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Scientific Article

Uridine increases endurance and improves the rehabilitation of experimental animals after physical performance

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BACKGROUND: The pharmacological correction of metabolic processes, providing an increase in the efficiency and duration of physical performance and contributing to rapid rehabilitation, is an important component of the regulation of adaptation. Previously, we found that the pyrimidine nucleoside uridine exhibits antihypoxic properties, activates mitochondrial K^+_{ATP} channels (mitoK$_{ATP}$), normalizes energy metabolism, reduces lipid peroxidation, activates the antioxidant system, and increases glycogen content. The substance with such properties was assumed to increase endurance and improve recovery after physical performance.

AIM: To examine the effect of uridine on the endurance of experimental animals in the forced swimming test under different intensities of physical performance and their rehabilitation.

MATERIALS AND METHODS: Experiments were performed on male Wistar rats (350–380 g) and male outbred mice (25–30 g). In the first series, the effect of uridine on the rat's endurance was studied in the forced swimming test with a load of 5%, 7%, or 10% of the animal weight. In the second series, the effect of uridine on the first phase of recovery was evaluated in a three-load swimming test. Mice with 10% load were subjected to a swimming test three times, after which the trail index —the ratio of time of the third trail to the first trail — was determined. The frequency of animals with low, medium, and high recovery ability was estimated. Uridine 30 mg/kg or physiological saline (control) was administered 30 min before testing, 5-hydroxidecanoate (5-HD, mitoK$_{ATP}$ blocker) 5 mg/kg 45 min before testing, and mexidol (reference drug) 200 mg/kg 50 min before testing.

RESULTS: Uridine increased the critical swimming duration by 58% and 44% at 5% and 7% exercise, respectively, in comparison with control. At 7% load, the drug increased the period before the appearance of the first signs of fatigue by 100%. After the blockade of mitoK$_{ATP}$ channels, the effect of uridine decreased by 40% in the presence of fatigue and 24% in critical swimming duration. In the three-load swimming test, uridine increased the trail index by 1.5 times, which was comparable to the effect of mexidol, and increased the number of animals with a high ability to recover by 2.6 times. The use of uridine after mitoK$_{ATP}$ channel blockade did not lead to a decrease of its positive effect and the blockade of channels with 5-HD did not affect rehabilitation.

CONCLUSIONS: Uridine increases the endurance of rats with a medium load in the forced swimming test and the rehabilitation of mice in the three-load swimming test. It also increases the number of animals with a high ability to recover after a swimming performance. The mechanism of its effects was realized both through the activation of mitoK$_{ATP}$ channels and, probably, the stimulation of glycogenesis.

Keywords: uridine; endurance; rehabilitation; forced swimming test; physical performance; mitoK$_{ATP}$ channel.

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Научная статья

Уридин повышает выносливость и улучшает восстановление работоспособности экспериментальных животных после физической нагрузки

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Актуальность. Фармакологическая коррекция метаболических процессов, обеспечивающих увеличение эффективности и длительности выполняемой работы и способствующих скорейшему восстановлению организма после физических нагрузок, является важным компонентом регуляции адаптационных возможностей организма. Ранее нами было установлено, что пиримидиновый нуклеозид уридин проявляет антигипоксические свойства, способен активировать митохондриальные $К^{+}_{АТФ}$ каналы (митоК$_{АТФ}$), нормализует энергетический обмен, снижает интенсивность перекисного окисления липидов, активирует антиоксидантную систему, а также увеличивает содержание гликогена. Можно предположить, что соединение с такими свойствами будет повышать выносливость и способствовать более быстрому восстановлению сил после физических нагрузок.

Цель — изучение влияния уридина на работоспособность экспериментальных животных в тесте вынужденного плавания с утяжелением при физических нагрузках разной интенсивности и на восстановление их работоспособности.

Материалы и методы. Опыты выполнены на крысах-самцах линии Вистар (350–380 г) и самцах белых беспородных мышей (25–30 г). В первой серии экспериментов определяли влияние уридина на работоспособность крыс в тесте вынужденного предельного плавания с утяжелением массой 5, 7 или 10 % от веса животного. Физическую работоспособность оценивали по продолжительности плавания до появления первых признаков утомления и/или времени предельного плавания до гибели. Во второй серии в трехнагрузочном плавательном тесте оценивали влияние уридина на первую фазу процессов восстановления. Мышей с 10 % грузом 3 раза подвергали плавательной пробе, после чего определяли индекс пробы, равный отношению времени выполнения нагрузки 3 к нагрузке 1. Оценивали частоту встречаемости животных с низкой, средней и высокой способностью к восстановлению. Уридин объемом 30 мг/кг или физиологический раствор (контроль) вводили за 30 мин, 5-гидроксидеканоат (5-ГД, блокатор митоК$_{АТФ}$ каналов) 5 мг/кг — за 45 мин, мексидол (препарат сравнения) 200 мг/кг — за 50 мин до начала тестирования.

Результаты. Уридин увеличивал продолжительность предельного плавания на 58 и 44 % при 5 и 7 % нагрузке соответственно. При 7 % нагрузке под действием препарата период до появления первых признаков утомления возрастал на 100 %. Эффект уридина, введенного на фоне блокады митоК$_{АТФ}$ каналов, снижался на 40 % в случае утомления и на 24 % в случае ПП. В трехнагрузочном плавательном тесте уридин в 1,5 раза увеличивал эффективность восстановления сил, что было сопоставимо с действием мексидола. Препарат в 2,6 раза увеличивал долю животных с высокой способностью к восстановлению. Применение уридина на фоне блокады митоК$_{АТФ}$ каналов не приводило к ослаблению его положительного эффекта, а блокада каналов 5-ГД не влияла на способность животных к восстановлению сил.

Заключение. Уридин увеличивает выносливость животных в тесте вынужденного предельного плавания при предъявлении им нагрузок средней интенсивности, повышает способность к восстановлению работоспособности в трехнагрузочном плавательном тесте и увеличивает количество животных с высокой способностью к восстановлению. Механизм его действия реализуется как через активацию митоК$_{АТФ}$ каналов, так и, вероятно, через стимуляцию гликогенеза.

Ключевые слова: уридин; выносливость; восстановление сил; тест вынужденного предельного плавания; физическая нагрузк, митоК$_{АТФ}$ каналы.

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BACKGROUND

To increase performance and recover rapidly after intense physical activity are issues in various areas of human life, i.e., labor, sports, and military service. Therefore, possible solutions, particularly those related to the pharmacological correction of metabolic changes during heavy physical loads, are desired [1]. Hypoxia, which is referred to as exercise hypoxia [2] or physiologic hypoxia [3], underlies the decline in performance. Oxygen deficiency during prolonged or intense exercise limits the body's ability to use the aerobic pathway of energy production, which subsequently activates anaerobic glycolysis. Owing to the rapid depletion of its substrate supply, this opportunity to replenish energy resources becomes inefficient, resulting in fatigue and decreased performance. Antihypoxants and antioxidants may be used as nondoping drugs to increase work volume and duration and accelerate recovery [4].

The pyrimidine nucleoside uridine, a metabolic precursor of uridine diphosphate (UDP), an endogenous activator of mitochondrial adenosine triphosphate (ATP)-sensitive K(+) (mitoK_{ATP}) channels, was found to exhibit antihypoxic properties in experimental models of hypoxic conditions such as hypoxic hypoxia with hypercapnia and local circulatory hypoxia (acute myocardial ischemia) [5]. Uridine normalizes energy metabolism, reduces the intensity of lipid peroxidation, and activates the antioxidant system in the ischemic myocardium [6]. When it was used along with mitoK_{ATP} channel blockade, its main effect was assumed to be the activation of these channels [7]. Activation leads to the preservation of the morphofunctional organization of mitochondria and thus increases the efficiency of the aerobic component (oxidative phosphorylation) in the cellular energy supply system. In the presence of acute myocardial ischemia, uridine metabolites may participate in glycogenesis [8, 9], replenishing glycogen stores, which plays an important role in both aerobic and anaerobic pathways of energy supply to muscle tissues. Therefore, a compound with such properties may increase work capacity (endurance) and improve recovery from physical performance.

This study aimed to examine the effect of uridine on the endurance of experimental animals in the forced swimming (FS) test under different intensities of physical performance and their rehabilitation.

MATERIALS AND METHODS

Experiments were performed on 76 (each group including 6–14 animals) male Wistar rats (350–380 g) and 48 male white outbred mice (25–30 g). The animals were obtained from the Rappolovo nursery and kept under standard vivarium conditions at a room temperature of 20°C–22°C, relative humidity of 60%–70%, and 12-h day/night cycle with free access to water and food.

Experiments were conducted in compliance with the requirements of the European Convention for the Protection of Vertebrate Animals Used for Experimental or Other Scientific Purposes (Strasbourg, 1986), in accordance with the ethical principles outlined in the Directive of the European Parliament and the Council of the European Union 2010/63/US dated September 22, 2010, and with the approval of the Bioethics Commission of the Institute of Experimental Medicine. The experimental work was performed in accordance with the methodological guidelines for the study of drugs that affect physical performance [10].

Two series of experiments were conducted. In series 1, the effect of uridine on rat performance in the FS test with weighting was determined. A load corresponding to 5%, 7%, or 10% of the animal's weight was attached to the base of the sacrum 15 min before testing [1]. The water depth in the pool was 80 cm, and the water temperature was 22°C.

Rats were intraperitoneally injected with uridine at a dose of 30 mg/kg or saline solution 30 min before pool immersion (control group [CG]). In addition, the effects on the performance of the mitoK_{ATP} channel blocker 5-HD, which was administered 45 min before the experiment at a dose of 5 mg/kg, and the combined application of 5-HD and uridine were examined in a 5% loading experiment. In the latter case, 5-HD was administered 15 min before uridine. The criterion for study termination was the death of the animal, and the parameters that reflect physical performance were the duration of swimming before the first signs of fatigue (before the first dive) and/or the time of FS before death.

In series 2, the three-load swimming test was used, which is a modified FS test and is conducted to assess the effect of drugs on the first phase of recovery (first hour) [10]. The experiment was performed on male white outbred mice weighing 25–30 g, which were divided into groups (Table 1). A 10% load was attached to sacral base, and in the swimming test, the animals were immersed in a pool with water temperature of 22 °C. The criterion for the termination of swimming load 1 was the inability of the animals to continue swimming (diving to the bottom of the pool without swimming movements for 30 s or the appearance of rotational movements or agonal convulsions). After the refusal to continue the load, the mice were quickly removed from the water and dried. After 5 min, they were reimmersed in the pool for the second swimming test (load 2), after which they rested for 45 min. Subsequently, all animals were subjected to a third swimming test (load 3). The duration of each load test was recorded. The ability to recover, i.e., the so-called the test index (TI), was analyzed, which was equal to the ratio of the time of performing load 3 to load 1. The TI was characterized as low (<0.5), medium (0.51–0.8), and high (>0.8) recovery ability. Moreover, animals with low, medium, and high recovery ability were assessed. Uridine 30 mg/kg or saline (CG) was injected intraperitoneally 30 min before testing, and 5-HD 5 mg/kg was injected 45 (CG) or 15 min before uridine administration. Mexidol at a dose of 200 mg/kg, which was administered intraperitoneally 50 min before testing, was used as the comparison drug.

Statistical data analysis was performed using GraphPad Prism 6 (GraphPad Software, USA). Experimental groups were compared using the one-factor analysis of variance, Student's *t*-test, and Fisher's nonparametric criterion. Between-group differences were considered statistically significant at $p < 0.05$. Data are presented as mean and standard error ($M \pm SEM$).

RESULTS

FS test with weighting

Under FS conditions with a 5% load, the period before the emergence of signs of fatigue (time of the first dive) in control animals ($n = 6$) was 170 ± 17 s, and the FS duration was 526 ± 37 s (Fig. 1). The administration of uridine to rats ($n = 11$) at a dose of 30 mg/kg did not significantly change the swimming time to fatigue, which was 185 ± 40 s. By contrast, the duration of the uridine-induced FS increased by 58% compared with the CG. Under these conditions, the mitoK$_{ATP}$ channel blocker 5-HD ($n = 6$) significantly decreased rat performance, reducing the swimming time to fatigue by 3.9-fold and the time to FS by 2.4-fold compared with the CG (Fig. 1), indicating the involvement of mitoK$_{ATP}$ channels in the energy supply during physical activity. The effect of uridine administration along with mitoK$_{ATP}$ channel blockade was reduced by 40% in the presence of fatigue and by 24% in the case of FS.

Increasing the load to 7% (Fig. 2) resulted in a significantly faster fatigue onset and decreased the endurance of the animals. Thus, the time to the first dive and FS time in the CG decreased by 5.3- and 2.9-fold, respectively, compared with a 5% load. Uridine increased the period until the first signs of fatigue by 100%. The FS duration after uridine administration was 44% higher than that of the CG. Thus, with increased load, drug efficiency improved, which was manifested as an increase of both the FS time and duration before fatigue onset.

Increasing the load up to 10% of body weight resulted in further decreased performance of the CG and the inability to clearly distinguish the time up to the first dive, as fatigue occurred very quickly. In these animals, uridine did not positively affect the FS time.

Three-load swimming test

The results are presented in Fig. 3. In the CG, the TI was 0.57 ± 0.04. In the uridine-treated group, the recovery was more effective, as evidenced by a 1.5-fold increase in TI (0.85 ± 0.04; $p < 0.001$ vs. CG). The activity of uridine was comparable to that of mexidol, which increased TI by 1.5-fold (0.82 ± 0.05; $p < 0.001$ vs. CG). The use of uridine along with mitoK$_{ATP}$ channel blockade did not significantly weakened its positive effect (0.78 ± 0.04; $p > 0.05$ vs. uridine), and 5-HD channel blockade did not affect the animals' ability to recover (0.60 ± 0.07; $p > 0.05$ vs. CG).

If the investigated drug exerts a positive effect on the first phase of recovery, it should cause both a significant increase in the group average TI and a change in the occurrence patterns of animals with low, medium, and high ability for effective recovery. The results demonstrate pronounced uridine-induced changes in the distribution of animals with different recovery abilities (Table 1).

Uridine increased the proportion of animals with a high recovery ability by 2.6-fold and had superior efficiency to the comparison drug mexidol. The mitoK$_{ATP}$ channel blocker did not significantly change the distribution of animals into groups. However, a preliminary blockade of mitoK$_{ATP}$ channels by 27% reduced the positive effect of uridine.

DISCUSSION

In the FS test, the load determines the mode of physical performance, i.e., 5% of the animal's weight correspond to a moderate load of medium duration and is recommended to be used to assess the aerobic component of work, and

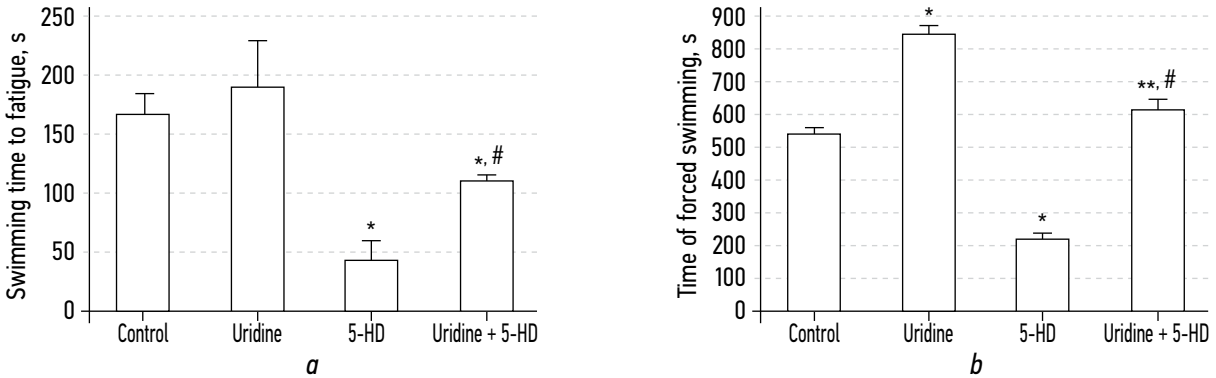

Fig. 1. Influence of uridine on the performance of rats in the forced swimming test with a 5% load; *a*, time until fatigue appear; *b*, time of ultimate swimming. *$p < 0.05$ to the control group; **$p < 0.01$ between 5-HD and uridine + 5-HD groups; #$p < 0.05$ between uridine and uridine + 5-HD groups

Рис. 1. Влияние уридина на работоспособность крыс в тесте вынужденного предельного плавания с утяжелением 5 %; *a* — время до появления признаков утомления; *b* — время предельного плавания. *$p < 0,05$ по отношению к контрольной группе; **$p < 0,01$ между группами 5-ГД и уридин + 5-ГД; #$p < 0,05$ между группами уридин и уридин + 5-ГД

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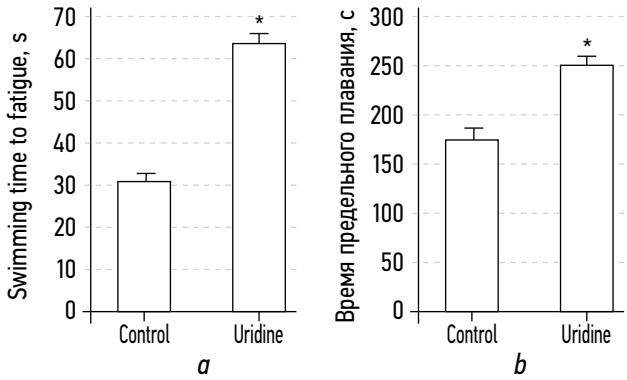

Fig. 2. Influence of uridine on the performance of rats in the forced swimming test with a 7% load; *a*, time until fatigue appear; *b*, time of ultimate swimming. *$p < 0.05$ to the control group

Рис. 2. Влияние уридина на работоспособность крыс в тесте вынужденного предельного плавания с утяжелением 7 %; *a* — время до появления признаков утомления; *b* — время предельного плавания. *$p < 0,05$ по отношению к контрольной группе

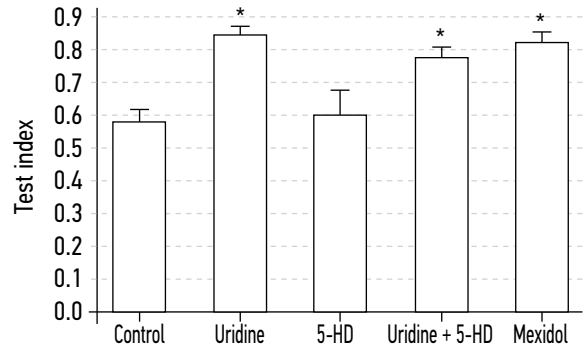

Fig. 3. Effect of uridine on the first phase of rehabilitation of mice in the three-load swimming test. *$p < 0.05$ to the control group

Рис. 3. Влияние уридина на первую фазу восстановления сил у мышей в трехнагрузочном плавательном тесте. *$p < 0,05$ по отношению к контрольной группе

Table 1. Effect of uridine on mouse groups (%) with low, medium, and high ability in the physical performance rehabilitation

Таблица 1. Влияние уридина на распределение мышей (%) по группам с низкой, средней и высокой способностью к восстановлению работоспособности

Group	*n*	Ability to physical performance rehabilitation		
		Low	Medium	High
Control	18	22	45	33
Uridine	7	0* $p < 0.0001$	14* $p < 0.0001$	86* $p < 0.0001$
5-HD	8	25	37.5	37.5
Uridine + 5-HD	8	$12^{\#}$ $p = 0.0004$	$25^{*\#}$ $^{*}p = 0.003$ $^{\#}p = 0.0496$	$63^{*\#}$ $^{*}p < 0.0001$ $^{\#}p = 0.0002$
Mexidol	7	$29^{\#}$ $p < 0.0001$	14* $p < 0.0001$	$57^{*\#}$ $^{*}p = 0.0006$ $^{\#}p < 0.0001$

Note: * significant difference when compared with the control group; # significant difference when compared with uridine.

7% and 10% refer to a medium and high levels of loading intensity, respectively [10].

The results of the FS test with weighting indicate that uridine increases rat performance at a moderate and, to a greater extent, at a medium level of loads. Thus, the effect of the drug is manifested by the dominance of the aerobic component of work during aerobic–anaerobic loading. At a high load level (10% of the animal weight), in which a rapid transition from aerobic to anaerobic pathways of energy formation occurs and the animal spends most of the time in anaerobic conditions (underwater), the endurance of rats exposed to uridine did not increase. However, evidence suggested that uridine can increase the endurance of rats with initially low exercise tolerance at a 20% load [11]. In this case, its effect is attributed to the activation of mitoK_{ATP} channels and the acceleration of the K+ transport in mitochondria. However, despite under the same experimental conditions, uridine decreased the swimming time of highly resistant animals. In our experiment, the average group endurance was determined, whereas the initial tolerance of the animals was not considered. This may be the reason why no drug activity was observed at maximal loading. When assessing the antihypoxic activity of uridine in pathological hypoxia models and animals of different sexes, the protective effect of uridine on the initial resistance to hypoxia was noted; however, the drug did not aggravate the condition of the animals [5]. The decreased effect of uridine on exercise duration accompanied by mitoK_{ATP} channel blockade suggests that the effect of the substance is partially mediated by their activation. The preservation of drug activity during mitoK_{ATP}

channel blockade is most likely due to the ability to intensify glycogen synthesis, which is a source of substrate supply for aerobic and anaerobic pathways of energy production. Glycogen is actively broken down during muscle contractions, resulting in the generation of ATP needed to perform physical work. In humans, glycogenolysis provides 40%–50% of ATP production during physical performance, particularly in sports [12, 13]. During exercise, the key factor of performance is a sufficient supply of glycogen in muscles, and its resynthesis directly affects overall recovery and performance [14, 15]. In addition, the recovery after physical activity is primarily associated with the restoration of the energy potential of the organism and replenishment of glycogen stores [1]. Previously, uridine administration led to increased glycogen in cardiomyocytes during acute myocardial ischemia in rats [16]. Furthermore, UDP and uridine triphosphate (UTP) in the myocardium increased over twofold 60 min after uridine administration in both intact animals and animals with myocardial infarction [7]. These findings support the possibility of including exogenous uridine in metabolic transformations to form uridine nucleotides. In turn, UTP formed from uridine participates in the synthesis of UDP glucose, which is an activated form of glucose and is directly involved in polymerization reaction, resulting in the build-up of glycogen molecules [17]. The absence of the effect of the mitoK_{ATP} channel blocker and uridine on the TI along with channel blockade suggests that the positive effect of uridine on recovery is more related to intensified glycogenesis.

CONCLUSIONS

1. In the FS test, uridine increased the endurance of rats when presented with moderate-intensity loads.

2. In the three-load test, uridine enhanced the recovery ability of mice and increased the proportion of animals with high recovery ability.

3. The effect of uridine on animal performance is partially realized through the activation of mitoK_{ATP} channels, and the positive effect of the drug on recovery is probably associated with enhanced glycogenesis.

ADDITIONAL INFORMATION

Authors contribution. Thereby, all authors made a substantial contribution to the conception of the study, acquisition, analysis, interpretation of data for the work, drafting and revising the article, final approval of the version to be published and agree to be accountable for all aspects of the study. The contribution of each author: E.N. Selina — manuscript drafting, writing and pilot data analyses; I.B. Krylova — general concept of paper.

Competing interests. The authors declare that they have no competing interests.

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ДОПОЛНИТЕЛЬНАЯ ИНФОРМАЦИЯ

Вклад авторов. Все авторы внесли существенный вклад в разработку концепции, проведение исследования и подготовку статьи, прочли и одобрили финальную версию перед публикацией. Вклад каждого автора: Е.Н. Селина — написание статьи, анализ данных; И.Б. Крылова — разработка общей концепции.

Конфликт интересов. Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с публикацией настоящей статьи.

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REFERENCES

1. Gridin LA, Ikhalainen AA, Bogomolov AV, et al. *Metody issledovaniya i farmakologicheskoi korrektsii fizicheskoi rabotosposobnosti cheloveka*. Ushakov IB, editor. Moscow: Meditsina, 2007. 104 p. (In Russ.)

2. Shustov EB, Kapanadze GD, Stankova NV, et al. Hypoxia of physical activity at the atlets and laboratory animals. *Biomedicine*. 2014;(4):4–16. (In Russ.)

3. Li J, Li Y, Atacan MM, et al. The molecular adaptive responses of skeletal muscle to high-intensity exercise/training and hypoxia. *Antioxidants (Basel)*. 2020;9(8):656. DOI: 10.3390/antiox9080656

4. Pitkevich EhS, Lositskii EA, Krest'yaninova TYu, Derkach IN. *Farmakologicheskaya korrektsiya rabotosposobnosti v sporte. Metodicheskie rekomendatsii*. Vitebsk: VGU imeni P.M. Masherova, 2013. 52 p. (In Russ.)

5. Krylova IB, Safonova AF, Evdokimova NR. Correction of hypoxic state by metabolic precursors of endogenous activator of mitochondrial ATP-dependent K+channels. *Reviews on Clinical Pharmacology and Drug Therapy*. 2018;16(3):25–32. (In Russ.) DOI: 10.17816/RCF16325-31

6. Bulion VV, Krylova IB, Selina EN. Cardioprotection of ischemic myocardium. *Reviews on Clinical Pharmacology and Drug Therapy*. 2018;16(2):13–17. (In Russ.) DOI: 10.17816/RCF16213-17
7. Krylova IB, Selina EN, Bulion VV, et al. Uridine treatment prevents myocardial injury in rat models of acute ischemia and ischemia/ reperfusion by activating the mitochondrial ATPdependent potassium channel. *Sci Rep*. 2021;11(1):16999. DOI: 10.1038/s41598-021-96562-7
8. Bul'on VV, Krylova IB, Rodionova OM, et al. Comparative study of cardioprotective effects of uridine-5'-monophosphate and uridine-5'-triphosphate during the early periods of acute myocardial ischemia. *Bull Exp Biol Med*. 2007;144(3):322–325. DOI: 10.1007/s10517-007-0323-4
9. Aussedat J. Effect of uridine supply on glycogen resynthesis after ischaemia in the isolated perfused rat heart. *Cardiovasc Res*. 1983;17(3):145–151. DOI: 10.1093/cvr/17.3.145
10. Karkishchenko NN, Karkishchenko VN, Shustov EB, et al. *Biomeditsinskoe (doklinicheskoe) izuchenie lekarstvennykh sredstv, vliyayushchikh na fizicheskuyu rabotosposobnost'. Metodicheskie rekomendatsii*. Moscow: Nauchnyi tsentr biomeditsinskikh tekhnologii FMBA Rossii, 2017. 134 p. (In Russ.)
11. Mankovskaya IN, Nosar VI, Gonchar OA, et al. The effect of uridine on the endurance of animals with different resistance to physical stress: the role of mitochondrial ATP-dependent potassium channel. *Biophysics*. 2014;59(5):941–945. (In Russ.)
12. Cheetham ME, Boobis LH, Brooks S, Williams C. Human muscle metabolism during sprint running. *J Appl Physiol*. 1985;61(1):54–60. DOI: 10.1152/jappl.1986.61.1.54
13. Girard O, Mendez-Villanueva A, Bishop D. Repeated-sprint ability-part I: factors contributing to fatigue. *Sports Med*. 2011;41(8): 673–694. DOI: 10.2165/11590550-000000000-00000
14. Burke LM, van Loon LJC, Hawley JA. Postexercise muscle glycogen resynthesis in humans. *J Apl Physiol*. 2017;122(5):1055–1067. DOI: 10.1152/japplphysiol.00860.2016
15. American College of Sports Medicine. *ACSM's advanced exercise physiology. 2nd ed*. Farrell PA, Joyner M, Caiozzo V, editors. Wolters Kluwer Health/Lippincott Williams and Wilkins, 2012. 719 p.
16. Bul'on VV, Krylova IB, Selina EN, et al. Antiarrhythmic effect of uridine and uridine-5'-monophosphate in acute myocardial ischemia. *Bull Exp Biol Med*. 2014;157(6):728–731. DOI: 10.1007/s10517-014-2653-3
17. Katz A. A century of exercise physiology: key concepts in regulation of glycogen metabolism in skeletal muscle. *Eur J Appl Physiol*. 2022;122(8):1751–1772. DOI: 10.1007/s00421-022-04935-1

СПИСОК ЛИТЕРАТУРЫ

1. Гридин Л.А., Ихалайнен А.А., Богомолов А.В., и др. Методы исследования и фармакологической коррекции физической работоспособности человека / под ред. И.Б. Ушакова. Москва: Медицина, 2007. 104 с.
2. Шустов Е.Б., Капанадзе Г.Д., Станкова Н.В., и др. Гипоксия физической нагрузки у спортсменов и лабораторных животных // Биомедицина. 2014. № 4. С. 4–16.
3. Li J., Li Y., Atacan M.M., et al. The molecular adaptive responses of skeletal muscle to high-intensity exercise/training and hypoxia // Antioxidants (Basel). 2020. Vol. 9, No. 8. ID656. DOI: 10.3390/antiox9080656
4. Питкевич Э.С., Лосицкий Е.А., Крестьянинова Т.Ю., Деркач И.Н. Фармакологическая коррекция работоспособности в спорте. Методические рекомендации. Витебск: ВГУ имени П.М. Машерова, 2013. 52 с.
5. Крылова И.Б., Сафонова А.Ф., Евдокимова Н.Р. Коррекция гипоксических состояний метаболическими предшественниками эндогенного активатора митохондриальных АТФ-зависимых K^+каналов // Обзоры по клинической фармакологии и лекарственной терапии. 2018. Т. 16, № 3. С. 25–32. DOI: 10.17816/RCF16325-31
6. Бульон В.В., Крылова И.Б., Селина Е.Н. Кардиопротекция при ишемическом повреждении миокарда. Обзоры по клинической фармакологии и лекарственной терапии // 2018. Т. 16, № 2. С. 13–17. DOI: 10.17816/RCF16213-17
7. Krylova I.B., Selina E.N., Bulion V.V., et al. Uridine treatment prevents myocardial injury in rat models of acute ischemia and ischemia/ reperfusion by activating the mitochondrial ATP-dependent potassium channel // Sci Rep. 2021. Vol. 11, No. 1. ID 16999. DOI: 10.1038/s41598-021-96562-7
8. Bul'on V.V., Krylova I.B., Rodionova O.M., et al. Comparative study of cardioprotective effects of uridine-5'-monophosphate and uridine-5'-triphosphate during the early periods of acute myocardial ischemia // Bull Exp Biol Med. 2007. Vol. 144, No. 3. P. 322–325. DOI: 10.1007/s10517-007-0323-4
9. Aussedat J. Effect of uridine supply on glycogen resynthesis after ischaemia in the isolated perfused rat heart // Cardiovasc Res. 1983. Vol. 17, No. 3. P. 145–151. DOI: 10.1093/cvr/17.3.145
10. Каркищенко Н.Н., Каркищенко В.Н., Шустов Е.Б., и др. Биомедицинское (доклиническое) изучение лекарственных средств, влияющих на физическую работоспособность. Методические рекомендации. Москва: Научный центр биомедицинских технологий ФМБА России, 2017. 134 с.
11. Маньковская И.М., Носарь В.И., Горбачева В.С., и др. Влияние уридина на выносливость животных с разной устойчивостью к физической нагрузке: роль митохондриального АТФ-зависимого калиевого канала // Биофизика. 2014. Т. 59, № 5. С. 941–945.
12. Cheetham M.E., Boobis L.H., Brooks S., Williams C. Human muscle metabolism during sprint running // J Appl Physiol. 1985. Vol. 61, No. 1. P. 54–60. DOI: 10.1152/jappl.1986.61.1.54
13. Girard O., Mendez-Villanueva A., Bishop D. Repeated-sprint ability-part I: factors contributing to fatigue // Sports Med. 2011. Vol. 41, No. 8. P. 673–694. DOI: 10.2165/11590550-000000000-00000
14. Burke L.M., van Loon L.J.C., Hawley J.A. Postexercise muscle glycogen resynthesis in humans // J Apl Physiol. 2017. Vol. 122, No. 5. P. 1055–1067. DOI: 10.1152/japplphysiol.00860.2016
15. American College of Sports Medicine. ACSM's advanced exercise physiology. 2nd ed. / P.A. Farrell, M. Joyner, V. Caiozzo, editors. Wolters Kluwer Health/Lippincott Williams and Wilkins, 2012. 719 p.
16. Bul'on V.V., Krylova I.B., Selina E.N., et al. Antiarrhythmic effect of uridine and uridine-5'-monophosphate in acute myocardial ischemia // Bull Exp Biol Med. 2014. Vol. 157, No. 6. P. 728–731. DOI: 10.1007/s10517-014-2653-3
17. Katz A. A century of exercise physiology: key concepts in regulation of glycogen metabolism in skeletal muscle // Eur J Appl Physiol. 2022. Vol. 122, No. 8. P. 1751–1772. DOI: 10.1007/s00421-022-04935-1

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