonic mechanokinetic chart, built within the coordinates [Δl; t]), then, according to the ratio (4), we get:

$$ln\left(\frac{\Delta l_R}{\Delta l_C}\right) = -k \cdot \Delta t + n \cdot ln\left(1 + \frac{\Delta t}{t}\right). \quad (5)$$

Our experiments demonstrate that the initial mechanokinetic curve, re-built within double logarithmic coordinates $[ln\left(\frac{\Delta l_R}{\Delta l_C}\right); ln\left(1 + \frac{\Delta t}{t}\right)]$ according to the ratio (5) for the complete cycle of spontaneous isotonic contraction-relaxation of smooth muscle preparations, was linearized very well (R^2 = 0.99) [22, 26]. Thus, it may be assumed that equation (4) is an absolutely reliable description for the mechanokinetics of the contractile response of the smooth muscle on the level of the complete cycle of the process of spontaneous isotonic contraction-relaxation. Therefore, using a linear chart, built within double logarithmic coordinates $[ln\left(\frac{\Delta l_R}{\Delta l_C}\right); ln\left(1 + \frac{\Delta t}{t}\right)]$, based on the abovementioned linearized ratio (5), one can estimate empirical basic constants n and k, which are a part of this ratio: tangent of the angle (α) of the slope of the linearized chart tgα = n, and the interval, reflected during the extrapolation of the chart to the axis of ordinates, is $-k\Delta t$ (as stated above, the value of Δt is set by the researcher, and it is fixed).

Using equations (3) and (4), it is possible to demonstrate that under the isotonic mode of muscle contraction-relaxation, there are the following equations for the change in the length of a muscle stripe $\Delta l_{\tau C}$ and $\Delta l_{\tau R}$ at time moments τ_C and τ_R respectively, which correspond to inflexion points on the mechanokinetic curve on the level of contraction and relaxation phases:

$$\Delta l_{\tau_C} = \Delta L_{max} \cdot \left(\frac{n-\sqrt{n}}{n}\right)^n \cdot e^{\sqrt{n}} \quad (6)$$

$$\Delta l_{\tau_R} = \Delta L_{max} \cdot \left(\frac{n+\sqrt{n}}{n}\right)^n \cdot e^{-\sqrt{n}}. \quad (7)$$

Then the equations for the maximal velocities of contraction and relaxation of a muscle stripe $V_{\tau_C} = \left[\frac{d(\Delta l)}{dt}\right]_{\tau_C}$ and $V_{\tau_R} = -\left[\frac{d(\Delta l)}{dt}\right]_{\tau_R}$ at time points τ_C and τ_R are reasonable:

$$V_C = k \cdot \Delta L_{max} \cdot \left(\frac{n-\sqrt{n}}{n}\right)^{n-1} \cdot \frac{e^{\sqrt{n}}}{\sqrt{n}} \quad (8)$$

$$V_R = -k \cdot \Delta L_{max} \cdot \left(\frac{n+\sqrt{n}}{n}\right)^{n-1} \cdot \frac{e^{-\sqrt{n}}}{\sqrt{n}}. \quad (9)$$

The estimation of mechanical energy parameters. The work ΔA, done by a smooth muscle during the isotonic contraction-relaxation. According to equation (4) for mechanical work $\Delta A = f \cdot \Delta l$ of the isotonic contraction-relaxation of the muscle at any time point t, we can write:

$$\Delta A = f\left(\frac{ke}{n}\right)^n \Delta L_{max} t^n e^{-kt}, \quad (10)$$

and for the maximal work (for time $t = \tau_0$) $\Delta A_{max} = \Delta A_{\tau 0}$, we will get:

$$\Delta A_{max} = f \Delta L_{max}. \quad (11)$$

According to equations (10) and (3) for the value of mechanical work $\Delta A_{\tau C}$ at an inflexion point $t = \tau_C$ on the level of the contraction phase, we have:

$$\Delta A_{\tau C} = e^{\sqrt{n}} \left[\left(n - \sqrt{n}\right)/n\right]^n f \Delta L_{max}. \quad (12)$$

Then, we can introduce the notion of relative work, done by the smooth muscle in the isotonic mode, namely:

- for non-dimensional instant work, done by the muscle at the time moment t and normalized for its maximal (amplitude) value $\frac{\Delta A}{\Delta A_{max}}$, according to equations (10) and (11), we will have an equation:

$$\frac{\Delta A}{\Delta A_{max}} = \left(\frac{ke}{n}\right)^n t^n e^{-kt}, \qquad (13)$$

- for non-dimensional instant work, done by the muscle at the time moment t and normalized for its value on the level of the contraction phase $\frac{\Delta A}{\Delta A_{\tau C}}$ at the inflexion point $t = \tau_C$, according to equations (10) and (12), we will have an equation:

$$\frac{\Delta A}{\Delta A_{\tau_C}} = \left(\frac{ke}{n-\sqrt{n}}\right)^n t^n e^{-kt} \qquad (14)$$

- for non-dimensional work, done at a time moment $t = \tau_C$ and normalized for its maximal (amplitude) value $\frac{\Delta A\tau}{\Delta A_{max}}$, according to equations (12) and (11), we will have the following equation:

$$\frac{\Delta A_{\tau C}}{\Delta A_{max}} = e^{\sqrt{n}} \left[\left(n-\sqrt{n}\right)/_n\right]^n. \qquad (15)$$

As seen, if the values of relative work $\frac{\Delta A}{\Delta A_{max}}$ and $\frac{\Delta A}{\Delta A_{\tau C}}$ on the level of the complete mechanokinetic curve in case of isotonic contraction-relaxation depend, according to equations (13) and (14), on two characteristic constants – *n* and *k*, then the relative work $\frac{\Delta A_{\tau C}}{\Delta A_{max}}$ on the level of a contraction phase proper, according to (15), is determined only by parameter *n*.

Power N, developed by the smooth muscle during the isotonic contraction-relaxation. For instant power of the isotonic contraction of the muscle *N* at a time moment *t*, we have an equation: $N = d\Delta A/dt$. Therefore, taking into account equation (10), after the differentiation, we will have the formula for the instant power of the contraction *N* at any time moment *t*:

$$N = f\left(\frac{ke}{n}\right)^n \Delta L_{max} t^n e^{-kt}\left(\frac{n}{t} - k\right). \qquad (16)$$

It is evident that in case of merely the contraction phase, the value of maximal power N_{max} will be achieved at a time moment $t = \tau_C$ (i.e. at a temporal inflexion point of the mechanokinetic curve on the level of the contraction phase), i.e. $N_{max} = N_{\tau C}$; thus, considering equations (16) and (3), for the maximal power of the contraction N_{max}, we will get the equation:

$$N_{max} = k\Psi(n) f \Delta L_{max}, \qquad (17)$$

where $\Psi(n)$ – the characteristic function of parameter *n*, which satisfies the equation

$$\Psi(n) = e^{\sqrt{n}}\left(n-\sqrt{n}\right)^{n-1} n^{\frac{1-2n}{2}}. \qquad (18)$$

The chart of the characteristic function $\Psi(n)$ is presented in Fig. 1.

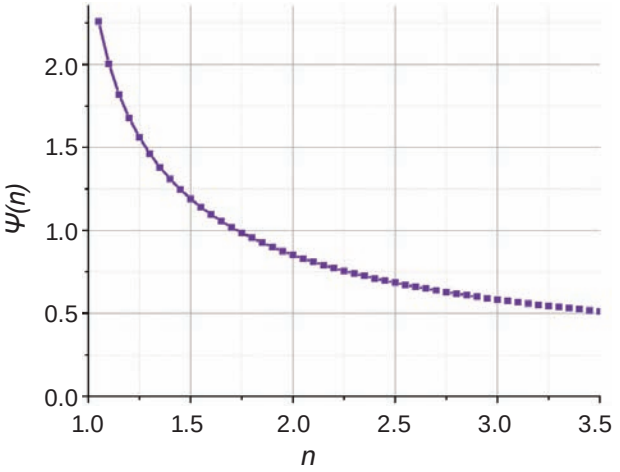


Fig. 1. The chart of the characteristic function Ψ(n). Estimated according to equation (18)

Let us introduce the notion of a relative non-dimensional power N/N_{max} of the smooth muscle contraction, i.e. instant power *N*, normalized by its maximal value N_{max}. Thus, for relative non-dimensional power N/N_{max} at any time moment *t*, according to equations (16) and (17), we will get the equation:

$$\frac{N}{N_{max}} = \frac{\left(\frac{ke}{n}\right)^n \cdot t^n \cdot e^{-kt} \cdot \left(\frac{n}{t-k}\right)}{k \cdot \psi(n)}. \qquad (19)$$

It is also reasonable to introduce the notion of the mean power of the muscle contraction N_m in the time interval $0 - \tau_0$ of the contraction phase, i.e. $N_m = \frac{\Delta A_{max}}{\tau_0} = f\Delta L_{max}/\tau_0$, or, taking into account (3), we get:

$$N_m = kf\Delta L_{max}/n. \qquad (20)$$

We can also introduce the corresponding notion of the relative non-dimensional power N/N_m of the smooth muscle contraction, i.e. power *N*, normalized by its mean value N_m. Thus, for relative non-dimensional power N/N_m at any time moment *t*, according

to equations (16) and (20), we will get the following equation:

$$\frac{N}{N_m} = [n(ke/n)^n t^n e^{-kt}\left(\frac{n}{t} - k\right)]/k\,. \quad (21)$$

As seen, according to equations (19) and (21), in case of the isotonic contraction, the relative non-dimensional power of the contraction N/N_{max} and the relative non-dimensional power of the contraction N/N_m depend on two characteristic constants – both n and k.

Comparing equations (17) and (20), we get a simple association (22) between the capacities of the muscle contraction N_{max} and N_m via the characteristic function $\Psi(n)$:

$$\frac{N_m}{N_{max}} = [n \cdot \Psi(n)]^{-1}\,. \quad (22)$$

What is the relevance of the relative parameters $\Delta A/\Delta A_{max}$, $\Delta A/\Delta A_{\tau C}$, N/N_{max} and N/N_m suggested by us to describe the energy of the isotonic muscle contraction? They are relevant because their value does not depend on the weight of the muscle preparation, arbitrarily chosen in the experiment, the load f and the amplitude of the isotonic contraction ΔL_{max}, it depends only on the values of the characteristic constants n and k. It means that, while studying the energy of the isotonic contraction of the smooth muscle, it is useful to use not the absolute values of the mechanical work ΔA, ΔA_{max}, $\Delta A_{\tau C}$ and power N, N_{max} and N_m for the objective characterization of the contractile process, but normalized values – $\Delta A/\Delta A_{max}$, $\Delta A/\Delta A_{\tau C}$ and N/N_{max} and N/N_m. Therefore, while conducting comparative studies *in vitro* in the sphere of biophysics, physiology, and pharmacology of smooth muscles on the level of studying the classic experimental "norm–pathology" or "control–effect of physiologically active/pharmacological substances, the effect of physical-chemical factors", it is reasonable to provide the interpretation of the isotonic contraction energy using the terms of the abovementioned non-dimensional parameters – $\Delta A/\Delta A_{max}$, $\Delta A/\Delta A_{\tau C}$, N/N_{max} and N/N_m.

As seen from equations (13) and (19), there is a connection between the values of the normalized mechanical work of the muscle contraction $\Delta A/\Delta A_{max}$ and the normalized power of this contraction $/N_{max}$:

$$\frac{\Delta A}{\Delta A_{max}} = \left[k \cdot \Psi(n) \Big/ \left(\frac{n}{t} - k\right)\right]\left(\frac{N}{N_{max}}\right). \quad (23)$$

In other words, according to equation (23) for any mechanogram, in case of the isotonic contraction of the smooth muscle at any time moment t, there should be the mentioned relation between the energy parameters (ΔA, ΔA_{max}, N, N_{max}) and empirical mechanokinetic parameters (n and k). Thus, equation (23) is a strict quantitative criterion for the accuracy of the researcher's determination of mechanokinetic and energy parameters.

Experimental part

At the first stage of our experimental studies, we investigated the mechanokinetic regularities of the selective inhibitor of Mg^{2+}, ATP-dependent sodium pump, calix[4]arene C-1130 (10 μM), on the contraction-relaxation of the myometrium preparation, induced by K^+-depolarization (80 mM KCl) (Fig. 2, Table).

In Fig. 2, we have charts, illustrating the possibility of using the mechanokinetic equation (4) to describe the contraction-relaxation of the myometrium preparation, induced by K^+-depolarization (weight – 38 mg) in the isotonic mode (f = 10 mN, the initial preparation length – 10 mm) in control and at the effect of calix[4]arene C-1130 (10 μM) under preliminary incubation of this compound for 30 min.

It is evident that on the level of the complete cycle of the isotonic contraction-relaxation, the initial mechanokinetic curves, presented in panel A of Fig. 2, are linearized very well (R^2 = 0.98), according to equation (5), while using the double logarithmic coordinates $\left[ln\left(\frac{\Delta l_R}{\Delta l_C}\right); ln\left(1 + \frac{\Delta t}{t}\right)\right]$ (panel B, Fig. 2). It means that, firstly, both in the control and in case of the effect of calix[4]arene C-1130, the mechanokinetics on the level of a complete contraction-relaxation cycle, induced by K^+-depolarization, is reliably described by equation (4). Secondly, the use of linearized charts (panel B, Fig. 2) allows us to calculate the basic mechanokinetic parameters n and k according to equation (5): in case of control we have k = 0.026 s^{-1}; n = 2.08; and in case of calix[4]arene C-1130, the calculation yields k = 0.007 s^{-1}; n = 1.12. As seen, in case of applying calix[4]arene C-1130, the inhibitor of Mg^{2+}, ATP-dependent sodium pump, there is a 3.7-fold decrease, as compared to the control, in the empirical mechanokinetic constant k, and a 1.9-fold decrease, as compared to the control, in the non-dimensional empirical parameter n.

According to the data, presented in Fig. 2, in case of the control mechanokinetic curve, the value

of ΔL_{max} = 1.99 mm, and the values of $\Delta l_{\tau C}$ and $\Delta l_{\tau R}$ were 0.73 mm and 1.41 mm, respectively (estimated using equations (6) and (7)). The values of characteristic time parameters τ_0, τ_C and τ_R had the values of 80.7, 25.03 and 136.4 s, respectively (calculated using equation (3)). And finally, in case of control, the values of the maximal velocities on the level of contraction and relaxation phases $V_{\tau C}$ and $V_{\tau R}$ were 0.042 and 0.015 mm/s, respectively (calculated using equations (8) and (9)) (see also Table).

In case of the effect of calix[4]arene C-1130 (10 μM) on the muscle preparation, the value of ΔL_{max} = 2.96 mm (148.4% from the control value), and the values of $\Delta l_{\tau C}$ and $\Delta l_{\tau R}$ were 0.34 mm (46.4% from the control value) and 2.16 mm (153.5% from the control value), respectively (calculated using equations (6) and (7)). The values of characteristic temporal parameters τ_0, τ_C and τ_R were 163.0 s (202.0% from the control value), 9.14 s (36.5% from the control value) and 316.8 s (232.3% from the control value), respectively (calculated using equation (3)). And finally, the values of maximal velocities on the level of contraction and relaxation phases $V_{\tau C}$ and $V_{\tau R}$ were 0.039 mm/s (92.8% from the control value) and 0.007 mm/s (48.3% from the control value), respectively (calculated using equations (8) and (9)) (see also Table).

Generally, the abovementioned data (see also Table) confirm that calix[4]arene C-1130 (10 μM), a selective inhibitor of Mg^{2+}, ATP-dependent sodium pump, has a considerable impact on mechanokinetic parameters of the contraction-relaxation of the myometrium preparation, induced by K^+-depolarization (80 mM KCl). For instance, under the effect of calix[4]arene on the muscle contraction, there is a considerable increase (up to 148.4% from the control value) in its amplitude ΔL_{max}, controlled by the superposition of the functioning of membrane-bound systems of passive energy-independent transportation of Ca ions (Ca^{2+}-channels of the plasma membrane and sarcoplasmic reticulum) and energy-dependent transportation of this cation (Mg^{2+},ATP-dependent calcium pumps of the plasma membrane and sarcoplasmic reticulum, Na^+-Ca^{2+} exchanger of the plasma membrane, Ca^{2+}-uniporter of mitochondria), i.e. controlled by the concentration of ionized Ca in

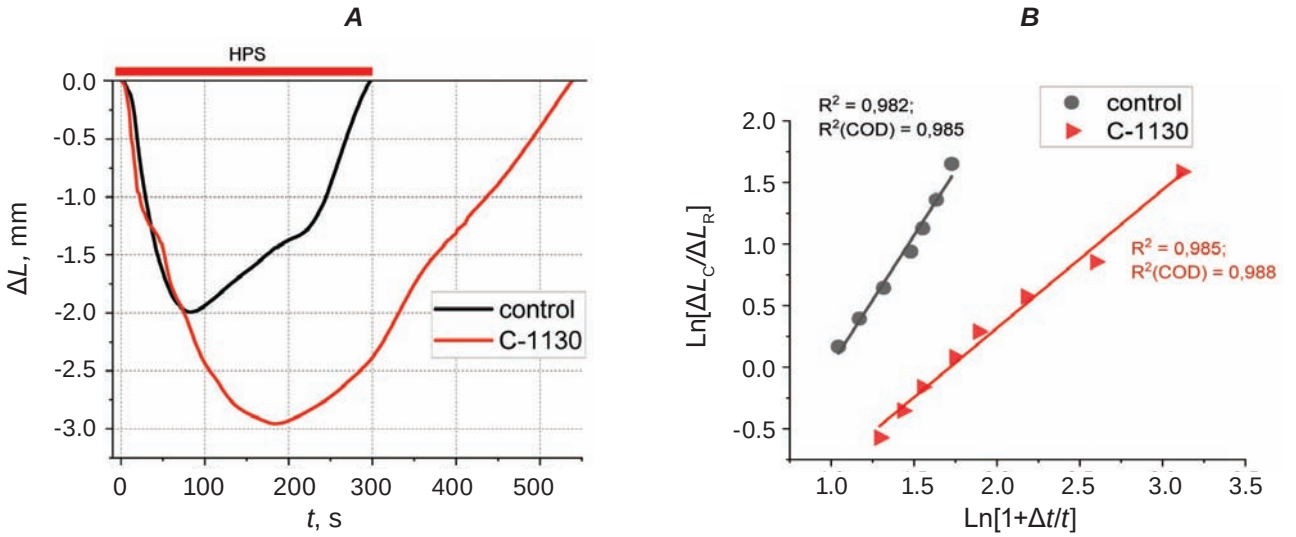


*Fig. 2. The mechanokinetic analysis of the complete isotonic contraction-relaxation cycle of the myometrium tissue stripe, induced by K^+-depolarization (load f = 10 mN) in the control and under the effect of calix[4]arene C-1130, a selective inhibitor of the sodium pump. Typical mechanokinetic charts are presented. The concentration of calix[4]arene – 10 μM. **A** – initial mechanokinetic curves; **B** – linearization of initial mechanokinetic curves, presented in panel A, which was done according to equation (5) (see Research Methods). The weight of the tissue preparation and its initial length were 38 mg and 10 mm, respectively. In case of the control chart and the chart, obtained under the effect of calix[4]arene, the set values were Δt 80 and 280 s, respectively. The values of mechanokinetic constants, estimated using the linearized charts according to equation (5), were as follows: in control k = 0.026 s^{-1}, n = 2.08; under the effect of calix[4]arene C-1130 – k = 0.007 s^{-1}, n = 1.12. The timing of high-K^+ solution application showed by a horizontal bar above recorded mechanokinetic curves*

Table. Mechanokinetic and energy characteristics of the isotonic (f = 10 mN) contraction-relaxation of the myometrium preparation, induced by K^+-depolarization, at norm and under the effect of calix[4]arene C-1130 (10 μM). The results of the typical mechanokinetic experiment are presented in Fig. 2. The weight of the tissue preparation and its initial length were 38 mg and 10 mm, respectively

Mechanokinetic or energy parameter	Parameter value, control	Parameter value under the effect of calix[4]arene	Reference to the equation for parameter estimation
k, s^{-1}	0.026	0.007	(5)
n	2.08	1.12	(5)
ΔL_{max}, mm	1.99	2.96	
τ_0, s	80.70	163.00	(3)
τ_C, s	25.03	9.14	
τ_R, s	136.40	316.80	
$\Delta l_{\tau C}$, mm	0.73	0.34	(6)
$\Delta l_{\tau R}$, mm	1.41	2.16	(7)
$V_{\tau C}$, mm/s	0.042	0.039	(8)
$V_{\tau R}$, mm/s	0.015	0.007	(9)
ΔA_{max}, μJ	19.90	29.60	(11)
$\Delta A_{\tau C}$, μJ	7.22	3.36	(12)
$\Delta A_{\tau C}/\Delta A_{max}$	0.36	0.11	(13)
N_{max}, μW	0.42	0.39	(17)
N_m, μW	0.25	0.18	(20)
N_m/N_{max}	0.60	0.46	(22)

Note. As seen from this Table, in the kinetic aspect, under the effect of calix[4]arene C-1130, there is a considerable, 3.7-fold as compared to the control, decrease in the empirical mechanokinetic constant k and a 1.9-fold decrease in the non-dimensional empirical parameter n. Here, the amplitude value of the contractile activity ΔL_{max} increases by 48.4%. The values of characteristic time parameters τ_0 (notable for the contraction amplitude) and τ_R (the inflexion point in case of the relaxation phase) under the effect of calix[4]arene increased by 102% and 132%, respectively, and the value τ_C (the inflexion point in case of the contraction phase) decreased by 63.5% to the control. Under the effect of calix[4]arene, the value of linear contraction $\Delta l_{\tau C}$ at a characteristic time point τ_C decreased by 53.6%, and the value of linear contraction $\Delta l_{\tau R}$ at a time point τ_R increased by 53.5%. However, under the effect of calix[4]arene on the background of the control experiment, there was practically no change in the characteristic velocity parameter $V_{\tau C}$ on the level of the contraction phase, the value of this velocity decreased merely by 7.2 %, whereas the velocity parameter $V_{\tau R}$ had considerable changes on the level of the relaxation phase – it decreased by 51.7%. Under the effect of calix[4]arene on the muscle contraction, there were subsequent changes in the energy parameters. As compared to the control, there was a considerable increase in the maximal (at a time moment $t = \tau_0$) value of the isotonic work ΔA_{max} – by 48.4%, and the value of the mechanical work at the time point τ_C decreased by 53.4%. As for the non-dimensional ratio of these works, $\Delta A_{\tau C}/\Delta A_{max}$, under the effect of calix[4]arene C-1130 it decreased by 69.5% compared to the control. However, under the effect of calix[4]arene C-1130, the maximal value of the contraction power Nmax at a time point $t = \tau_C$ practically did not change regarding the control (the difference is only 7%), and the average value of the power Nm even decreased by 28%. As for the non-dimensional ratio N_m/N_{max}, under the effect of calix[4]arene C-1130, it decreased by 23.3% compared to the control

the cell. Therefore, on the level of intact muscle tissue, we see the confirmation of our previous results, obtained on the cellular level using the method of laser confocal microscopy, which demonstrated that under the effect of the mentioned calix[4]arene, there is indeed an increase in the ionized Ca concentration in myometrium cells [16]. Simultaneously, under the effect of calix[4]arene C-1130, there is a considerable decrease (to 48.3% from the control value) in the maximal (at the inflexion point $t = \tau_R$) velocity of the

muscle stripe relaxation $V_{\tau R}$, with practically no observed change in the maximal (at the inflexion point $t = \tau_C$) velocity of the muscle stripe contraction $V_{\tau C}$ (92.8% from the control value).

It is well known that to the predominant degree, the dynamics of the muscle contraction phase is controlled by the systems of passive energy-independent transportation of Ca ions, which ensure the increase in the concentration of these ions in myocytes, and the dynamics of the relaxation phase is controlled by the systems of active energy-dependent transportation of the mentioned cation, which induce the decrease in this concentration in the myoplasm [17, 27, 28]. Therefore, the fact of a considerable (almost two-fold) decrease in the velocity of muscle stripe relaxation $V_{\tau R}$ under the impact of calix[4]arene C-1130 – the inhibitor of Mg^{2+},ATP-dependent sodium pump – Na^+,K^+-ATPase at the practically unchangeable value of the velocity of the muscle stripe contraction $V_{\tau C}$ gives grounds for the following assumption: the result of the impact of this calix[4arene on the contractile activity of the myometrium stripe is the inhibition of the Na^+-dependent release of Ca ions from myocytes, mediated by the functioning of the sodium pump, due to the decrease in the transmembrane sodium gradient, directed into muscle cells, and thus, a decrease in the activity of the non-electrogenic $2Na^+$-Ca^{2+} exchanger of the plasma membrane, releasing Ca ions from myocytes which promotes the increase in Ca ion concentration in them.

On the second stage of our study, we conducted energy-wise interpretation of the regularities in the myometrium contraction-relaxation in the control experiment and under the effect of calix[4]arene C-1130, the inhibitor of the sodium pump, using the smooth muscle (Fig. 3 and 4, see also Table).

When the smooth muscle preparation was used (the tissue weight – 38 mg, the initial preparation length – 10 mm, the load f = 10 mN), the data about the mechanokinetics of the contraction-relaxation of which are reflected in Fig 2, the involvement of equations (11), (12) and (20), (22) allowed for calculating the corresponding energy characteristics ΔA_{max}, $\Delta A_{\tau C}$, N_{max} and N_m.

It was found that during the control experiment (the values of the characteristic constants k = 0.026 s^{-1}; n = 2.08), the value of the maximal work of the muscle stripe contraction ΔA_{max} was 19.9 μJ, and the value of the work $\Delta A_{\tau C}$ at the moment of characteristic time τ_C – 7.22 μJ. Thus, during the control experiment, the ratio $\Delta A_{\tau C}/\Delta A_{max}$ was 0.36. And under the effect of calix[4]arene C-1130 on the muscle preparation (the values of the characteristic constants were k = 0.007 s^{-1}; n = 1.12), the values of ΔA_{max} and $\Delta A_{\tau C}$ were 29.6 μJ (compared to the control value – 148.4%) and 3.36 μJ (compared to the control value – 46.6%). That is, in case of the effect of calix[4]arene, the ratio $\Delta A_{\tau C}/\Delta A_{max}$ was 0.11, which was much less than in the control experiment. As for the values of the contraction power, in case of the control experiment for the maximal power N_{max} we had the value of 0.42 μW, and for the average power N_m – 0.25 μW. Therefore, during the control experiment, the ratio N_m/N_{max} was 0.6. In case of the effect of calix[4]arene C-1130 on the muscle preparation, the values of N_{max} and N_m were 0.39 μW (compared to the control value – 92.0%) and 0.18 μW (compared to the control value – 72.9). Thus, under the effect of calix[4]arene] C-1130 on the muscle contraction, the ratio N_m/N_{max} was 0.46.

It is evident that in the energy aspect, the effect of calix[4]arene C-1130 on the isotonic contraction of the myometrium preparation is revealed in the increase in the maximal contraction work ΔA_{max} (by 48.4%) and the decrease in the work $\Delta A_{\tau C}$, done as of the moment of characteristic time τ_C (by 53.4%). As for the power of the contraction N under the effect of calix[4arene, its maximal value N_{max} at the time point τ_C practically did not change, and the average value for power N_m even decreased – by 27.1%. Therefore, in the energy aspect, the stimulating impact of calix[4]arene C-1130, the selective inhibitor of Mg^{2+},ATP-dependent sodium pump, on the isotonic contraction of the myometrium preparation, induced by K^+-depolarization, was revealed in the increase in the maximal work of the contraction ΔA_{max} practically without any changes in the maximal power of the contraction (as of the moment of reaching the characteristic time τ_C).

However, the abovementioned calculations of the energy parameters of the smooth muscle were related to specific quantitative characteristics of the muscle preparation (as stated before, the weight – 38 mg, the initial length – 10 mm, the load value f – 10 mN), which are usually subjectively selected by the researcher. Thus, the further energy analysis in the process of isotonic myometrium contraction-relaxation in the control experiments and under the effect of calix[4]arene C-1130 was conducted according to equations (13), (14), (19), and (21), in terms of non-dimensional energy parameters –

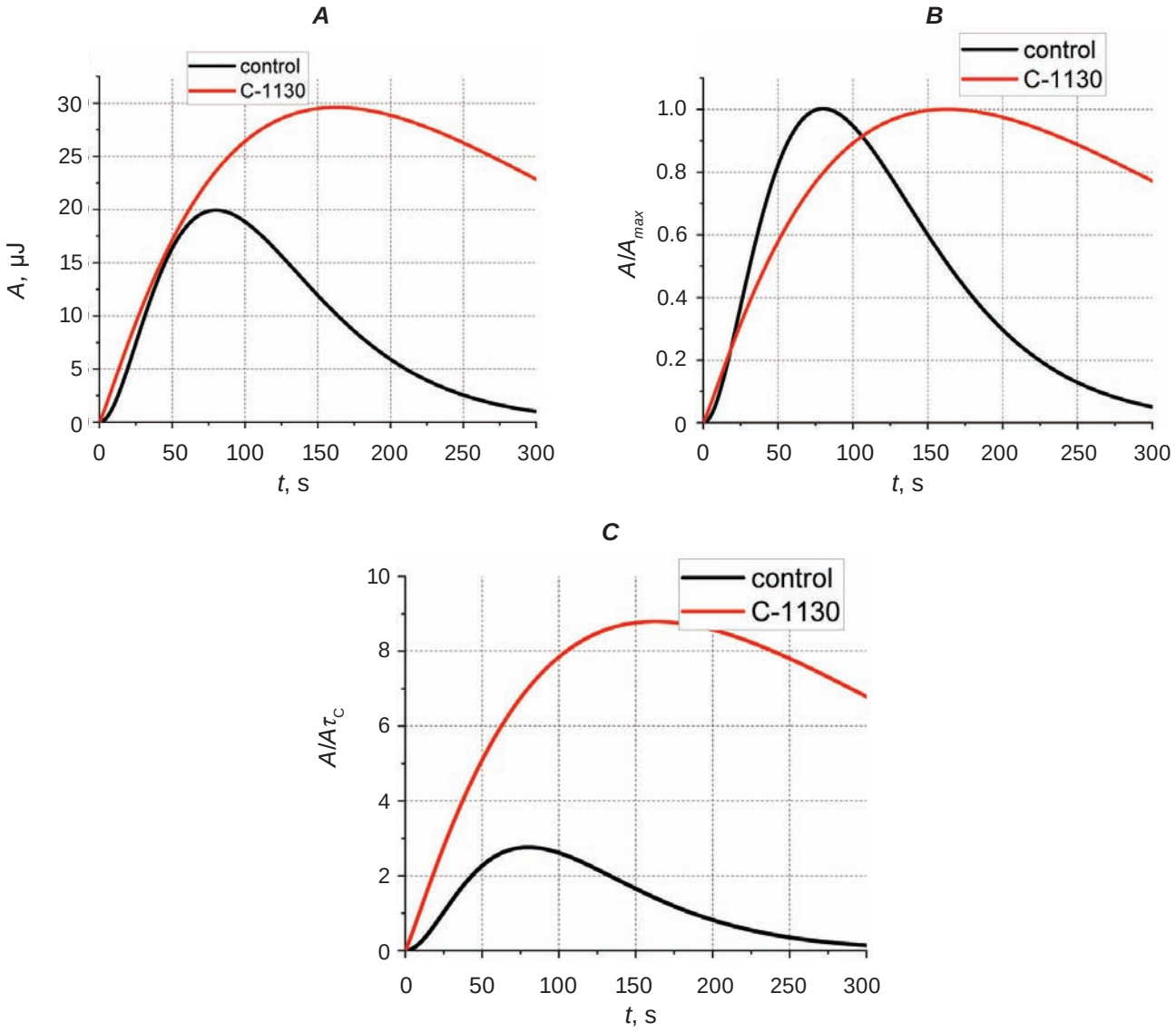


*Fig. 3. The dynamics in the change of the instant work ΔA in case of the complete cycle of isotonic contraction-relaxation of the myometrium tissue stripe, induced by K^+-depolarization, in control and under the effect of calix[4]arene C-1130 (10 μM). The values of mechanokinetic constants k and n were estimated using the linearized charts (Fig. 2, panel B): in control – k = 0.026 s^{-1}, n =2.08; under the effect of calix[4]arene C-1130 – k = 0.007 s^{-1}, n = 1.12. **A** – dependence of the absolute value of the instant work ΔA on time t (load f = 10 mN). The values of the weight of the tissue preparation and its initial length were 38 mg and 10 mm, respectively. At the same time, the values of ΔA in time were estimated according to equation (10); **B** – dependence of the instant work, done by the muscle at the time moment t and normalized by its maximal (amplitude) value $\Delta A/\Delta A_{max}$ regarding time t. The change in the value of $\Delta A/\Delta A_{max}$ in time t was estimated according to equation (13). **C** – dependence of the instant work, done by the muscle at the time moment t and normalized by its value in case of the characteristic time τ_C $\Delta A/\Delta A_{\tau C}$, regarding time t. The change in the value of $A/\Delta A_{\tau C}$ in time t was estimated according to the ratio (14)*

normalized work $\Delta A/\Delta A_{max}$, $\Delta A/\Delta A_{\tau C}$ and normalized power N/N_{max}, N/N_m. Obviously, these relative characteristics, according to equations (13), (14), (19) and (21), do not depend on the weight and length of the muscle preparation or the load f and the contraction amplitude ΔL_{max}, but are determined solely by characteristic parameters *k* and *n*.

Firstly, the data, presented in Fig. 3, are evidence in favor of the fact that under the effect of calix[4]arene C-1130 (10 μM) on the myometrium con-

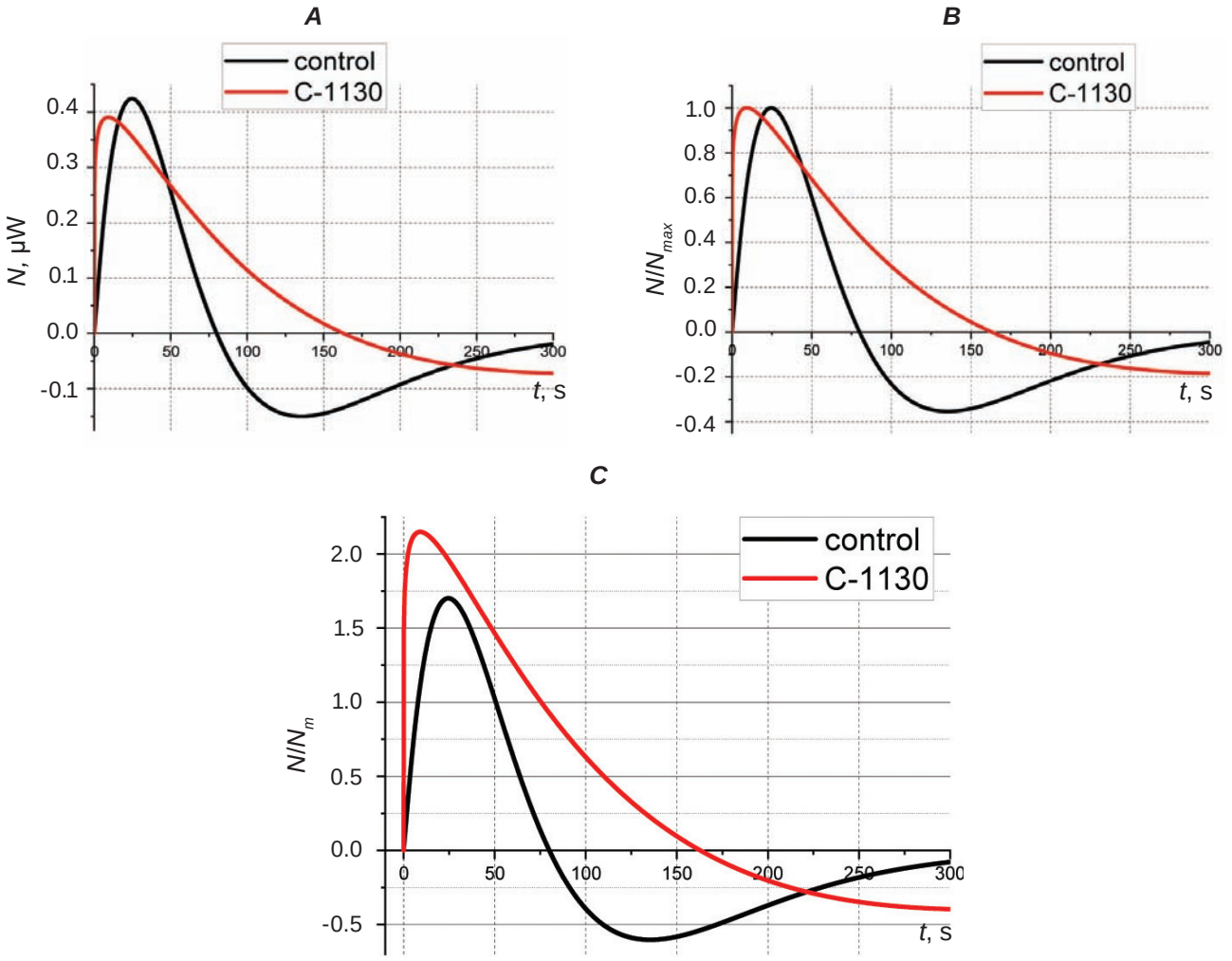


Fig. 4. The dynamics of the change in the instant power N in case of the complete cycle of the isotonic contraction-relaxation of the myometrium tissue stripe, induced by K^+-depolarization, in control and under the effect of calix[4]arene C-1130 (10 μM). The values of mechanokinetic constants k and n, estimated using the linearized charts (Fig. 2, panel B): in control k = 0.026 s^{-1}, n = 2.08; under the effect of calix[4]arene C-1130 k = 0.007 s^{-1}; n =1.12. ***A*** *– dependence of the absolute value of the instant power N on time t (load f = 10 mN). The value of the weight of the tissue preparation and its initial length were 38 mg and 10 mm, respectively. Here, the change in the value N in time was estimated according to equation (16);* ***B*** *– dependence of the non-dimensional instant power at the time moment t and normalized by its maximal value N/N_{max} on time t. The change in the value of N/N_{max} in time t was estimated according to equation (19), using the characteristic function Ψ(n) = 0.82 and 1.92 in control and under the effect of calix[4]arene C-1130, respectively, which is determined by equation (18);* ***C*** *– dependence of the non-dimensional instant power at the time moment t and normalized by its average value N/N_m, on time t. The change in the value of N/N_m in time was estimated according to equation (21)*

traction, induced by K^+-depolarization, the maximal value of the work (at $t = \tau_0$) in the "work-time" cycle is achieved when, under control, this cycle practically comes to its completion; this conclusion relates not only to the absolute value of the work ΔA (panel A), but also its relative values $\Delta A/\Delta A_{max}$ (panel B) and $\Delta A/\Delta A_{\tau C}$ (panel C).

Secondly, as seen in Fig. 3, under the effect of calix[4]arene C-1130 on the smooth muscle on the level of the complete contraction-relaxation cycle, induced by K^+-depolarization, both for the absolute value of the work ΔA (panel A), and for its relative values $\Delta A/\Delta A_{max}$ and $\Delta A/\Delta A_{\tau C}$ (panels B and C, respectively), there is considerable relaxation inhibi-

tion of these energy parameters till the complete relaxation of the muscle. It means that under the effect of the mentioned calix[4]arene, the smooth muscle not only becomes capable of increasing the maximal isotonic mechanical work ΔA_{max} (Fig. 3, panel A), but also demonstrates a much higher, compared to the control, ability to conduct this work in time (Fig. 3, panels A, B, and C): for instance, in control, in case of all three parameters, we have complete relaxation of the muscle after 250–300 s, but under the effect of calix[4]arene C-1130, at this moment, a rather prolonged higher level of conducting mechanical work is still observed.

At the same time, as seen in Fig. 4, under the effect of calix[4]arene C-1130 on the muscle (at $t = \tau_C$) in case of "power-time" cycle, the maximum for all three power parameters – N, N/N_{max} and N/N_m is observed in time t earlier than in control. And if, similar to the use of the absolute power value N (panel A), and its relative value N/N_{max} (panel B), the maximal values of these characteristics in control practically correspond to those, registered under the effect of calix[4]arene C-1130, then in case of such a relative characteristic as N/N_m, they differ (panel C): in case of the effect of calix[4]arene, this ratio is obviously higher than in control. However, noteworthy is the following fact: while in the control experiment, all three power parameters – N, N/N_{max} and N/N_m reach the zero value after 75–80 s, then under the effect of calix[4]arene C-1130, the smooth muscle still has a considerable power potential – 30–40% from its maximal value.

It should be noted that, as it turned out, at any time moment t for each mechanokinetic curve, studied by us in the isotonic mode of contraction-relaxation, the combination of mechanokinetic (n, k, $\Psi(n)$) and energy $\left(\frac{\Delta A}{\Delta A_{max)}}, \frac{N}{Nmax}\right)$ parameters corresponds to equation (23) rather reliably, which indicates that the abovementioned analysis of kinetics and energy of the contraction-relaxation of the uterine smooth muscle is quite accurate.

Thus, in general, the abovementioned mechanokinetic and energy analysis of the effect of calix[4]arene C-1130, the new selective inhibitor of Mg^{2+}, ATP-dependent sodium pump of the plasma membrane of myocytes, on the isotonic contractile activity of myometrium, induced by K^+-depolarization, demonstrates that this inhibitor is capable of inducing the increase in the maximal value of the mechanical work ΔA_{max} (observed at $t = \tau_0$), promoting its relaxation without a considerable change in the contraction power. However, while in the control experiment, all three power parameters – N, N/N_{max} and N/N_m reach a zero value after 75–80 s, then under the effect of calix[4]arene C-1130, the smooth muscle still has a considerable power potential – 30–40% from its maximal value.

Taking into consideration the fact that the mentioned calix[4]arene is a selective inhibitor of the sodium pump [16], one can assume that mechanokinetic and energy effects, discovered by us and observed under its effect on the uterine muscle, are mediated by the inhibition of the functioning of non-electrogenic $2Na^+$-Ca^{2+} exchanger, the presence of which in the plasma membrane of myometrium cells is not under doubt [17, 18].

At present, there is a series of publications in scientific literature in the field of investigating the mechanokinetics of smooth muscle contraction-relaxation [29-32]. Based on our previously developed method of mechanokinetic analysis of the isotonic contraction of the smooth muscle [22, 26], we elaborated the methodology of estimating the energy characteristics of this process – mechanical work A and power N at any time moment t in case of the complete contraction-relaxation cycle. We obtained equations to determine both instant absolute and relative $\Delta A/\Delta A_{max}$, $\Delta A/\Delta A_{\tau C}$, N/N_{max} and N/N_m values of these parameters. A criterion for estimating the accuracy of the conducted analysis of mechanokinetic and energy indices of the contraction-relaxation process was suggested. However, it is obvious that the calculations of the absolute energy parameters of the smooth muscle contraction are usually related to specific quantitative characteristics of the muscle preparation (weight, initial length, load value), which in experiments *in vitro* are subjectively selected by researchers. The contraction amplitude ΔL_{max} depends on these characteristics. Therefore, we recommend conducting the objective analysis of the energy of the process of isotonic contraction-relaxation of the smooth muscle in terms of the abovementioned non-dimensional parameters of mechanical work and power, which do not depend on the subjectivity of the researchers.

The suggested method of estimating absolute and relative energy parameters was tested on the example of studying the effect of calix[4]arene C-1130, a new selective inhibitor of Mg^{2+},ATP-dependent sodium pump (Na^+, K^+-ATPase) (10 μM), on the isotonic contraction of the uterine smooth mus-

cle, myometrium, induced by K^+-depolarization. The obtained results give grounds for the assumption that this inhibitor mediates its effect on mechanokinetic and energy characteristics of the contractile activity of myometrium, induced by K^+-depolarization, via the inhibition of the functioning efficiency of the non-electrogenic $2Na^+$-Ca^{2+}-exchanger of the plasma membrane, ensuring the release of Ca ions from myocytes due to the energy of transmembrane sodium gradient, directed from the extracellular space into the cell.

We believe that the methodology of determining the energy parameters of the smooth muscle contraction-relaxation process, developed by us, may be useful for the strict interpretation of the experiment results in biophysics and physiology of smooth muscles in case of model tensometric studies in vitro while investigating the effect of biologically active substances, pharmacological compounds on the dynamics of the complete contraction-relaxation dynamics. This method may also be considered reasonable for quantitative characterization of the contraction process in biomedicine in the "norm-pathology" mode or for comparative determination of mechanokinetic characteristics in case of different smooth muscles.

We do not rule out that if the method, developed by us, is successfully tested in simulated experiments, conducted on skeletal muscles, it may be useful in solving urgent problems of sport biophysics and sport medicine.

Conclusions

1. The method of determining energy parameters – mechanical work A and power N at any time moment t in case of the complete cycle of isotonic contraction-relaxation of smooth muscle preparations was developed and tested in the tensometric experiments.

2. The method was used while studying the energy regularities of the effect of calix[4]arene C-1130, the new selective inhibitor of Mg^{2+},ATP-dependent sodium pump (Na^+, K^+-ATPase), on the isotonic contraction of the myometrium smooth muscle, induced by K^+-depolarization.

3. Based on the analysis of the mechanokinetics and energetics results, it has been assumed that calix[4]arene C-1130 mediates its effect on the contractile activity of myometrium, induced by K^+-depolarization, inhibiting the functioning efficiency of the non-electrogenic $2Na^+$-Ca^{2+}-exchanger of the plasma membrane, which ensures the release of Ca ions from myocytes due to the energy of the transmembrane sodium gradient.

4. The proposed methodology of determining the energy parameters of the process of contraction-relaxation of the smooth muscles may be useful during the interpretation of experimental results in biophysics and physiology of the smooth muscles in case of model tensometric studies *in vitro* while investigating the effect of biologically active substances, pharmacological compounds, and physical-chemical factors on the dynamics of the complete contraction-relaxation cycle. This methodology may be reasonable during quantitative characterization of the contractile process in biomedicine in the "norm-pathology" mode, or with the purpose of comparative determination of energy characteristics of this process in physiology and bioenergetics, in case of different smooth muscles.

Conflict of interest. The authors have completed the Unified Conflicts of Interest form at http://ukr-biochemjournal.org/wp-content/uploads/2018/12/coi_disclosure.pdf and declare no conflict of interest.

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НОВИЙ СЕЛЕКТИВНИЙ ІНГІБІТОР НАТРІЄВОЇ ПОМПИ КАЛІКС[4]АРЕН С-1130 ЯК МОДУЛЯТОР ЕНЕРГЕТИКИ СКОРОЧЕННЯ ГЛАДЕНЬКОГО М'ЯЗА МАТКИ

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Відомо, що функціонування неелектрогенної системи $2Na^+$-Ca^{2+}-обміну, локалізованої в плазматичній мембрані клітин міометрія, забезпечується енергією трансмембранного градієнта натрію, що створюється Mg^{2+}, АТР-залежним натрієвим насосом. Метою дослідження було визначити, як інгібітор цього насоса калікс[4]арен С-1130 впливає на механокінетику та енергетику скорочення-розслаблення міометрія. Експерименти проводилися на самках щурів Вістар. Скоротливу активність поздовжніх гладеньких м'язів матки вивчали за допомогою тензометричного методу. Розроблено та випробувано в тензометричних експериментах метод визначення механічної роботи *A* та потужності *N* у будь-який момент часу *t* повного циклу ізотонічного скорочення-розслаблення гладких м'язів. Калікс[4]арен С-1130 розчиняли в диметилсульфоксиді та вводили в робочі розчини в концентрації 10^{-5} М. Було виявлено, що під впливом калікс[4]арену С-1130 відносні максимальні значення механічної роботи *A* досягалися в момент, коли цикл скорочення-релаксації в контрольних умовах практично завершувався, тоді як максимальні значення потужності *N* досягалися швидше, ніж у контролі. Ці результати свідчать про те, що калікс[4]арен С-1130 здатний підвищувати максимальне значення механічної роботи гладеньких м'язів, сприяючи їх розслабленню без суттєвої зміни потужності скорочення. Розроблена методика може бути корисною для порівняльного вивчення впливу фармакологічних препаратів на скоротливу активність гладеньких м'язів у форматі «норма-патологія».

Ключові слова: калікс[4]арен С-1130, гладенькі м'язи міометрія, скоротлива активність, кінетика та енергетичні параметри.

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