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Impact of C_{60} fullerene on the dynamics of force-speed changes in *soleus* muscle of rat at ischemia-reperfusion injury

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The effect of C_{60} fullerene nanoparticles (30-90 nm) on dynamics of force response development to stimulated soleus muscle of rat with ischemic pathology, existing in muscle during the first 5 hours and first 5 days after 2 hours of ischemia and further reperfusion, was investigated using the tensometric method. It was found that intravenous and intramuscular administration of C_{60} fullerene with a single dose of 1 mg/kg exert different therapeutic effects dependent on the investigated macroparameters of muscle contraction. The intravenous drug administration was shown to be the most optimal for correction of the velocity macroparameters of contraction due to muscle tissue ischemic damage. In contrast, the intramuscular administration displays protective action with respect to motions associated with generation of maximal force response or continuous contractions elevating the level of muscle fatigue. Hence, C_{60} fullerene, being a strong antioxidant, may be considered as a promising agent for effective therapy of pathological states of the muscle system caused by pathological action of free radical processes.

Key words: C_{60} fullerene, soleus muscle of rat, ischemia-reperfusion injury, dynamics of muscle contraction, dynamic light scattering.

Ischemic muscle injury may be viewed as a series of biochemical reactions initiated under conditions of hypoxia already after few minutes of ischemia as a consequence of insufficient blood supply [1]. As a rule this pathology is related to a secondary effect commonly developed after insults, infarcts or mechanical injuries. Destruction of the majority of cells occurs due to activation of chemical agents produced during and after ischemia. Ischemic cascade usually proceeds within 2-3 hours after ischemia, although in certain cases it may last several days even after recovery of normal blood stream. Quick determination of the level of ischemic injury is of crucial importance for its further therapy [2]. The action of ischemia decreases the force of muscle contraction by 40% after 1 hour of ischemia, and by 90% after 2 hours. Recovery of muscle force generation was observed only by the end of second week after ischemia [3]. After the ischemia pathologic processes are operating in muscle within few days and are usually characterized by progressive dynamics. The processes of regeneration start by the end of the first week after 2 hours of ischemia. Experimental data point out that the initial pathologic effects after continuous ischemia-reperfusion may be incomplete thus extending the ischemic state for up to several days [4]. Increase of the duration of ischemia from 1 to 2 hours significantly slows down the processes of regeneration [3].

Complexity of molecular mechanisms of muscle contraction and insufficient knowledge

of their operation under conditions of ischemic injury often do not allow interpreting of large amount of experimental data. The general picture of the pathologies being developed is complicated by the fact that fast and slow muscle filaments differently respond to ischemic injury. Recovery of their kinetic characteristics also occurs for different time intervals independent of their location [5].

The pristine C_{60} fullerene as a unique class of carbon allotropes is able to penetrate through the cell membrane [6], to exhibit antioxidant properties [7, 8] and, being nontoxic (at low concentration at least) [9], to exert specific health effects [10]. Biomedical applications require the dispersal of C_{60} fullerene in a solvent, with aqueous dispersions being preferred because of biocompatibility, safety, or environmental concerns. Although pristine C_{60} fullerene has extremely low water solubility, it can form stable colloid solution containing individual C_{60} fullerenes as well as C_{60} fullerene aggregates (clusters) in water [11] when subjected to extended mixing, sonication or solvent exchange [12].

It is known that C_{60} molecule is able to bind 34 methyl radicals [13]. C_{60} fullerene can effectively immobilize and inactivate either superoxide anion-radical and hydroxyl radicals [14]. C_{60} fullerene derivatives are now considered as strong adsorbents of free radicals, which are being produced as a consequence of ischemic injury of small intestine [15]. In [16] it was shown that intravenous administration of C_{60}(FC4S) 15 minutes before occlusion in 10 and 100 μg/kg doses significantly lowers the level of focal cerebral ischemia. In this case the pH level and gas content in blood do not change, as well as the frequency of heart contraction and arterial pressure remain unaltered. Hence, it may be assumed that C_{60} fullerene, as a strong antioxidant, may exert protective effects against ischemic injuries of tissues. That is why the main goal of the present work was to investigate the influence of pristine C_{60} fullerene on dynamics of evolution of the processes of force response development to stimulated excitation of *soleus* muscle of rat with ischemic pathology, appearing during the first 5 hours and first 5 days after 2 hours of ischemia and further reperfusion. The evolution of the processes of force response change in ischemic muscle determined during the experiment enables establishing important relationships between the macroscopic parameters of ischemic muscle state and the level of its efferent activity.

METHODS

Highly stable reproducible pristine C_{60} fullerene aqueous colloid solution (C_{60}FAS) in 0.15 mg/ml C_{60} fullerene concentration used in the experiments, was prepared according to protocol [17, 18].

Measurement of the *hydrodynamic* size distribution for C_{60} fullerene aggregates was performed by dynamic light scattering (DLS) at 25 °C on a Zetasizer Nano ZS (Malvern Ins. Ltd) with upload of Multiple narrow modes (high resolution). DLS instrument equipped with a HeNe gas laser (max. output power: 4 mW) operating at a wavelength of 633 nm, was used. The measurements were performed at 173° scattering angle (Non-Invasive Back-Scatter (NIBS) technology). The autocorrelation function of the scattered light intensity was analyzed by the Malvern Zetasizer software. In DLS measurements the C_{60} fullerene refraction index was equal to 1.90.

Experiments were performed on 60 male Wistar rats in the age of 3 months, having weight of 170±5 g. Administration of C_{60}FAS at a dose of 1 mg/kg [19] was carried out in two ways: intravenously (20 animals per group) and intramuscularly (20 animals per group) 2 hours before the beginning of each experiment. The control group (not received C_{60}FAS) also contained 20 animals.

The protocol of injecting of C_{60} fullerenes was based on experimental work [7] reporting that C_{60} fullerenes administered intraperitoneally to rats (the maximum tolerated dose was

500 mg/kg) were subjected to clearance from the organism within 2-4 days.

Animals were anesthetized by intraperitoneal administration of nembutal (40 mg/kg). For muscle ischemia the branch of the femoral artery which provides blood supply in experimental muscle was dragged by ligatures. In this case the so-called incomplete ischemia of the muscle was induced, because within few hours after the operation the blood supply to the muscle was reduced by 25-30% due to the accession of small lateral collaterals to the femoral artery. Preparation of the experiment also included cannulation (*a. carotis communis sinistra*) for drug administration and pressure measurement, tracheotomy and laminectomy at the lumbar spinal cord level. *Soleus* muscle of rat was separated from the surrounding tissues. Its tendon portion was transversely cut in the distal part. The ventral roots were cut in points of their exit from the spinal cord to stimulate efferent fibers in L7-S1 segments.

The animals used in this study were treated in accordance with international principles of the European Convention for the protection of vertebrate animals used for experimental and other scientific purposes (Strasbourg, 1986).

Variations of muscle contraction were measured using hypersensitive strain gauges, which are based on measuring the change in resistance of an array of single-walled carbon nanotubes (SWCNTs) by deformation [20]. SWCNTs were located in the back of the micropipette, and its front part was attached to the investigated muscle tendon. The programmable signal generators of the special shape were used to form the stimulating electrical signals with duration of 2, 3, 4 and 5 sec.

The muscle contraction force was measured during the first 5 hours (the first series of experiments) and on the 1^{st}, 2^{nd}, 3^{rd}, 4^{th} and 5^{th} day (the second series of experiments) after 2 hours of ischemia.

The study of dynamic properties of muscle contraction was performed under conditions of muscle activation using the modulated stimulation of efferent fibers. Five filaments of the cut ventral roots were fixed on stimulating electrodes, and a special device was used for cyclic sequence distribution of electrical signals to stimulate the filaments. The distributed stimulation allowed one to get monotonous and uniform muscle contraction at low stimulation frequencies of individual filaments. Stimulation of efferent fibers in L7-S1 segments was performed by rectangular shape electric pulses (duration was 2 msec), formed by means of a pulse generator controlled by ADC through the platinum electrodes (voltage was 7 V). The characteristics of stimulating signal were programmed and transmitted from the ADC-DAC device to a generator. Controlling of external load on the muscle was carried out with the help of mechanical stimulator. The electromagnetic linear motor was used for perturbation load.

The experimental curves obtained reflect the change in the studied parameters as a percentage of intact control muscle parameters taken as 100%. Each of these curves is a result of averaging $10\text{-}12^{th}$ similar measurements.

The statistical analysis of the results was carried out by the methods of variation statistics, using the Statistica 8.0 (“StatSoft”, USA) software. Testing of the datasets for their match to normally distributed population was performed using Shapiro-Wilk test. To determine the most probable differences between the mean values of the sampled populations the U-criterion of Mann-Whitney test was used. Statistical significance of any differences was set to $p \leq 0.05$.

RESULTS AND DISCUSSION

Knowledge of structural state of C_{60} fullerene in solution is important for estimation of nanostructure bioactivity and perspectives of its biomedical application [21]. In order to characterize the structural state of C_{60}FAS the DLS investigation was performed.

Fig. 1a demonstrates the experimental distribution of the scattered light intensity

over the hydrodynamic sizes of light scattering C_{60} fullerene particles in C_{60}FAS at room temperature. The presence of two peaks in DLS spectrum of C_{60}FAS shows the existence of C_{60} fullerene aggregates with different hydrodynamic sizes. As one can see in Fig. 1b the C_{60}FAS contains C_{60} fullerene aggregates with hydrodynamic sizes from 30 nm to 90 nm (~92% of the total number of particles), and small number (~8%) of aggregates having dimensions from 100 nm up to 300 nm. Moreover, according to the DLS data the dimensions of C_{60} fullerene aggregates do not depend on time during the period 70-270 days starting from the day of C_{60}FAS preparation.

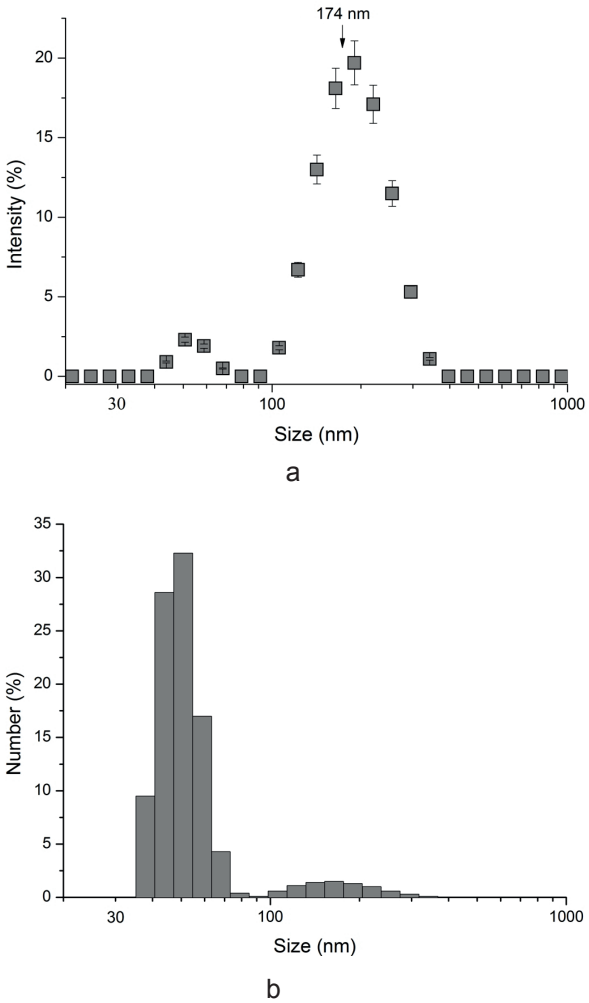

Fig. 1. DLS results of C_{60}FAS (0.15 mg/ml) at room temperature: (a) distribution of the scattered light intensity over the hydrodynamic sizes of light scattering C_{60} fullerene particles; (b) distribution of the number of light scattering C_{60} fullerene particles over their hydrodynamic sizes

Skeletal muscles possess higher resistance to ischemia than other organs, however, continuous ischemia may result in various pathologies, in particular, muscle necrosis and apoptosis. Usually the main goal during ischemia treatment is fast recovery of blood supply (reperfusion) in the injured zones. However, the reperfusion therapy leads to a new pathophysiological process called reperfusion trauma, which also induces significant tissue damage [22]. The principal pathological processes, which invoke the cascade of ischemic pathologies in the injured muscle, are occurring during the first hours after reperfusion [23]. Based on this, the first step in our study was the investigation of the changes in the dynamics of contraction within the first 5 hours after the reperfusion of the ischemic rat *soleus* muscle. By means of comparative analysis of intravenous and intramuscular C_{60}FAS administration we have been trying to select an optimal method for achieving the maximal therapeutic effect.

Note, the changes in ischemic muscle contraction force by using similar stimulus pools were described in detail in our previous work [24].

The change in the force of contraction of the ischemic rat *soleus* muscle during the first 5 hours after its reperfusion activated by stimulating pools with duration of 5 sec, is given in Fig. 2. In the control (ischemic muscle in the absence of the drug) the decrease of maximal force response was observed either on increase of time passed after ischemia and on increase of the duration of stimulating excitation signal (Fig. 3(I)). Independent of the method of C_{60} fullerene administration an insignificant decrease of the force response was observed on increasing the duration of the excitation signal, which was mainly dependent on the time passed after the reperfusion.

The results of calculation of such important biomechanical indicator as the integrated power of muscle contraction (calculated from the total

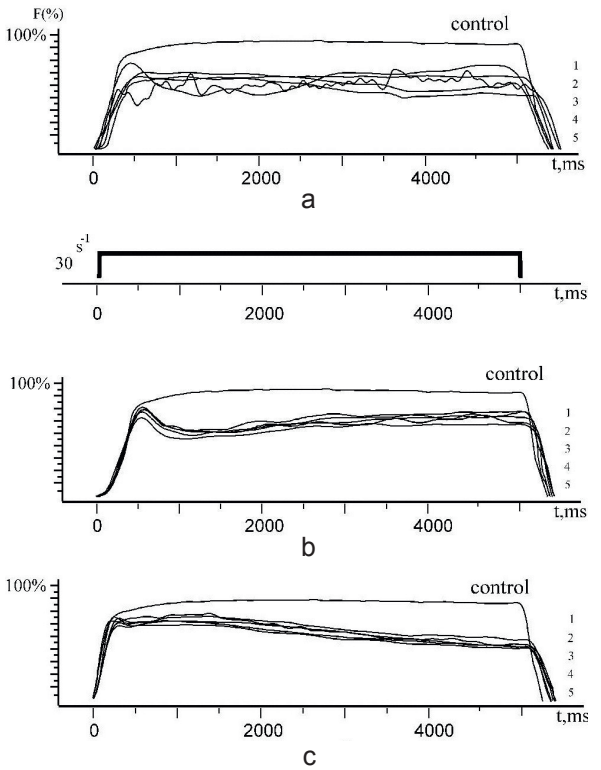

Fig. 2. Curves of contraction force generation, F(%), of ischemic rat *soleus* muscle: (a) – the control (in the absence of C_{60}FAS); (b) – intravenous injection of C_{60}FAS; (c) – intramuscular injection of C_{60}FAS. 1, 2, 3, 4, 5 – hours passed after reperfusion of ischemic muscle

area under the force curve, S(f)) are given in Fig. 3(II). It was found that the decrease of the integrated power on increase of the time passed after the reperfusion and increase of the stimulating signal duration to much extent was compensated by the action of C_{60}FAS independent of the method of its administration. It is worth noting that this protective effect of C_{60} fullerene can be observed already during the first hours of ischemic injury, when the initiation of the main ischemic cascades of muscle tissue damaging occurs.

Taking into account that the muscle contraction is a dynamic oscillating process involving interdependent reactions, it is possible to assume that under the condition of appearing of pathological changes in muscle filaments induced by artificial ischemia, an optimal interrelation of the parameters of stimulation which can involve the maximal number of sarcomer structures for the most optimal course of contraction, must exist. Although the heterogeneity of the contractile component of the skeletal muscle complicates the estimation of the damage of each particular element, the overall picture of the development of pathological

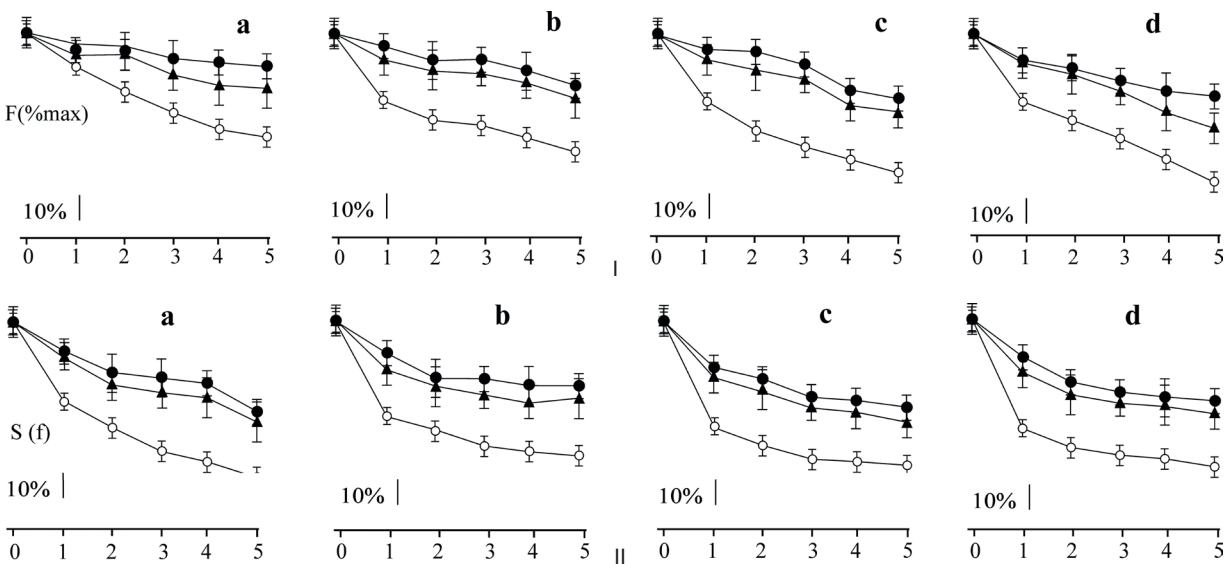

Fig. 3. Maximal contraction force change, F(%max) (I), and integrated power change, S(f) (II), of ischemic rat *soleus* muscle for different duration of modulated electrostimulation: a, b, c, d – stimulation during 2, 3, 4, 5 sec, respectively; (○) – the control (in the absence of C_{60}FAS); (▲) – intravenous injection of C_{60}FAS; (●) – intramuscular injection of C_{60}FAS. 1, 2, 3, 4, 5 – hours passed after reperfusion of ischemic muscle; *$p<0.05$

process may be tracked by means of measuring the changes of maximal force of contraction during several days (Fig. 4). In the control the muscle activity exerts a tendency of linear decrease of the force response on increasing the time after the reperfusion, which may be due to development of muscle fatigue. However in contrast to the processes of fatigue, fluctuating components can be clearly seen on the force curves starting from the 2nd day of experiment. If the force decrease is associated with the decrease in the number of molecular force generators (i.e. decrease in the number of active cross-bridges), in the case of fluctuating contractions the damages must be observed nearly for all contractile components of myocyte. It is therefore reasonable to say just about relative resemblance of the force responses in fatigue and artificial ischemia. Significant dependence of dynamic characteristics of contraction on the activity of the main types of proprioceptors strongly complicates controlling of the motion activity of injured muscle by central nervous system (CNS), if the uncontrolled fluctuating responses of the ischemia injured muscle appear as a reaction to even a simple stimulating signal. Removal of these oscillating components of contraction (Fig. 4) due to the action of C_{60}FAS independent of the method of its administration is a very important feature of the protective effect of this compound.

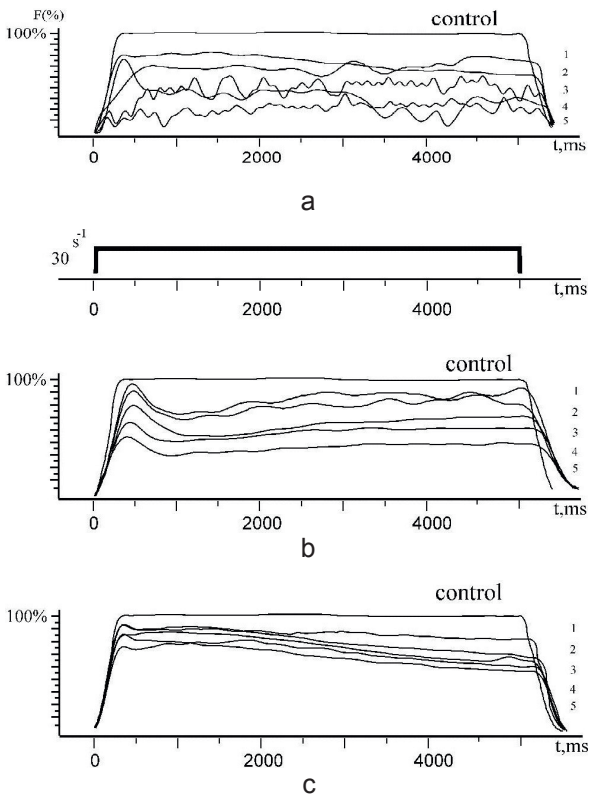

Fig. 4. Curves of contraction force generation, F(%), of ischemic rat *soleus* muscle: (a) – the control (in the absence of C_{60}FAS); (b) – intravenous injection of C_{60}FAS; (c) – intramuscular injection of C_{60}FAS. 1, 2, 3, 4, 5 – a day after reperfusion of ischemic muscle

It is seen that on applying the modulated stimulation one can observe qualitative and quantitative differences in the contraction of ischemic injured *soleus* muscle of rat in the control and after the action of C_{60}FAS (Fig. 4). In the all studied processes the control values of maximal force of contraction and the integrated power were decreasing on increasing the duration of period after the reperfusion as well as the duration of the stimulated excitation (Fig. 5). Administration of C_{60} fullerene had revealed its apparent protective action on the studied characteristics of the force of contraction. In particular, the pronounced protective effects were observed on the 5th day after the ischemia at the maximal 5 sec duration of the stimulated excitation. It was found that the protective effect associated with the maximal force response amounted to 30-35%, whereas the same effect with respect to integrated power was more than 50% as compared to the control values. In all cases the intramuscular administration of C_{60}FAS displayed 10-15% greater protection with respect to the intravenous administration.

Differences in the dynamics of force and integrated power of ischemic injured muscle on intravenous and intramuscular drug administration (Fig. 5) indicate complexity of molecular mechanisms of contraction, which, presumably, differ from each other depending on the state in which the muscle exists, and different mechanisms of developing the antioxidant action of C_{60} fullerene. At the

same time on C_{60}FAS injection directly into the injured muscle the concentration of C_{60} fullerene must be significantly higher specifically in the hearth of damage in muscle as compared with the intravenous administration of this compound (Fig. 5). In such case it is reasonable to say about the concentration dependence of the protective effect of C_{60} fullerene with respect to maximal force and integrated power of the ischemic injured muscles.

The above-discussed effects may be related to the fact that during the 2 hours of ischemia of rat *soleus* muscle the ATP concentration is getting significantly lowered which is accompanied by considerable elevation of the lactate level. After 3 hours of ischemia the lowering of ATP level reaches approximately 95%, whereas the glycogen appears to be outspent by 88% [25]. These results confirm hypothesis that large amount of high-energy phosphates is being utilized by the injured muscle cell for maintaining homeostasis altered due to ischemic injury. As a consequence it leads to elevation of the level of muscle fatigue, further resulting in lowering the maximal force response on increasing the duration of stimulating signal. It has recently been shown [26], that C_{60}FAS is capable to induce the ATPase activity and the superprecipitation reaction of rabbit skeletal muscle actomyosin. This may be due to the binding of C_{60} fullerene with aminoacid residues of the active site of myosin. Alternatively, the protective effect of C_{60} fullerene with respect to the processes of generation of maximal force response of ischemic injured muscle may be connected with its antioxidant properties, whereas the most pronounced therapeutic effects observed on C_{60}FAS intramuscular administration can be explained by its injection directly to the hearth of damage.

In the modern theories of motor control it is commonly assumed that when muscle pathologies are being developed the CNS restricts the motions of limb in such a way to minimize the number of degrees of freedom which are associated with movement of certain segments. The synergies (involvement of non-damaged or weakly damaged muscle filaments) are thought to lie behind this process, which may lead to more difficult managing of actions and thereby worsen the control over execution of purposeful motions. Because the structure

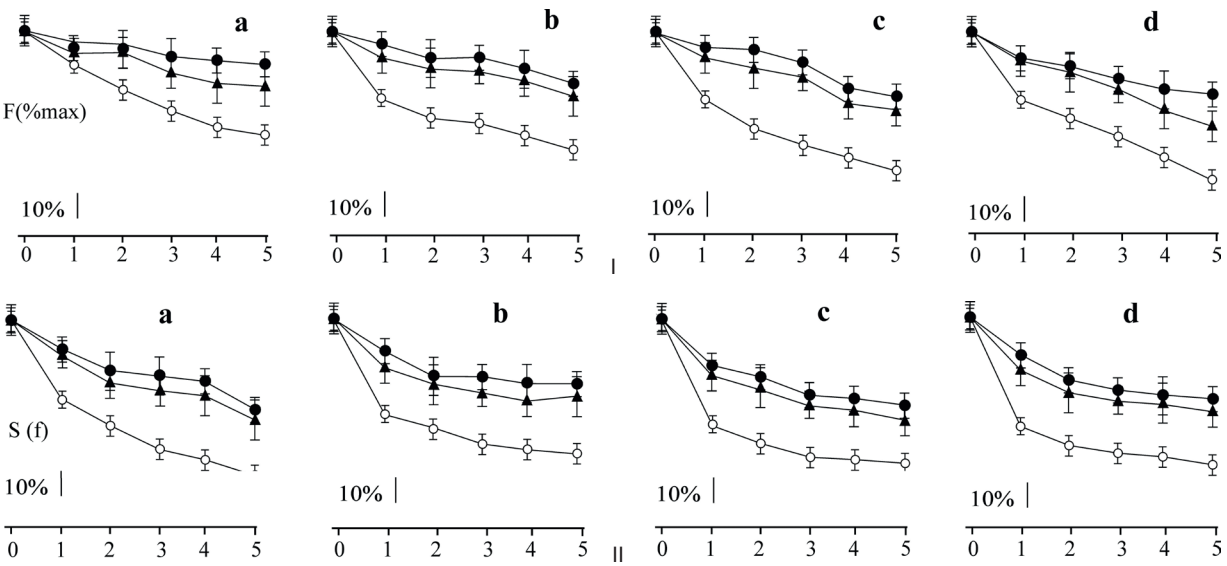

Fig. 5. Maximal contraction force change, F(%max) (I), and integrated power change, S(f) (II), of ischemic rat *soleus* muscle for different duration of modulated electrostimulation: a, b, c, d – stimulation during 2, 3, 4, 5 sec, respectively; (○) – the control (in the absence of C_{60}FAS); (▲) – intravenous injection of C_{60}FAS; (●) – intramuscular injection of C_{60}FAS. 1, 2, 3, 4, 5 – a day after reperfusion of ischemic muscle; *$p<0.05$

of dynamic component of stimulation, i.e. the interrelation of its amplitude and duration, determines the speed and amplitude of motion, the change in the character of efferent activity by ischemic muscle results in errors in precision of positioning of the joint as a whole. When making even simple motions there is the possibility of establishing cause-effect relation between the mechanical activity of ischemic injured muscles of the joint and the main dynamic parameters of the motions. The accuracy of such analysis may be improved by means of analysis of totetanic areas of contraction accompanied by controlling mechanical parameters of motion. Hence, investigations of changes in dynamics of contraction of ischemic injured muscle specifically on totetanic areas of contraction makes possible to trace the level of muscle damage and the quality of therapeutic action of the studied drug.

Fig. 6(I) demonstrates the changes in force response of ischemic rat *soleus* muscle during the application of stimulating signal with increased time of totetanic phase during the first 5 hours after the reperfusion. As one can see, already within the first hour after the reperfusion in control studies the decrease of maximal force of contraction and increase of the time needed for achieving it are observed. The force curves exhibit a marked smoothing of the transition from dynamic to steady-state phase of contraction (the transition between Δt_3 and Δt_4 regions). Hence, the use of C_{60}FAS independent of the method of its administration has apparently affected the force curves, viz. resulted in clear separation of the dynamic and steady-state regions of contraction.

Increase of the time needed to reach the maximal level of contraction force in rat *soleus* muscle already after 1 hour after reperfusion, and linear increase of retention time during the next 5 hours, most likely is due to the growing inability of ischemic muscle to fully activate the targeted accuracy descending pools of afferent activity. The most pronounced influence of C_{60} fullerene on totetanic regions of contraction, than on maximal force response, from our viewpoint, is connected with induction of irreversible pathologic changes in generation of the contraction force in the most affected molecular components belonging to the elements of the muscle contraction system, which are being activated on different stages of contraction. However, the observed insignificant protective effect of C_{60} fullerene on totetanic regions of contraction is of great importance because it specifically affects further development of pathologic injures neutralizing free radicals on the very beginning of ischemic muscle injury.

Slowing down of dynamic processes on increase of the time passed after the reperfusion within the first hours of experiment, at least in part, may be associated with destruction of the myocyte membranes which occurs already on the first stages of ischemic injury [23] before the administration of C_{60}FAS. This process obviously emphasizes the role of rigidity of muscle contraction, and its impact is getting most pronounced under condition of ischemic damage of muscle filaments. A proof to this assumption comes from the fact that the increase in time required to reach the maximal contraction force and decrease of the magnitude of maximal force, occur on similar level.

Investigations of the changes in dynamic parameters of contraction by means of electrostimulation during 5 days (Fig. 6(II)) enabled establishing direct dependence of lowering the velocity of reaching the maximal level of force on the time passed after the reperfusion in control groups. Administration of C_{60}FAS strongly influences this process, viz. decrease of this velocity after the first day after the ischemia did not significantly change during the next 4 days of experiment. Intravenous drug administration demonstrated better protective effect (by 10%) with respect to intramuscular administration. More apparent transition from the dynamic component of contraction to maintaining of equilibrium level of force may be due to the fact that C_{60} fullerene favors the involvement of energetically favorable mechanisms which are able to minimize the level of ischemic damage.

The velocity by which the muscle reaches the maximal force response is one of the important biomechanical characteristics of the fast muscle filaments. Increase of this parameter in the ischemic muscles under the action of C_{60}FAS may facilitate involvement of motoneuron pools of activity encoding the limb motion. As reported in [27] the pattern of pathologic processes development in slow and fast muscles is similar during the first 2 weeks after the ischemia. Hence, the effects observed on slow rat *soleus* muscle must also be spread

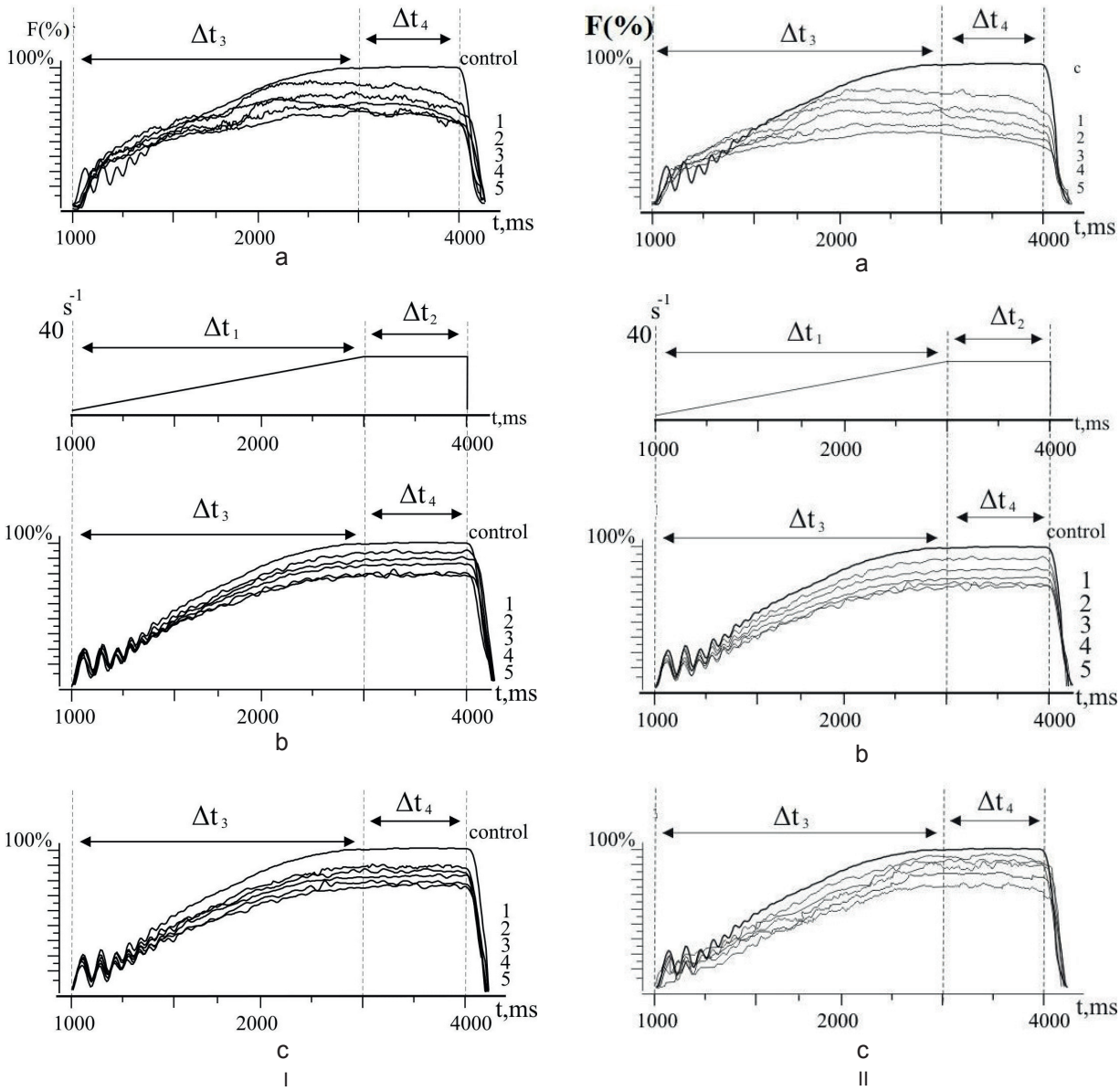

Fig. 6. Curves of contraction force generation, F(%), of ischemic rat *soleus* muscle on applying stimulating signal with increased totetanic phase of the growing frequency of excitation: (a) – the control (in the absence of C_{60}FAS); (b) – intravenous injection of C_{60}FAS; (c) – intramuscular injection of C_{60}FAS. Δt_1 – the time of growing of the stimulating frequency; Δt_2 – retention time of the maximal frequency of excitation; Δt_3 – the time of growing of the contraction force; Δt_4 - retention time of the maximal contraction force. 1, 2, 3, 4, 5 – hours (I) and days (II) after reperfusion of ischemic muscle

onto the fast muscle filaments, where the effects of precise positioning are of utmost importance in muscle dynamics.

The observed high correlation between the duration of ischemia and viability of muscle filament [2] might be one of the important factors of lowering the maximal force response on increase of time passed after the ischemia not only due to the decrease in the number of viable muscle filaments, but also due to the increase of the fraction of collagen structures in muscle. Ischemia lasting 3 hours causes muscle necrotic changes and nerve degrading. The necrosis fraction in the muscle tissue may reach 60% [28]. In such case the therapeutic action of C_{60} fullerene as an antioxidant will not give any positive effect. So the use of C_{60} fullerene as a therapeutic agent in ischemic injures may have pronounced positive effect mainly on early stages of development of such pathologies.

The data obtained and discussed above demonstrate complexity of building the detailed model of the protective effect of C_{60} fullerene with respect to ischemic muscle contraction. Biomechanical analysis of the protective action of C_{60} fullerene on ischemic injured muscle filaments should involve detailed investigation of kinematic and dynamic parameters of motion.

CONCLUSIONS

The results obtained in the present work evidence a pronounced protective effect of C_{60} fullerene nanoparticles in rat *soleus* muscle contraction dynamics after ischemic injury. Specifically it was found that low-dose intravenous and intramuscular administration of C_{60}FAS have different therapeutic effects depending on the studied macroparameters of skeletal muscle contraction. It was determined that the intravenous drug administration is the most optimal for correction of the velocity macroparameters of contraction on ischemic damage of muscle tissue, whereas the intramuscular C_{60}FAS administration exerts more strong protective action with respect to the motions which generate the maximal force responses or continuous contractions characterized by elevated level of muscle fatigue. These results suggest that further development of medical nanotechnologies, which utilize antioxidant properties of C_{60} fullerene, and the absence of any acute intoxication after administration of this drug opens up new possibilities for therapy and prevention of ischemic pathologies. It is reasonable to propose that the development of this area may also result in improvement of the therapy of other pathologic states of the muscle system, which are associated with pathologic action of free radicals.

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ВПЛИВ C_{60} ФУЛЕРЕНУ НА ЗМІНИ СИЛА-ШВИДКІСТЬ В *SOLEUS* MUSCLE ЩУРА ЗА ІШЕМІЇ-РЕПЕРФУЗІЇ

Досліджено вплив наночастинок C_{60} фулерену (30-90 нм) на динаміку процесів розвитку силової відповіді у разі стимуляційного подразнення м'яза *soleus* щура на фоні ішемічної патології, яка виникає упродовж перших 5 год та перших 5 днів після 2 год ішемізації і наступної реперфузії. Встановлено, що внутрішньовенне та внутрішньом'язове введення C_{60} фулерену (1 мг/кг) мають різні терапевтичні ефекти залежно від досліджуваних макропараметрів скорочення м'яза. Найбільш оптимальним для корекції швидкісних макропараметрів скорочення за ішемічного ушкодження м'язової тканини є внутрішньовенне введення препарату, а внутрішньом'язове проявляє більш захисну дію за рухів, пов'язаних з генерацією максимальної силової відповіді або тривалих скорочень, які збільшують рівень втомлюваності м'язу. Отже, C_{60} фулерен можна розглядати як перспективний агент для ефективної терапії патологічних станів м'язової системи, в основі розвитку яких лежить патологічна дія вільнорадикальних процесів.

Ключові слова: C_{60} фулерен; *soleus* м'яз щура; ішемія-реперфузія; динаміка м'язового скорочення; динамічне розсіювання світла.

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ВЛИЯНИЕ C_{60} ФУЛЛЕРЕНА НА ИЗМЕНЕНИЯ СИЛА-СКОРОСТЬ В *SOLEUS MUSCLE* КРЫСЫ ПРИ ИШЕМИИ-РЕПЕРФУЗИИ

Исследовано влияние наночастиц C_{60} фуллерена (30-90 нм) на динамику процессов развития силового ответа на стимуляционное раздражение мышцы *soleus* крысы на фоне ишемической патологии, которая возникает в мышце в течение первых 5 ч и первых 5 дней после 2-часовой ишемизации и следующей реперфузии. Установлено, что внутривенное и внутримышечное введение C_{60} фуллерена (1 мг/кг) имеют разные терапевтические эффекты в зависимости от исследованных макропараметров сокращения мышцы. Наиболее оптимальным для коррекции скоростных макропараметров сокращения при ишемическом повреждении мышечной ткани является внутривенное введение препарата, а его внутримышечное проявляет более защитное действие при движениях, связанных с генерацией максимального силового ответа или длительных сокращений, которые увеличивают уровень утомляемости мышцы. Таким образом, C_{60} фуллерен можно рассматривать как перспективный агент для эффективной терапии патологичных состояний мышечной системы, в основе развития которых лежит патологическое действие свободнорадикальных процессов.

Ключевые слова: C_{60} фуллерен; *soleus* мышца крысы; ишемия-реперфузия; динамика мышечного сокращения; динамическое рассеяние света.

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