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Creatine as an essential pharmaconutrient in the practice of training athletes in martial arts

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Aim: to form modern ideas about the properties of creatine as a pharmaconutrient, its biological role in the body, and rational dosage during physical exertion.

Materials and methods. To determine the level of development of the research problem, a search was conducted in the databases MEDLINE, PubMed, Scopus, Directory of Open Access Journals and ScienceDirect; the keywords used included physical exercise, creatine supplementation, oxidative stress, mitochondria, energy metabolism. We focused on English-language articles published between 2019 and 2025.

Results. The use of creatine loading schemes during high-intensity interval training provides an increase in physical fitness indicators by an average of 10–20 % due to an increase in the concentration of muscle phosphocreatine. According to modern ideas, creatine belongs, on the one hand, to the group of myostatin inhibitors, and on the other hand, to the protectors of mitochondrial function. The results of 50 studies showed that compared to placebo, creatine, both alone and in combination with bicarbonate, produced a statistically significant increase in average and peak power in martial artists. Increasing cellular creatine levels promoted metabolic channeling, demonstrated antiapoptotic properties, promoted the survival of dopaminergic neurons, and produced a pronounced antidepressant effect, helping athletes remain psychologically stable during training, and before competitions.

Conclusions. Thus, from the literature data, it becomes clear that the course use of creatine leads to a significant increase in the efficiency of the training process, and this makes it an indispensable tool for improving the indicators of physical and functional fitness, as well as the overall quality of life of athletes. Creatine is a universal ergogenic food supplement, but due to its predominantly positive effect on the body with chiefly aerobic energy supply, typical of Olympic martial arts, it is fully suitable for improving the effectiveness of the training process in boxing, judo, taekwondo, jiu-jitsu (jujutsu), fencing, etc. The neuroprotective and antidepressant effects of ergogenic supplements with creatine are very important in sports such as martial arts, as they contribute to the development of discipline, emotional control, mental stability, and help athletes' brains become more resistant to stress, especially before competitions. The course use of such a pharmaconutrient as creatine can rightfully be attributed to health-saving technologies – a new direction in sports pharmacology, and nutriology.

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Креатин як необхідний фармаконутрієнт у практиці підготовки спортсменів у єдиноборствах

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Мета роботи – формування сучасних уявлень про властивості креатину як фармаконутрієнта, його біологічної ролі в організмі та раціонального дозування при фізичних навантаженнях.

Матеріали і методи. Для визначення рівня розробки досліджуваної проблеми пошук здійснено у базах даних MEDLINE, PubMed, Scopus, Directory of Open Access Journals та ScienceDirect за такими ключовими словами: фізичні вправи, креатинові добавки, оксидативний стрес, мітохондрії, енергетичний обмін. Аналізували передусім англомовні статті, що опубліковані у період 2019–2025 рр.

Результати. Використання схем навантаження креатином під час високоінтенсивних інтервальних тренувань забезпечує підвищення показників фізичної підготовленості в середньому на 10–20 % унаслідок зростання концентрації м'язового фосфокреатину. Згідно з сучасними уявленнями, креатин належить, з одного боку, до групи інгібіторів міостатину, а з іншого, – до протекторів функції мітохондрій. Результати 50 досліджень підтвердили, що порівняно з плацебо креатин окремо та в поєднанні з бікарбонатом зумовлює достовірне статистично значуще підвищення середньої і пікової потужності в єдиноборців. Підвищення рівнів клітинного креатину сприяло метаболічному каналуванню та виживанню дофамінергічних нейронів, чинило антиапоптотичний вплив і виражену антидепресивну дію, що допомагало атлетам залишатися психологічно стабільними під час тренувань і перед змаганнями.

Висновки. Курсове застосування креатину зумовлює суттєве підвищення ефективності процесу підготовки, що робить його незамінним засобом для покращення показників фізичної та функціональної підготовленості, а також загальної якості життя спортсменів. Креатин є універсальною харчовою добавкою ергогенної спрямованості, але через переважно позитивний вплив на організм при аеробному енергозабезпеченні, властивому олімпійським видам єдиноборств, є повністю придатним для поліпшення ефективності тренувального процесу в боксі, дзюдо, тхеквондо, джиу-джитсу (дзю-дзюцу), фехтуванні тощо. Нейропротективна й антидепресивна дія ергогенних добавок із креатином дуже важлива для спортсменів-єдиноборців, оскільки сприяє розвитку дисципліни, емоційного контролю, психічної стійкості, допомагає мозку атлетів стати стійкішим до стресу, особливо перед змаганнями. Курсове застосування такого фармаконутрієнта, як креатин, належить до здоров'язберігальних технологій – нового напряму в спортивній фармакології та нутриціології.

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The term "pharmaconutrient" is relatively new in nutrition in general and in particular in sports nutrition. At the same time, pharmaconutrients are an important component of nutritional and metabolic support (NMS) of the athlete training process and belong to a separate type of special food additives (supplements) [1]. Pharmaconutrients are natural metabolites (or their derivatives) of the body obtained from plant and/or biological sources, as well as by chemical synthesis. Their action is based on involvement in both extracellular and intracellular biochemical processes that promote the absorption of energy sources, and plastic materials in their deficiency, as well as improve nutritional status in various physiological and pathological conditions.

Pharmaconutrients are used in cases where usual dietary lifestyle modification or use of functional products is unable to meet the body's growing needs for energy and plastic substances, in order to increase the efficiency of macronutrient absorption. In the semantic meaning, the term "pharmaconutrient" refers to a narrower group of biologically active additives (nutraceuticals) that, when exogenously administered, exhibit the properties of a pharmacological agent in the body [2]. The classification of a substance (or their combinations) as a pharmaconutrient should ideally meet the following criteria [3,4]:

– identity in chemical structure with the endogenous metabolites and/or biosynthesis of such compounds as a result of biochemical transformations after entering the body;

– use in doses that provide concentrations in the body close to those observed in natural biochemical processes (usually varying within 6–40 g per day);

– the proven role of pharmaconutrients in shaping the nutritional status of the body, however, without performing the function of a direct source of energy, and due to the small doses used, also a source of plastic material;

– the proven role of a deficiency of a specific pharmaconutrient in the occurrence and development of absolute or relative nutritional deficiency and/or the presence of a positive effect from its exogenous administration to eliminate nutritional deficiency;

– the availability of schemes and methods of administration into the body, based on evidence-based medicine data (randomized placebo-controlled trials, meta-analyses, systematic reviews), identical to the use of pharmacological drugs (medicines): single and course (loading and maintenance) doses; duration and frequency of administration; different nutritional regimens (diets) recommended for different conditions; effectiveness during aerobic and anaerobic loads in untrained individuals and athletes of various qualifications, etc.

According to all these characteristics, creatine can be confidently classified as a pharmaconutrient [5].

Aim

To form modern ideas about the properties of creatine as a pharmaconutrient, its biological role in the body, and rational dosage during physical exertion.

Materials and methods

This study used theoretical analysis and generalization of data from scientific and scientific-methodological literature, information from the Internet and scientific databases in order to determine the level of development of the investigated problem. The search was performed in the MEDLINE, PubMed, Scopus, Directory of Open Access Journals and ScienceDirect databases. used keywords included physical exercise, creatine supplements, oxidative stress, mitochondria, energy metabolism. Keywords used included exercise, creatine supplementation, oxidative stress, mitochondria, energy metabolism. We focused on English-language articles published between 2019 and 2025.

After selecting articles and analysing their results on physical activity and creatine supplementation, information was collected focusing on the study objectives.

Results

The general biological significance of creatine and its properties. Creatine is synthesized in the liver and pancreas from the amino acids arginine, glycine, and methionine. Approximately 95 % of total body creatine is stored in skeletal muscle, two-thirds of which is presented as the high-energy compound phosphocreatine (PCr), and the rest is free creatine. The total creatine pool (PCr + free creatine) in skeletal muscle is on average 120 g in a person weighing 70 kg. At the same time, the average individual is able to accumulate up to 160 g of creatine under certain conditions. About 1–2 % of the total body creatine supply, or 1–2 g, is destroyed daily and then excreted in the urine *(Fig. 1)*. Creatine supplies are replenished by exogenous intake with food (about 1 g, mainly from meat and fish consumption), and approximately the same amount produced as a result of endogenous synthesis [6].

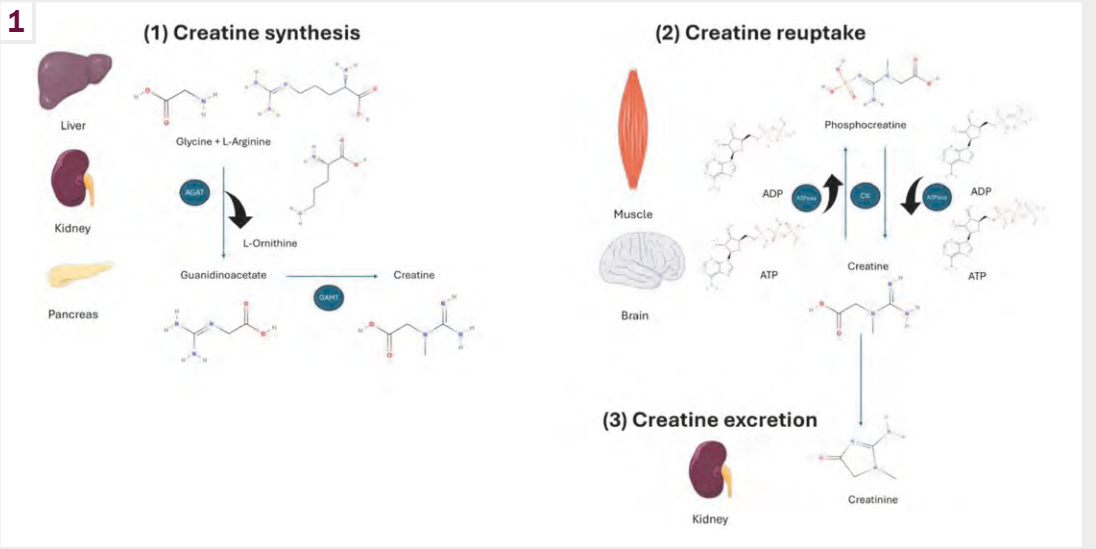

Fig. 1. Creatine synthesis, reuptake, and excretion. **1:** Creatine is synthesized from L-arginine and glycine in the liver, kidneys, and pancreas by L-arginine-glycine-amidinotransferase (AGAT) in the first step and by guanidinoacetate-N-methyltransferase (GAMT) in the second step. **2:** Creatine is released into the bloodstream and transported to skeletal muscle and the brain. Once inside the cell, creatine can be converted to phosphocreatine by creatine kinase (CK). The high-energy stores of phosphocreatine can be utilized in cells for ATP-dependent processes by ATPase enzymes. Both creatine and phosphocreatine are naturally metabolized to creatinine through a non-enzymatic reaction. **3:** Creatinine diffuses freely into the bloodstream for transport to the kidneys and is eventually excreted in the urine (by J. Gutiérrez-Hellín et al., 2022 [4]).

Food sources of creatine include meat and fish, but to obtain just one gram of creatine, we need to consume a significant amount of these foods, which is not always possible to provide through diet. Therefore, creatine monohydrate supplements (the form of creatine most often used in sports nutrition, and sports pharmacology today) is a cheap and effective alternative or addition to the specified products, without the excess fat intake and the need to digest large amounts of protein. However, it should be noted that many cheap powdered creatine supplements do not contain glucose, which is necessary for its effective absorption and transport into myocytes [5].

From the very beginning of its use, creatine has been recommended as an ergogenic aid that helps augment strength and power of movements, enhance muscle mass, stimulate muscle hypertrophy, and optimize the processes of adaptation to exercise training, primarily in sports games (football, American football, basketball, tennis, etc.). The use of creatine loading schemes during high-intensity interval training provides an increase in physical fitness indicators on average by 10–20 % due to an increase in muscle PCr concentration [7].

According to modern ideas, creatine belongs, on the one hand, to the group of myostatin inhibitors, and on the other hand, to the group of protectors of mitochondrial function. Important from the point of view of sports pharmacology are the antioxidant properties of creatine, which are manifested in its ability to enhance the activity of antioxidant enzymes and remove reactive oxygen species. The antioxidant effect of creatine is due to a reduction in the production of reactive oxygen species by damaged mitochondria, and an augmentation of the expression of intramitochondrial enzyme manganese superoxide dismutase (Mn-SOD) and G-protein coupled receptor 4 (GPR4) [8]. Furthermore, creatine's antioxidant properties may be related to the presence of arginine in its molecule. Arginine is a substrate for the NO synthase family and can enhance the formation of NO (a free radical that regulates metabolism, contraction, and glucose uptake by skeletal muscle). Creatine is also able to reduce the overexpression of inducible nitric oxide synthase (NOS) during intensive physical activity, and reduce the formation of cytotoxic NO derivatives, such as peroxynitrite ($ONOO^-$) and nitrosonium (NO^+) ions [9].

Creatine protects two distinct and important cellular targets, mitochondrial deoxyribonucleic acid (mtDNA) and RNA, from oxidative damage during exercise. Creatine supplementation may have a synergistic effect with exercise training [10]. From a biochemical point of view, the energy supply of ADP rephosphorylation to ATP during and after physical exertion largely depends on the reserves of PCr in the muscles. During exercise training, PCr levels reduce, and energy availability decreases due to insufficient rate of ATP resynthesis, necessary to maintain muscle metabolism owing to decreased bioavailability of PCr in muscles during training or competitive loads [11]. This can significantly affect the amount of energy generated during short periods of high-intensity activity [12]. Accordingly, the athlete's ability to maintain maximal effort for a sufficiently long time is reduced [13].

In addition, it has been hypothesized that increasing muscle creatine content through creatine supplementation may increase PCr availability and accelerate the rate of ATP resynthesis during and after short-term high-intensity exercise and competitive loads *(Fig. 2)* [14]. The current position of the International Society of Sports Nutrition (ISSN) on creatine, formulated in 2021, is that

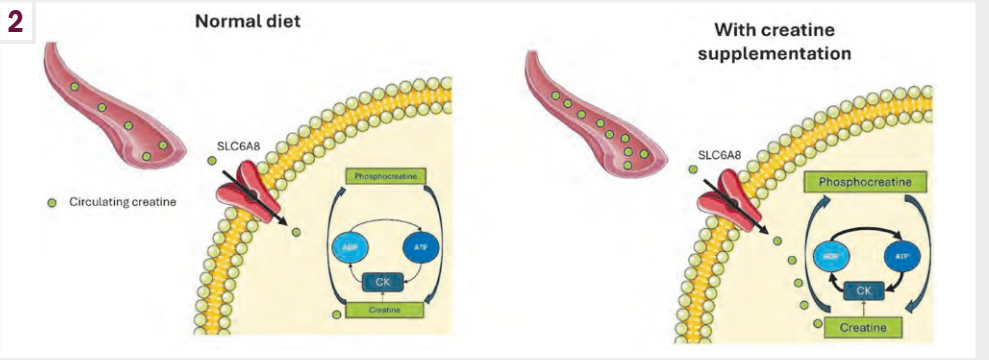

Fig. 2. Graphical representation of the amount of creatine present in the bloodstream and tissues from food (regular diet) or from creatine supplementation (creatine supplementation). Taking creatine supplements results in higher serum creatine concentrations than eating food. Creatine uptake from the bloodstream into cells is mediated by a creatine transporter known as SLC6A8. Higher serum creatine concentrations result in higher muscle creatine saturation, which in turn results in higher rates of ATP resynthesis (by J. Gutiérrez-Hellín et al., 2022 [4]).

a normal diet provides 1–2 g of creatine per day. This corresponds to maintaining the body's reserves of this pharmaconutrient at 60–80 % of the maximum [15], and the use of creatine supplements can increase the content of muscle creatine, and PCr by 20–40 % [4,14].

The most effective creatine intake regimen to increase muscle stores, according to evidence-based medicine, involves consuming approximately 5 g of creatine in the form of monohydrate, which corresponds to a dose of 0.3 g × kg^{-1} of body weight, four times a day (total 20 g per day) for 5–7 days. At the same time, to increase the concentration of creatine in brain to stimulate cognitive functions, larger amounts of creatine monohydrate (CM) may be required over a longer period of time [16,17].

According to a number of authors, creatine is able to improve the functionality of the central and peripheral nervous systems [18]. A number of studies have analyzed the effect of creatine supplements on increasing creatine levels in brain tissues of individuals of different age groups, and the associated improvement in cognitive functions, neuropsychological fitness, and sleep normalization [19]. Such effects have a clear competitive advantage in athletes who take creatine supplements compared to athletes who do not use exogenous creatine. However, the generally accepted optimal dose of creatine for improving cognitive function has not yet been definitively established but is estimated to be about 20 g per day [20].

Combining creatine with carbohydrates and proteins, for instance, taking it simultaneously with weight gainers, enhances and accelerates the replenishment of muscle creatine and PCr stores. An alternative option is a scheme for gradually accumulating creatine reserves by taking 3–5 g per day for 28 days, however, this option is considered less effective in terms of muscle adaptation in the case of intense training or competitive loads. Studies have shown that in this case, after a phase of increasing creatine levels in the muscles for 4–6 weeks, there is a rapid decrease to the initial levels. The peak concentration of creatine after oral administration is observed after 60 min, meaning that the best way to use creatine is to take it one hour before the start of physical activity – training or competition [5].

There is currently a strong consensus on the positive effects of creatine use in athletes, based on expert opinions from such reputable organizations as the ISSN, the American Dietetic Association (ADA), Dietitians of Canada (DC), the American College of Sports Medicine (ACSM), the Australian Institute of Sport (AIS), etc. Along with the ergogenic effect inherent in creatine, it reduces muscle microdamage and delayed muscle soreness that occur under the influence of physical exertion, accelerates recovery processes, increases the tolerance of large training volumes in conditions of elevated ambient temperature, accelerates rehabilitation after injuries, and has a protective effect on the central and peripheral nervous systems [21]. These data have recently been summarized in a fundamental review by D. G. Candow & T. Moriarty [22].

An important direction of the combined effect on physical fitness with the use of creatine (in order to optimize the ergogenic effect) is its combination with nutrients that increase insulin levels and/or insulin sensitivity of tissues. In particular, the combination of CM in a daily dose of 5 g with carbohydrates in a dose of 93 g increases the content of creatine in the muscles by 60 % [23]. It is known that the combination of CM with 47 g of carbohydrates and 50 g of protein per day is equally effective in increasing muscle creatine content, as is the combination of creatine-based nutritional supplements with carbohydrates at a dose of 96 g per day [24]. However, in experimental studies, although the use of such a combination increased the content of muscle creatine in the body, it was not more effective in increasing strength and endurance compared to the data in athletes who took creatine alone [7].

Provided that safety measures are followed and proper medical supervision is exercised, CM, which has anabolic effects, can serve as a safe alternative to potentially dangerous and WADA-banned steroids. The large amount of data accumulated over the past decade on the use of creatine, as well as special studies of its acute, subchronic, and chronic toxicity, give reason to assert a high level of safety in the use of this universal pharmaconutrient in the practice of training athletes.

The feasibility of using creatine in martial arts. Combat sports predominantly use anaerobic metabolism as an energy source, allowing for peak loads or sustained effort over very short periods

of time. In this context, the use of certain nutritional ergogenic aids (NEAs) can help athletes improve their performance in the specific combat skills (i. e. number of attacks, throws and strikes; jump height; grip strength, etc.), as well as in general physical aspects (time to exhaustion, strength, perception of fatigue, heart rate, use of anaerobic metabolism, etc.) [25].

After a thorough literature review, ISSN has developed an official position on nutritional strategies and the use of nutritional supplements to improve physical and functional fitness, and accelerate post-exercise recovery in martial artists, and weight loss for combat sports. It should be noted that while the type of martial arts, the length of the training camp, and the time between competitions are factors that affect nutritional strategies, similar following positions can be identified for different combat sports [26]. It should be considered that as the duration of combat bout increases to >4 min, the contribution of the aerobic system to the total energy pool can increase to more than 70 %, but the anaerobic alactic and anaerobic glycolytic pathways support high-performance bursts [27]. This fact is very important, considering that in combat sports, anaerobic power and anaerobic capacity determine athletic performance and dominant metabolic pathways. The reduction in performance during exercise, which is attributed to the cumulative effects of fatigue, including excessive accumulation of metabolites, depletion of energy substrates, and fluid and electrolyte imbalance, is of crucial importance [28].

The regulatory document on sports nutrition, "IOC Consensus 2018" emphasizes that any system of nutritional and metabolic support using nutritional ergogenic aids (NEAs) must consider the energy supply mechanisms of any sport [1,2], i. e., the predominant mechanism of formation of energy substrates in the form of ATP and creatine phosphate [29]. Given the close metabolic relationship between the precursors of the two main energy-generating substances ATP and PCr – adenosine diphosphate and creatine – it becomes clear that the use of creatine-based NEAs has profound biochemical and practical meaning in any locomotion, especially those provided predominantly aerobically [30]. Thus, it has been shown that in striking combat sports, the contribution of oxidative phosphorylation to the energy pool ranges from 62 % (in karate and taekwondo) to 86 % (in boxing); the contribution of the ATP system ranges from 10 % (in boxing) to 31 % (in taekwondo), and the contribution of glycolysis is only from 3 % (in taekwondo) to 21 % (in karate).

In throwing martial arts (judo), during a 4-minute match, the contribution of oxidative phosphorylation is 79 %, and the contribution of the glycolytic system is only 7 %. In fencing, the only Olympic combat sport based on the use of weapons, the contribution of oxidative phosphorylation to the total energy pool of oxidative metabolism ranges from 81 % to 90 %, and the contribution of the glycolytic system is only from 0.6 % to 7 %. Therefore, locomotion in Olympic martial arts is predominantly powered by the oxidative energy system [31].

With the growing body of research examining the effects of nutritional supplements on martial arts performance, researchers are actively seeking more effective NEAs for use in these sports. However, conflicting opinions on the subject remain. Consequently, a systematic review and Bayesian network meta-analysis were conducted to identify the most effective nutritional supplements in combat sports by synthesizing the available evidence. A comprehensive search was performed in the PubMed, Web of Science, Cochrane, Embase, and SPORTDiscus databases, covering the period from their inception to November 2, 2023. The aim of this systematic review was to identify randomized controlled trials that evaluated the benefits of various nutritional supplements for athletes specializing in martial arts [32].

Results from 50 studies included in the network meta-analysis showed that compared with placebo, creatine alone (SMD: 1.1, 95 % CrI: 0.45, 1.7), and in combination with sodium bicarbonate (SMD: 0.35, 95 % CrI: 0.11, 0.57) produced a statistically significant elevation in the average power of the fighters and a significant increase in peak power [32]. To optimize the performance of martial arts athletes, adequate recovery is necessary during training and competition. And although there is currently no clear consensus on strategies for stimulating the physical and mental performance of fighters, and accelerating post-exercise recovery processes, it is necessary to understand the basic mechanisms of fatigue in order to select the most reasonable composition of special ergogenic food supplements. It has been unequivocally proven that the combined use of traditional ergogenic food supplements in the form of carbohydrates and proteins is justified.

In addition, the use of supplements, the effectiveness of which is supported by evidence, in particular, creatine and β-alanine, which in itself does not have an ergogenic effect, but acts as a precursor for the synthesis of carnosine in human skeletal muscles [25]; as well as antioxidants (bioflavonoids); coronary dilators (red beet juice or extract, amaranth oil) or bicarbonates (alkaline water, 1–2 % sodium bicarbonate solution) significantly improve indicators of physical and functional fitness, and accelerate recovery processes after intense training and competitions [33].

Other researchers also emphasize that special attention should be paid to the consumption of amino acids, proteins, creatine, antioxidants, and omega-3 polyunsaturated fatty acids due to their therapeutic role in preventing the formation of muscle soreness syndromes, and delayed onset muscle soreness, which are the basis for the formation of fatigue and overtraining, as well as a decrease in muscle mass and the occurrence of anabolic resistance [15].

Important evidence for the feasibility of using creatine in the training process of martial artists is the high importance of the psychological state of athletes, which, of course, depends on the biochemistry of the tissues of the central nervous system [34]. Personality traits, in particular, conscientiousness, are recognized as crucial psychological factors contributing to the success of elite-level athletes. Emerging evidence suggests that individual differences in these traits depend on environmental influences, genetic variations, and metabolic changes in the CNS, especially in the dopaminergic system [35].

Creatine is a substrate for mitochondrial and cytosolic creatine kinases and buffers cellular ATP resources. In addition, increased cellular creatine levels promote metabolic channeling, and exhibit antiapoptotic properties. Therefore, exogenous creatine supplementation may offer a tool to improve the survival of dopaminergic neurons. An experimental study showed that the administration of creatine (5 mM) led to a significant increase (+35 %) in the density of immunoreactive cells (TH-ir) at 21 days of observation. Furthermore, the authors discovered that creatine administration provided

neuroprotection against TH-ir cell loss, resulting in a significantly higher density (+19 %) of TH-ir neurons in creatine-treated cultures compared to the corresponding control groups. Thus, these data indicate that creatine administration is beneficial for the survival of TH-ir neurons that are exposed to harmful conditions [36], and the training process of athletes, associated with the occurrence of oxidative stress, a decrease in ATP reserves, etc., are precisely unfavorable conditions for the functioning of brain tissue [31,37].

Additionally, creatine has been shown to produce a pronounced antidepressant effect [38], which helps athletes remain psychologically stable before competitions [39]. These results indicate that the antidepressant effect of creatine is most likely mediated by the activation of dopamine D_1- and D_2-receptors and therefore justify the use of this NEAs not only to maintain physical fitness parameters, but also the psychological state of wrestlers.

Conclusions

1. Thus, from the results of many clinical and experimental studies, it becomes clear that the course use of creatine leads to a significant increase in the efficiency of the training process, and this makes it an indispensable tool for improving the indicators of physical and functional fitness, as well as the overall quality of life of athletes.

2. Creatine is a universal ergogenic food supplement, but due to its predominantly positive effect on the body with predominantly aerobic energy supply, typical of Olympic martial arts, it is fully suitable for improving the effectiveness of the training process in boxing, judo, taekwondo, jiu-jitsu (jujutsu), fencing, etc.

3. The use of creatine-based NEAs also produces a protective effect on brain tissue and has a pronounced antidepressant effect, which is very important in sports such as martial arts, as it helps maintain the mental stability of athletes, especially before competitions.

4. The course use of a pharmaconutrient such as creatine can rightfully be attributed to health-saving technologies – a new direction in sports pharmacology and nutrition.

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