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C_{60} FULLERENE ATTENUATES THE SIGNS OF ACUTE RENAL FAILURE IN RATS UNDER RHABDOMYOLYSIS DUE TO INHIBITION OF OXIDATIVE STRESS

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Rhabdomyolysis, as an acute stage of myopathy is known to be associated with the accumulation of muscle breakdown products, acute renal failure and oxidative stress. The goal of the study was to evaluate the effect of C_{60} fullerene as an antioxidant on kidney damage in the model of glycerol-induced rhabdomyolysis in rats. The study was conducted on male Wistar rats, divided into the following experimental groups: control animals, animals intramuscularly injected with glycerol in a doses of 5, 10 and 15 mg/kg and those intraperitoneally injected daily with C_{60} fullerene aqueous solution (C_{60}FAS) in a dose of 1 or 2 mg/kg at 48 h after glycerol administration. Monitoring of the biochemical and morphological indicators was carried out on 3rd, 6th and 9th days of the experiment. A close correlation between the acute renal damage severity, increased creatinine and urea level, superoxide dismutase (SOD) and catalase (CAT) activity in the blood of rats was observed. It was shown that in rats which received 2 mg/kg of C_{60}FAS the renal glomeruli size and necrosis manifestations were attenuated, whereas SOD and CAT activity in the blood was significantly decreased. The results obtained may be useful for developing approaches to the treatment of pathological conditions of the muscular system caused by rhabdomyolysis and associated oxidative stress.

K e y w o r d s: rhabdomyolysis, acute renal failure, biochemical parameters, histopathology, muscle soleus, C_{60} fullerene.

In modern medical practice, nephropathies, which further lead to the development of organ failure, are becoming more and more relevant. Rhabdomyolysis, as an acute stage of myopathy, causes kidney damage [1]. The destruction of skeletal muscle cells leads to the release of intracellular elements involved in the pathogenesis of acute renal failure (ARF) - a homeostasis disorder caused by an irreversible decrease in functioning renal nephrons mass, which is manifested by a multisymptom complex and reflects the involvement of almost all organs and systems of the patient in this process [2]. Kidney damage induced by rhabdomyolysis occurs as the result of mechanical trauma (tearing or crushing of a skeletal muscle), burns (especially in case of damage to a large surface area), electric shock, overstrain during intense sports activities and manifestation of various forms of ischemia-reperfusion injuries, in particular, vascular occlusion with a tourniquet or thromboembolism [3]. Literature data [3, 4] indicate that this pathology is caused by the accumulation of muscle breakdown products and is associated with oxidative stress. Currently, its only adequate clinical treatment is aggressive infusion therapy [4].

The development of ARF is traditionally studied in an experimental model of glycerol-induced rhabdomyolysis [5]. It is characterized by hypovolemia, intraluminal myoglobin occlusion and its toxic effects, renal ischemia caused by releasing vasoconstrictors, and free radical oxidation activation [6-10]. At the same time, there is an increase in the products of lipid peroxidation (LPO), creatinine, urea in the blood plasma, and a decrease in the rate of glomerular filtration [1, 11-13]. When myoglo-

bin passes through the nephron, it causes damage with a cascading effect. The proximal tubular cells internalize myoglobin through their apical endocytic complex consisting of megalin, cubilin, and bezaminonoids [8]. Considering that one of the key links in renal epithelial damage in glycerol-induced nephropathy is LPO processes, one can assume the effective therapeutic use of antioxidant drugs [14]. One of them is C_{60} fullerene, which is able to effectively scavenge and inactivate free radicals in *in vivo* and *in vitro* systems [15, 16]. Our recent work has shown that the use of biocompatible water-soluble C_{60} fullerenes [17] after the initiation of skeletal muscle damage leads to significant positive therapeutic effects [18, 19].

Thus, based on the previous results, the purpose of this work was to evaluate the dose-dependent effect of C_{60} fullerene aqueous solution (C_{60}FAS) on the course of rhabdomyolysis-induced kidney damage of varying severity.

Materials and Methods

All experiments were carried out on laboratory animals in compliance with the international principles of the "European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes" (Strasbourg, 1986) and Article 26 of the Law of Ukraine "On the Protection of Animals from Cruelty" (No. 3447-IV, 21.02.2006), as well as generally accepted norms of bioethics and biological safety. The protocols of the experiments were approved by the Bioethics Commission of the ESC "Institute of Biology and Medicine" of Taras Shevchenko National University of Kyiv (protocol No. 2 dated September 2, 2022).

The study was conducted on male Wistar rats weighing 150–180 g, divided into the following experimental groups (n = 7 in each group): control, modeled pathology (on days 3, 6 and 9 after glycerol solution administration in three doses: 5, 10 and 15 mg/kg of animal weight (corresponding severity of ARF)) and modeled pathology under the conditions of C_{60}FAS administration in two doses: 1 and 2 mg/kg of animal weight.

The development of ARF was studied in the experimental model of glycerol-induced rhabdomyolysis in rats [5]. Rhabdomyolysis followed by kidney damage was modeled by intramuscular injection of a 50% glycerol solution into the soleus muscle.

To obtain C_{60}FAS, a method based on the transfer of C_{60} molecules from toluene into water, followed by sonication, was used [20]. The obtained C_{60}FAS at a maximum concentration of 0.15 mg/ml is a typical colloid containing both single C_{60} molecules and their nanoparticles [21] and it remains highly stable for 18 months at a temperature of 4°C.

C_{60}FAS was administered intraperitoneally 48 h after glycerol injections daily throughout the experiment.

It is important to note that the doses of C_{60}FAS used in our experiments are significantly lower than the LD_{50} value, which was 600 mg/kg of animal weight when administered orally to rats [22] and 721 mg/kg when administered intraperitoneally to mice [23].

The concentrations of creatinine and urea, hydrogen peroxide, catalase (CAT) and superoxide dismutase (SOD) activity in the blood of experimental animals as markers of kidney damage and indicators of pro- and antioxidant balance were determined using clinical diagnostic equipment – biochemistry analyzers (RNL-200 and JN-1101-TR2, Netherlands).

For histological analysis, the samples of a kidney were separated and fixed in 10% formalin, embedded in paraffin, cut into 5 μm sections, and stained with hematoxylin and eosin (H&E) [24]. Digital microphotographs of stained sections were taken at × 100 magnification using a computer-assisted image analyzing system (consisting of Olympus BX41 microscope and Olympus C-5050 Zoom digital camera). The histopathological features of the glomerular, tubular and interstitial damage of the kidney were determined by light microscopy observation according to EGTI system [25]. In addition, the cross-sectional area of renal glomeruli and the diameter of renal tubes were measured using ImageJ software.

The statistical analysis of the results was performed by the variance analysis methods in Statistica 8.0 program. Each biochemical measurement was carried out at least five times. The Shapiro-Wilk W-test was used to check the normality. ANOVA analysis of variance was used to assess the reliability of the detected changes, and the results are presented as M ± SD. Differences between groups were considered probable at a significance level of $P < 0.05$. Correlation analysis was performed using the OriginPro 2023 program (v. 10.0).

Results and Discussion

Renal function assessment. In most cases, an increase in blood creatinine levels is the main indicator of ARF to detect pathology in the genitourinary system [5, 8]. Creatinine concentration in the blood in case of ARF can increase by two or more times the baseline level [4, 5]. At the same time, the creatinine concentration increases no earlier than 48 h after the onset of rhabdomyolysis [6], and therefore, we recorded the change in creatinine on day 3 after the glycerin injection.

The intramuscular injection of glycerol led to the formation of rhabdomyolysis ARF, the increase in severity of which correlated with an increase in glycerol dose and the time after its administration.

It was found that after glycerol administration ARF occurred, which was characterized by hypercreatininemia. At a dose of glycerol of 5 mg/kg, the creatinine concentration was 102 ± 3 μM on day 3, 124 ± 4 μM on day 6, and 162 ± 3 μM on day 9 (at a normal value of 50 μM) (Fig. 1). At a dose of glycerol of 10 mg/kg, these values were 114 ± 3, 181 ± 4 and 224 ± 5 μM, respectively, on days 3, 6 and 9 of the experiment. With an increase in glycerol dose to 15 mg/kg, these values were 150 ± 3, 209 ± 4 and 269 ± 5 μM, respectively, on days 3, 6 and 9 of the experiment.

A significant increase (on (80–90)%) in creatinine level is noted from day 3 to day 6 of the experiment at all doses of glycerol used. The creatinine level on day 6 at a glycerol dose of 10 mg/kg almost corresponded to its level on day 9 at a dose of 5 mg/kg and on day 3 at a dose of 15 mg/kg, which indicated a significant acceleration of renal pathology with an increase in the dose of glycerol intramuscular injection (Fig. 1).

Intraperitoneal injection of C_{60}FAS at a dose of 1 mg/kg in a model of mild severity of ARF caused a decrease in creatinine levels by 25, 38 and 47% on days 3, 6 and 9, respectively, compared with the glycerol group (dose 5 mg/kg). With increasing severity of rhabdomyolysis, C_{60} fullerene therapy showed less quantitative positive effects: 16, 21 and 28% at a dose of 10 mg/kg of glycerol and 11, 18 and 21% at a dose of 15 mg/kg on days 3, 6 and 9, respectively. At the same time, with a doubling of the C_{60}FAS dose (2 mg/kg), its positive effect increased by 23 and 26% at glycerol doses of 10 and 15 mg/kg, respectively, on day 9 of the experiment (Fig. 1).

With the development of ARF, the concentration of nitrogenous toxins in the blood, which can only be excreted with the urine, increases significantly, which is a sign of impaired kidney function. Urea is one of the end products of protein metabolism that contains nitrogen. It is produced in the liver, transported by the blood to the kidneys, filtered through the vascular glomerulus, and then excreted from the body. Since this process is continuous, a certain amount of urea is always normally present in the blood. At the same time, with the development of rhabdomyolysis, its concentration increases significantly due to significant cell death. ARF manifests itself as a result of the loss of the glomerulus ability to filter blood metabolites through it. The result of the urea test in the blood is one of the main indicators of glomerular filtration efficiency in the development of ARF.

An increase in urea concentration from 10 ± 1 mM in the control to 32 ± 3, 38 ± 4 and 41 ± 3 mM on days 3, 6 and 9 of the experiment, respectively, indicates high ARF already at the minimum dose of glycerol (5 mg/kg) (Fig. 2). An increase in the dose of glycerol to 10 and 15 mg/kg increased the amount of urea in the blood by 19 and 14%, respectively, on day 9 of the experiment. C_{60}FAS injections at a dose of 1 mg/kg reduced the amount of urea by 26, 15 and 12% at glycerol doses of 5, 10 and 15 mg/kg, respectively, on day 9 of the experiment. With a twofold increase in the C_{60}FAS dose (2 mg/kg), this indicator decreased by 35, 28 and 21% at glycerol doses of 5, 10 and 15 mg/kg, respectively, on day 9 of the experiment (Fig. 2).

Evaluation of pro- and antioxidant balance indicators. During the development of rhabdomyolysis, an excessive amount of myoglobin is released into the bloodstream from damaged muscle cells, and free myoglobin is filtered by the glomerular filtration barrier and endocytosed by renal tubular cells. Ferrous myoglobin inside tubular cells is oxidized to the trivalent form, which leads to a hydroxyl radical formation and the subsequent conversion of trivalent myoglobin to ferrous myoglobin through a redox cycle with the formation of free radical compounds. The latter initiate LPO and excessive oxidative stress [1]. Antioxidant defense enzymes, such as CAT and SOD, play a key role in the mechanisms of regulation of free radical and peroxidative processes. The most powerful natural antioxidant and the first-line enzyme of antioxidant defense is SOD, which performs the reaction of dismutation of superoxide anion radicals and converts them into less reactive hydrogen peroxide molecules [26]. The further de-

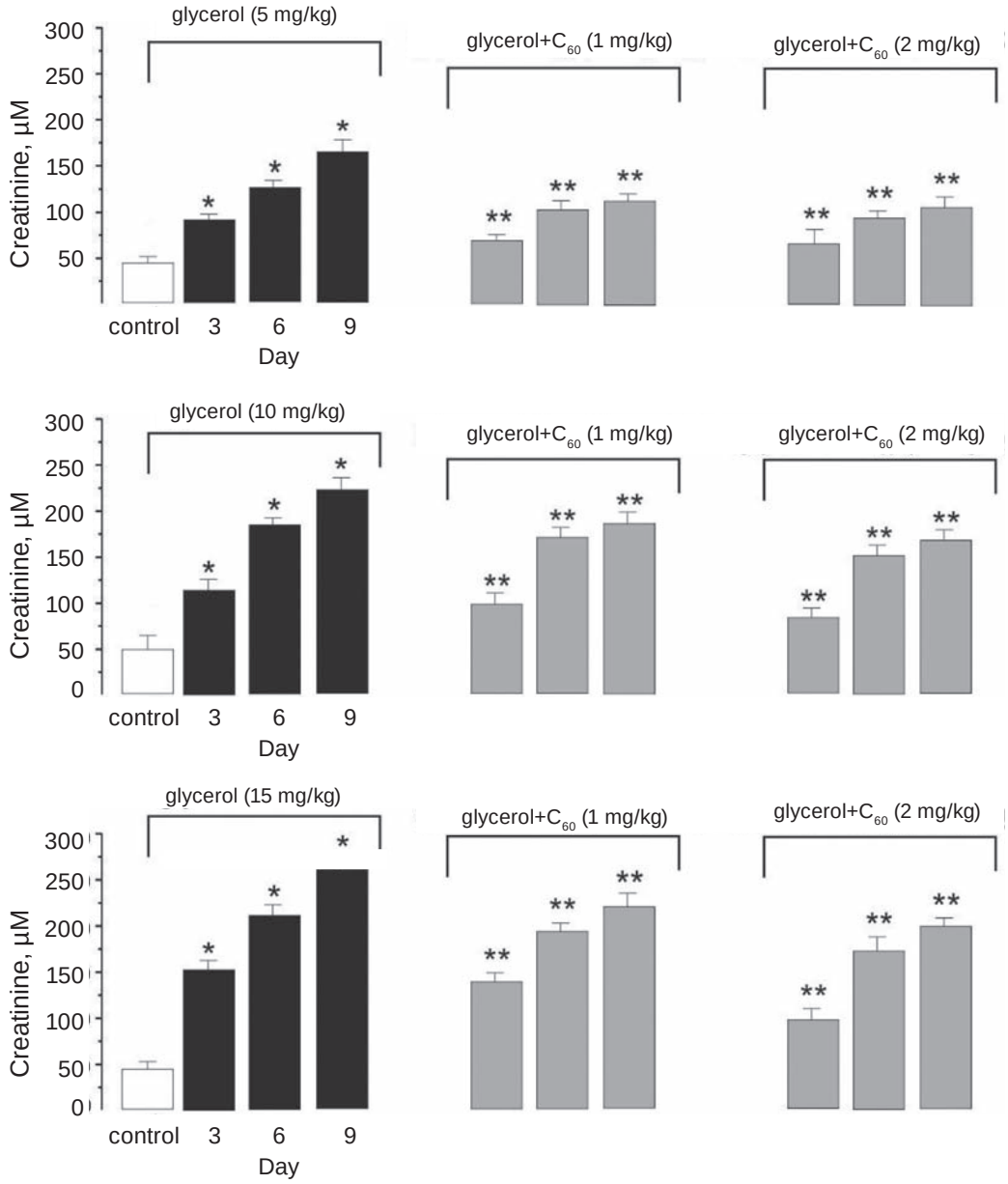


*Fig. 1. Creatinine concentration in blood of rats with ARF and administration of C_{60}FAS. *P < 0.05 vs. control group; **P < 0.05 vs. glycerol group*

composition of hydrogen peroxide into water and molecular oxygen is carried out by CAT, so the activity of these enzymes allows us to assess changes in the pro- and antioxidant balance in the body.

SOD activity in the blood increased by 67, 122 and 167% with the glycerol administration at doses of 5, 10, and 15 mg/kg, respectively, compared to the control on day 9 of the experiment (Fig. 3, *A*). The use of C_{60}FAS at a dose of 1 mg/kg reduced this indicator by 9, 22 and 24%, and when the dose was doubled (2 mg/kg), its positive effect was additionally 16, 15 and 12% when glycerol was administered at doses of 5, 10, and 15 mg/kg, respectively, on day 9 of the experiment (Fig. 3, *A*).

CAT activity in the blood increased from 1.9 ± 0.1 μmole/min/ml in the control to 4.1 ± 0.3, 5.2 ± 0.4 and 5.9 ± 0.6 μmole/min/ml after glycerol administration at doses of 5, 10 and 15 mg/kg, respectively, on day 9 of the experiment (Fig. 3, *B*). After C_{60}FAS injections at a dose of 1 mg/kg, CAT activity decreased to 3.2 ± 0.3, 4.2 ± 0.2 and 5.1 ± 0.3 μmole/min/ml, and with a doubling of the dose (2 mg/kg), its additional positive effect was 11, 13 and 16% when glycerol was administered at doses

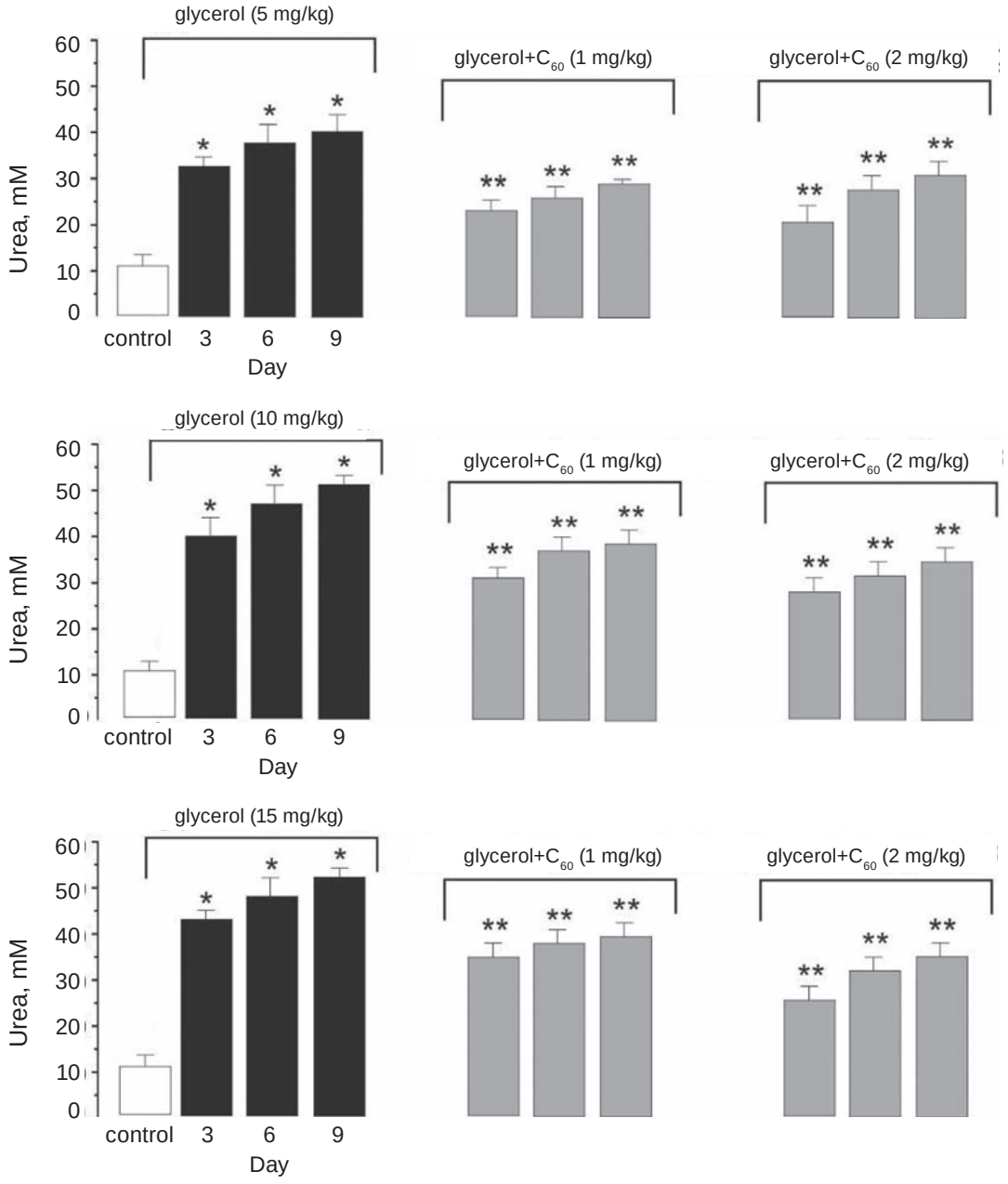
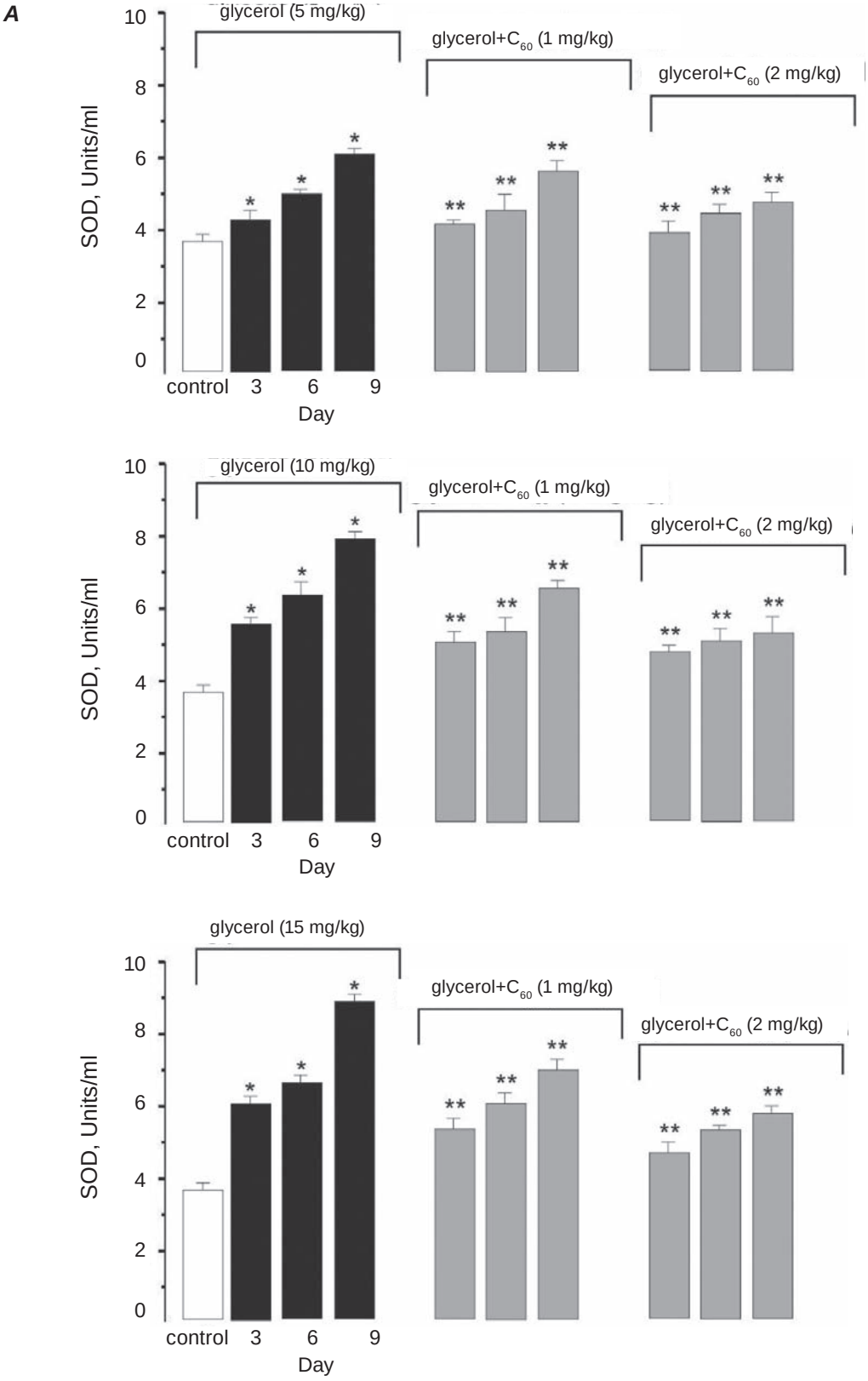


*Fig. 2. The urea concentration in the blood of rats with ARF and administration of C_{60}FAS. *P < 0.05 vs. control group; **P < 0.05 vs. glycerol group*

of 5, 10 and 15 mg/kg, respectively, on day 9 of the experiment (Fig. 3, *B*).

We next performed correlation analysis between the biochemical markers of kidney dysfunction and activities of SOD and CAT in the blood (Fig. 4). SOD activity, CAT activity and creatinine concentration in the blood of rats were expressed as fold change on the 3rd, 6th and 9th day after injection of glycerol at 5, 10 and 15 mg/kg and plotted in Fig. 4, *A, C*. Fig. 4, *B,D* shows the results of regression analysis of the combined data points, which revealed Pearson's correlation coefficient of 0.974 in the case of creatinine concentration-SOD activity relationship and 0.973 in the case of creatinine concentration-CAT activity relationship indicating tight correlation between the activity of these enzymes and the severity of ARF. The slope of this relationship was somewhat steeper (3.38 ± 0.25) for SOD activity compared to CAT activity (2.04 ± 0.15).


A
glycerol (5 mg/kg)
glycerol+C60 (1 mg/kg)
glycerol+C60 (2 mg/kg)
SOD, Units/ml
0
2
4
6
8
10
control
3
6
9
Day
glycerol (10 mg/kg)
glycerol+C60 (1 mg/kg)
glycerol+C60 (2 mg/kg)
SOD, Units/ml
control
3
6
9
Day
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SOD, Units/ml
control
3
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9
Day

B

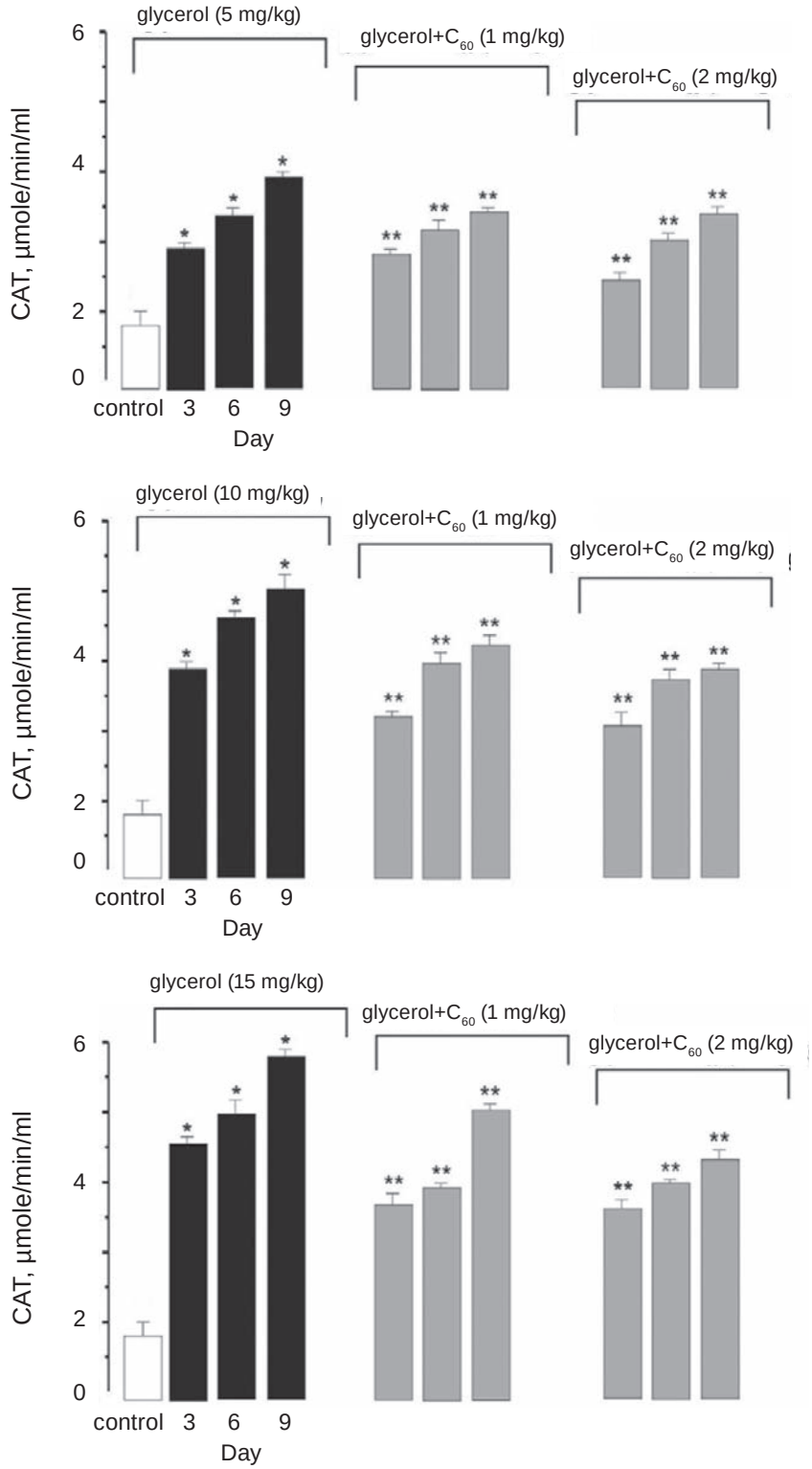

*Fig. 3. SOD (**A**) and CAT (**B**) activities in the blood of rats with ARF and administration of C_{60}FAS. *P < 0.05 vs. control group; **P < 0.05 vs. glycerol group*

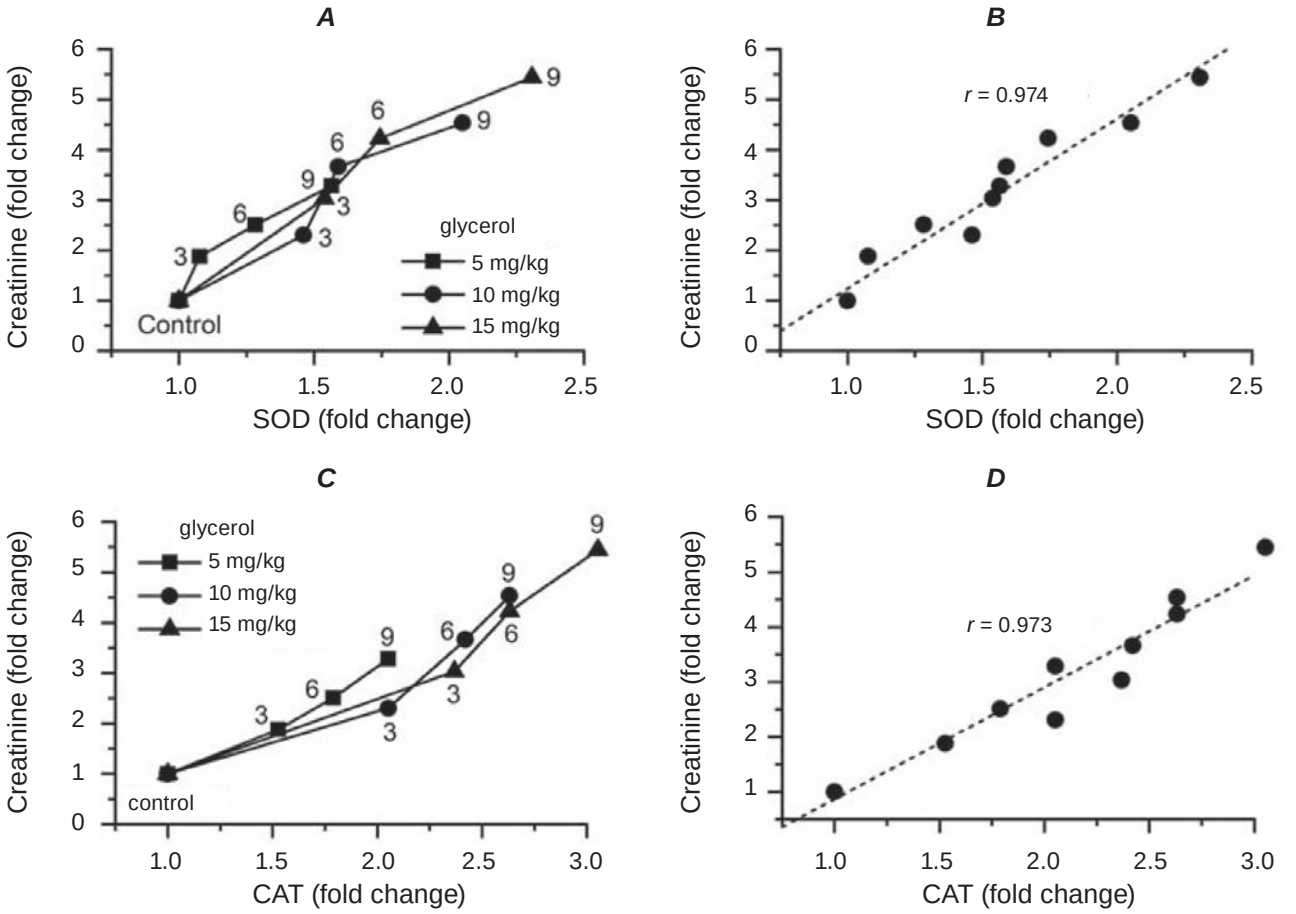

*Fig. 4. Correlation analysis of the degree of kidney dysfunction evaluated as fold-change in creatinine concentration and SOD (**A** and **B**) and CAT (**C** and **D**) activity in the blood of rats. **A** and **B**, the numbers near each symbol indicate the day of the experiment. **C** and **D**, combined data for all days of the experiment have been subjected to linear regression analysis (dotted lines) with Pearson's r values indicated*

A similar analysis was performed in order to quantitatively characterize the relationship between changes in urea concentration, SOD and CAT activity in the blood of rats (Fig. 5).

Again, a close correlation between the severity of ARF and the activity of SOD and CAT in the blood of rats was observed. The slopes of this relationship were similar in the case of urea: (1.49 ± 0.21) for SOD activity and 1.23 ± 0.10 for CAT activity.

We next addressed the question about how C_{60} fullerene treatment may affect these relationships. For this, pooled data from days 3, 6 and 9 obtained after C_{60}FAS treatment were plotted in Fig. 6. It can be seen that although C_{60} fullerene did not alter the relationships between creatinine or urea concentrations and activities of SOD and CAT in the blood of rats (note that data points are practically overlapping), it cause a significant decrease in the maximal values of all these parameters.

It should be noted that these results correlate well with the previously obtained data on C_{60}FAS effect on the functions of the body's antioxidant system in inflammatory and pathological processes [27, 28]. Activity of antioxidant enzymes, including CAT, SOD and glutathione peroxidase (GP_x), are often considered as biomarkers of oxidative stress, upregulation of which is important for preserving normal cell function and homeostasis under conditions of oxidative stress [29]. However, the relation between oxidative stress and the activity of antioxidant enzymes is complex, hence, future studies are warranted to investigate the role of oxidative stress in ARF due to rhabdomyolysis.

Inflammation caused by rhabdomyolysis can induce LPO processes in kidney tissue. To confirm this, we evaluated the level of secondary LPO products, in particular, the concentration of hydrogen peroxide in the blood of the studied animals.

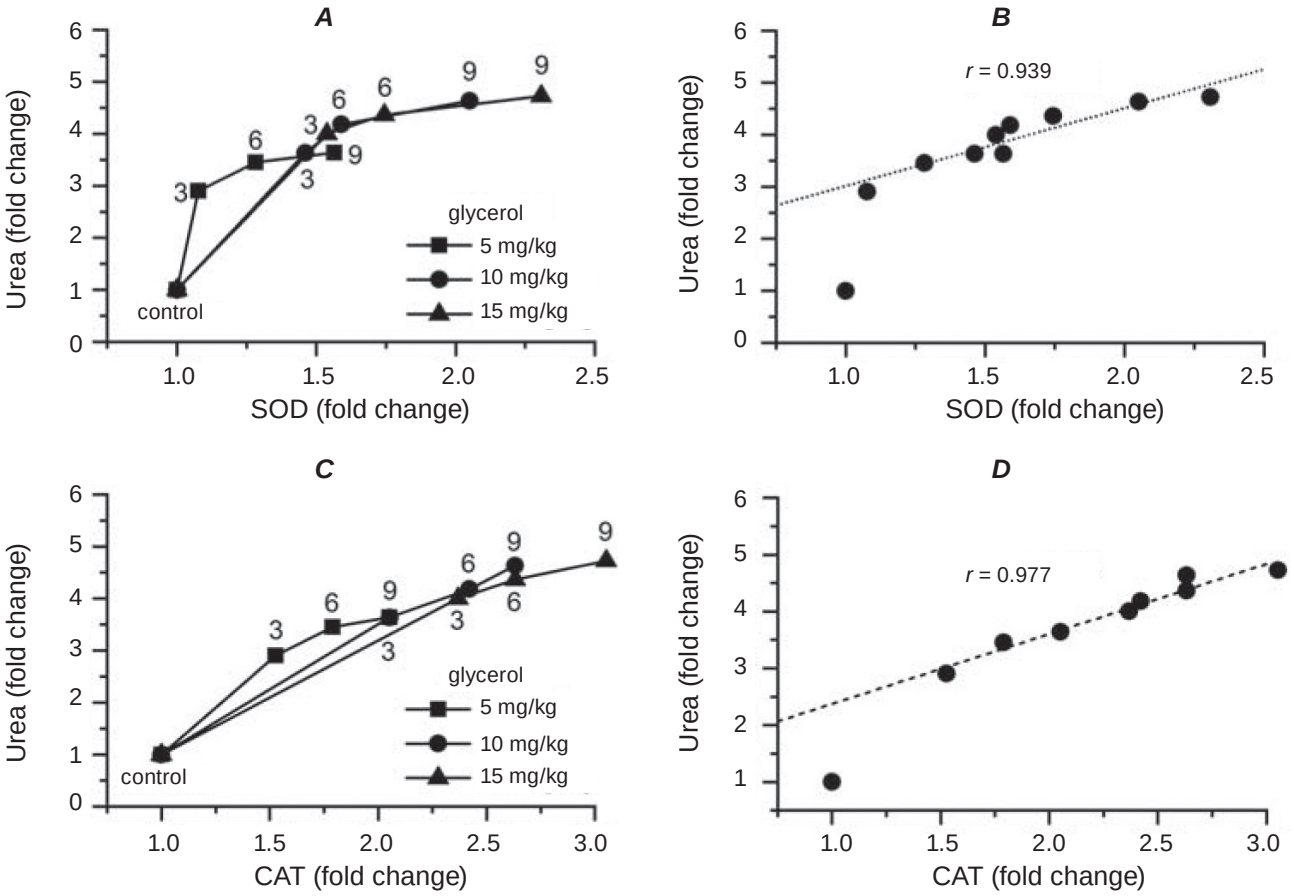

*Fig. 5. Correlation analysis of the degree of kidney dysfunction evaluated as fold-change in urea concentration and SOD (**A** and **B**) and CAT (**C** and **D**) activity in the blood of rats. **A** and **B**, the numbers near each symbol indicate the day of the experiment. **C** and **D**, combined data for all days of the experiment have been subjected to linear regression analysis (dotted lines) with Pearson's r values indicated*

When using glycerin injections at a dose of 5 mg/kg, the level of H_2O_2 in the blood increased from 0.94 ± 0.1 mM (control) to 1.3 ± 0.1, 1.5 ± 0.1 and 1.7 ± 0.2 mM on days 3, 6 and 9 of the experiment, respectively (Fig. 7).

C_{60}FAS injections at a dose of 1 mg/kg reduced these indicators by (5–7)% in all studied time intervals. Increasing the dose of C_{60}FAS to 2 mg/kg did not change these values. An increase in glycerol dose to 10 mg/kg increased the concentration of H_2O_2 to 1.7 ± 0.2, 2.0 ± 0.2 and 2.6 ± 0.2 μM on days 3, 6 and 9 of the experiment, respectively, compared to the control, i.e. its amount increased by (25–35)% compared to the previous glycerol dose. The use of C_{60}FAS at a dose of 1 mg/kg reduced these indicators by 10, 8 and 7%, and when its dose was increased to 2 mg/kg, they decreased by 17, 19 and 28% on days 3, 6 and 9, respectively. Glycerin injections at a dose of 15 mg/kg increased the concentration of H_2O_2 to 2.4 ± 0.2, 3.0 ± 0.3 and 4.1 ± 0.4 μM on days 3, 6 and 9 of the experiment, respectively, compared to the control. The use of C_{60}FAS at a dose of 1 mg/kg reduced the level of H_2O_2 by 14, 15 and 17%, and when its dose was increased to 2 mg/kg, it decreased by 16, 19 and 23% on days 3, 6 and 9, respectively (Fig. 7). Thus, these findings show that H_2O_2 concentration, which is a direct indicator of oxidative stress, is indeed progressively increased during the time course of the kidney pathology caused by rhabdomyolysis, and it decreases under the action of water-soluble C_{60} fullerenes.

Histopathological analysis of muscle soleus tissue. In control rats, no histopathological features in the kidney are observed (Table 1; Fig. 8, *A*).

In rats that received glycerol in a dose of 5 or 10 mg/kg, weak thickening of Bowman's capsule and moderate retraction of glomerular tuft are observed, as a result of which the cross-sectional area

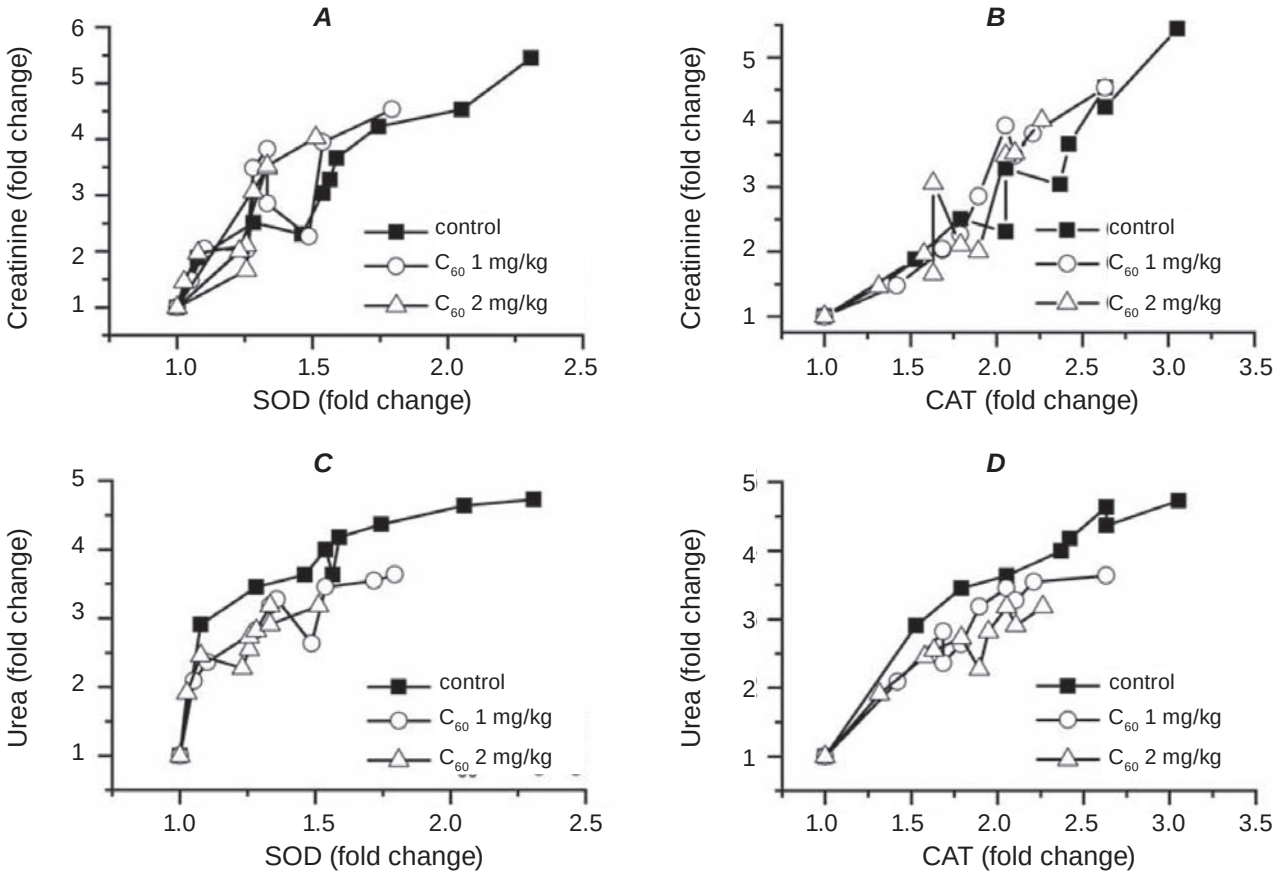

*Fig. 6. Correlation analysis of the degree of kidney dysfunction evaluated as fold-change in creatinine (**A**, **B**) and urea (**C**, **D**) concentration and SOD (**A** and **C**) and CAT (**B** and **D**) activity in the blood of rats in control (closed squares) and after C_{60} fullerene administration at 1 (open circles) and 2 (open triangles) mg/kg, as indicated*

of renal glomeruli decreases by 36–39%. Moderate tubular and interstitial necrosis (more intense in the kidney cortex) are also observed. In addition, weak inflammation and medium hemorrhage are observed (Table 1; Fig. 8, *B* and *D*).

Rats that received glycerol in a dose of 5 mg/kg or 10 mg/kg and C_{60}FAS (2 mg/kg) have similar histopathological features, but of lower intensity. Retraction of glomerular tuft is observed in a fewer number of renal glomeruli. The cross-sectional area of renal glomeruli is reduced compared to the control group by 25–30%, and it is larger by 15–17% compared to the group of rats that did not receive C_{60}FAS. The degree of necrosis in renal tubules and connective tissue is also lower (Table 1; Fig. 8, *C* and *E*).

In rats that received glycerol at a dose of 15 mg/kg, the degree of histopathological changes increases compared to rats that received glycerol at a lower dose. Strong necrosis of the renal tubules and moderate necrosis in the connective tissue of the kidney are observed. Inflammation, hemorrhage, thickening of Bowman's capsule and retraction of glomerular tuft of medium intensity and a decrease in the cross-sectional area of renal glomeruli are also observed. In addition, the tubular structure of part of the renal tubules in the medullary zone is disturbed. The diameter of renal tubes decreases by 8% (Table; Fig. 8, *F*).

In rats that received glycerol at a dose of 15 mg/kg and C_{60}FAS (2 mg/kg), the degree of histopathological changes is lower. Tubular necrosis of medium intensity, retraction of glomerular tuft is weak, cross-sectional area of renal glomeruli is less reduced, tubular structure of renal tubules is not disturbed and diameter of renal tubes is not reduced (Table; Fig. 8, *G*).

In our opinion, the above-described positive effects of exposure to C_{60} fullerenes on the ARF caused by rhabdomyolysis are related precisely to

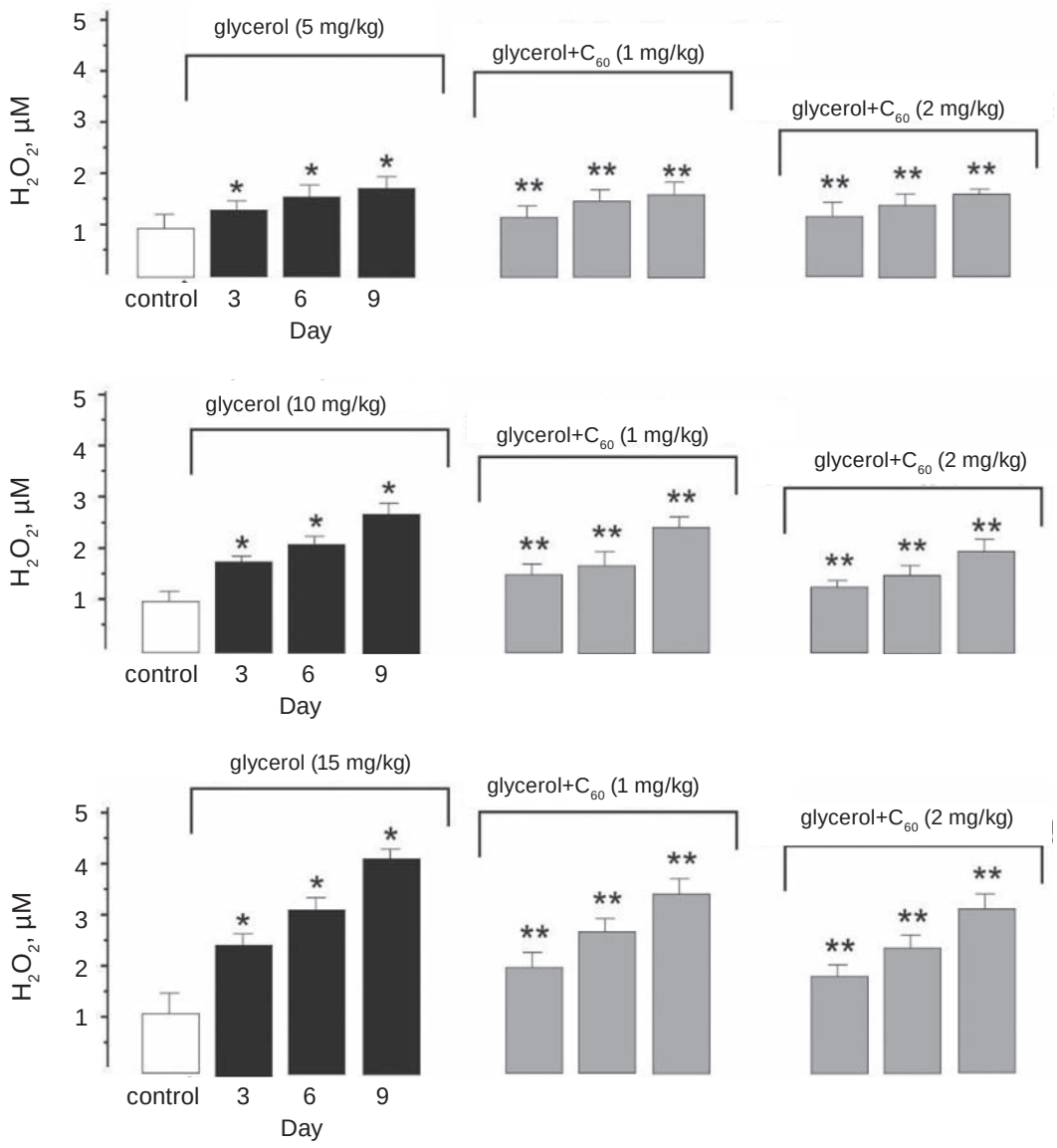

*Fig. 7. Concentration of H_2O_2 in the blood of rats with rhabdomyolysis kidney injury and administration of C_{60}FAS (C_{60}). *P < 0.05 vs. control group; **P < 0.05 vs. glycerol group*

their powerful antioxidant properties [15, 16, 22]: one C_{60} molecule simultaneously captures 34 methyl radicals, effectively inactivates the superoxidanion radical and hydroxyl radicals, protecting cell membranes from oxidation. By reducing the number of free radicals formed by the processes of rhabdomyolysis destruction, water-soluble C_{60} fullerenes reduce the number of damaged nephron membranes and, thus, reduce the severity of ARF.

Conclusions. Thus, there is a clear tendency to decreasing of the studied biochemical parameters values in the blood of rats (creatinine and urea concentrations, CAT and SOD activities) by about (20–30)% when using C_{60}FAS injections at a dose of 1 mg/kg and additionally by (12–15)% with an increase in its dose to 2 mg/kg in the model of glycerol-induced rhabdomyolysis. Moreover, the concentration of hydrogen peroxide also decreases under the action of water-soluble C_{60} fullerenes. Finally, the biochemical parameters were confirmed by the data of histopathological analysis.

Based on the analysis of the results obtained, it is possible to improve the generally accepted experimental model of glycerol-induced rhabdomyolysis, which is realized by intramuscular injection of a 50% glycerol solution at a dose of 10 mg/kg and is used to initiate ARF. So, the data obtained indicate that the injection of glycerol into a single muscle can

Ta b l e. Morphometrical features of the kidney in rats after glycerol and C_{60}FAS injection

Morphometrical features	Groups						
	Control	Glycerol (5 mg/kg)	Glycerol (5 mg/kg) + C_{60}FAS (2 mg/kg)	Glycerol (10 mg/kg)	Glycerol (10 mg/kg) + C_{60}FAS (2 mg/kg)	Glycerol (15 mg/kg)	Glycerol (15 mg/kg) + C_{60}FAS (2 mg/kg)
Cross-sectional area of renal glomeruli, μm²	5655±373	3429±298*	3960±357^	3621±341*	4212±401^	3504±314*	4046±396^
Diameter of renal tubes, μm	33.8±3.1	35.6±3.5*	33.5±3.1^	32.5±3.0*	31.9±2.9^	31.0±2.9*	32.9±3.0^

Notes: *P < 0.05 compare with control group; ^*P* < 0.05 compare with glycerol group in the same dose

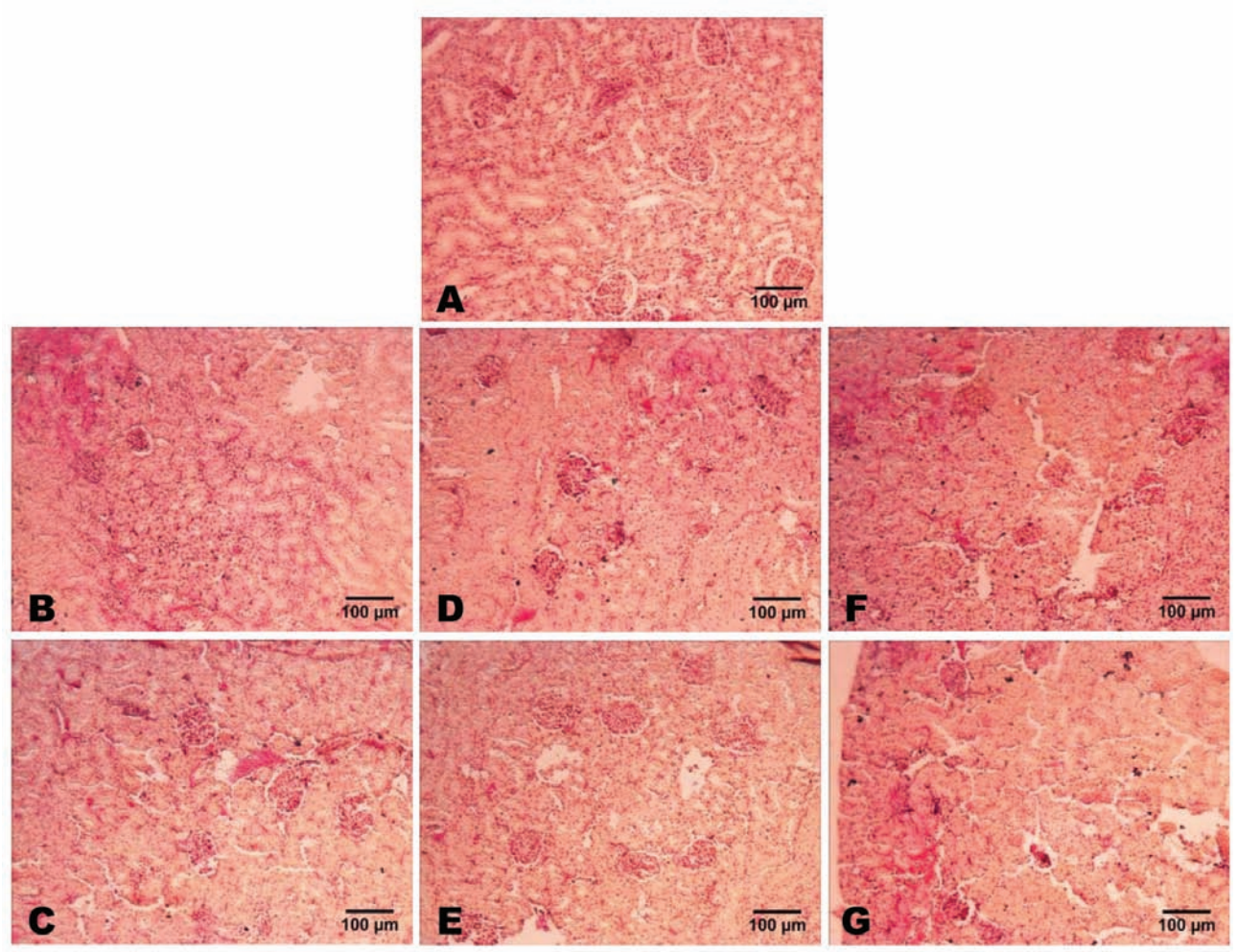

Fig. 8. Representative histological images of the kidney: ***A*** *– control group;* ***B*** *– glycerol (5 mg/kg);* ***C*** *– glycerol (5 mg/kg) + C_{60}FAS (2 mg/kg);* ***D*** *– glycerol (10 mg/kg);* ***E*** *– glycerol (10 mg/kg) + C_{60}FAS (2 mg/kg);* ***F*** *– glycerol (15 mg/kg);* ***G*** *– glycerol (15 mg/kg) + C_{60}FAS (2 mg/kg). H&E staining. Scale bar – 100 μm*

reduce the amount of glycerol used by half. In addition, the severity of ARF in this model depends on the time of the pathology initiation and reaches its maximum value on the 9th day.

C_{60}FAS has demonstrated a positive effect on the development of ARF *in vivo*, attenuating the features of renal due to a reduction in the oxidative stress degree. Therefore, the development of medicines using nanotechnology based on water-soluble C_{60} fullerenes, taking into account their powerful antioxidant properties, opens up new opportunities in the treatment and prevention of ARF caused by rhabdomyolysis damage to the musculoskeletal system.

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

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ФУЛЕРЕН C_{60} ПОСЛАБЛЮЄ ОЗНАКИ ГОСТРОЇ НИРКОВОЇ НЕДОСТАТНОСТІ У ЩУРІВ ПРИГНІЧЕННЯМ ОКИСНОГО СТРЕСУ ЗА РАБДОМІОЛІЗУ

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Відомо, що рабдоміоліз як гостра стадія міопатії пов'язаний з накопиченням продуктів розпаду м'язів, гострою нирковою недостатністю та окисним стресом. Метою дослідження було оцінити вплив C_{60} фулерену як антиоксиданту на пошкодження нирок у щурів з індукованим гліцерином рабдоміолізом. Дослідження проводили на щурах-самцях лінії Wistar, розділених на такі дослідні групи: контрольні тварини, тварини, яким внутрішньом'язово вводили гліцерин у дозах 5, 10 і 15 мг/кг та ті, яким щодня внутрішньоочеревинно вводили водний розчин C_{60} фулерену (C_{60}ФВР) в дозі 1 або 2 мг/кг через 48 год після введення гліцерину. Контроль за біохімічними та морфологічними показниками проводили на 3, 6 та 9 добу. Виявлено тісний кореляційний зв'язок між тяжкістю гострого ураження нирок, підвищенням рівня креатиніну та сечовини, активністю супероксиддисмутази (СОД) та каталази (КАТ) у крові щурів. Показано, що у щурів, які отримували 2 мг/кг C_{60}ФВР, розміри ниркових клубочків і прояви некрозу зменшувалися, а активність СОД і КАТ у крові значно знижувалася. Отримані результати можуть бути корисними для розробки підходів до лікування патологічних станів м'язової системи, спричинених рабдоміолізом та пов'язаним із ним оксидативним стресом.

Ключові слова: рабдоміоліз, гостра ниркова недостатність, біохімічні показники, патогістологічний аналіз, *muscle soleus*, C_{60} фулерен.

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