

случае шишковидное тело оказывается в борозде между передними зрительными буграми четверохолмия, а кровоснабжение в этом случае осуществляется одиночными кровеносными сосудами.

Ключевые слова: шишковидное тело, головной мозг, сосудистое сплетение, четверохолмие.

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the pineal body appears in the furrow between the anterior corpora quadrigemina, and the blood supply in this case is performed by single blood vessels.

Key words: pineal body, brain, vascular plexus, corpora quadrigemina.

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PHARMACOLOGICAL EFFECTS OF KB-28 COMPOUND UNDER CHRONIC IMMOBILIZATION STRESS CONDITIONS

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According to experimental studies, sodium 2-(tetrazolo[1,5-c]quinazoline-5-ylthio)acetate (KB-28 compound) shows an expressive actoprotective action under normal conditions. The work investigated the influence of KB-28 compound in the conditions of chronic immobilization stress. The study revealed that the administration of this substance maintains a high level of performance in rats. This confirms the presence in KB-28 of actoprotective effect. It has been also proven that the action of the test substance is maintained in the complicated conditions of the experiment. In addition, it is established that a stress-protective effect is inherent to sodium 2-(tetrazolo[1,5-c]quinazoline-5-ylthio)acetate which was manifested by rapid adaptation of animals to chronic immobilization stress. The effectiveness of KB-28 compound was significantly superior to the reference substance on the 12th and 18th day of the study.

Key words: sodium 2-(tetrazolo[1,5-c]quinazoline-5-ylthio)acetate, 2-ethylthiobenzimidazole hydrobromide, chronic immobilization stress.

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Decreased physical activity in modern society has reached a critical level. This issue is relevant regardless of nationality, age or gender. The reason for this phenomenon is a low culture of physical education and the reluctance of a person to leave the usual comfort zone (total automation and computerization of life and all areas of activities). However, it should be noted that the restriction of activity may be forced: for example, as a result of illness or injury or as a consequence of monotonous and stereotyped labour activity. Physical inactivity results in diseases of the cardiovascular, endocrine and nervous systems, excess weight gain; it speeds up the aging process. In turn, this may be one of the causes of premature death [5, 10, 11, 13]. It is also found that hypokinesia impairs cognitive functions. In general, it affects the employment potential and productivity and, consequently, defines the level of economic development of the country. Today, the problem of reduced motor activity has received considerable attention [1, 2, 4]. Despite this, the question of increasing the body resistance to hypokinesia and correction of its negative influence is still unresolved.

Promising in this respect are drugs from the group of actoprotectors [3, 12]. They act to increase the physical endurance and body capacity in normal and complicated conditions which also include hypokinesia. Today, the class of actoprotectors is limited to 2-ethylthiobenzimidazole hydrobromide (2-ETBI) alone. This drug has a number of side effects (hyperemia of face, gastralgias, etc.), which prevents its widespread use [3, 12]. This is what causes the need for search for new safe substances with actoprotective activity.

In this regard, our attention was drawn to quinazoline derivative – sodium 2-(tetrazolo[1,5-c]quinazoline-5-ylthio)acetate (KB-28 compound). The substance, according to preliminary experimental study, has shown a clear impact on performance in normal conditions [6, 16]. For in-depth study, it was appropriate to characterize the influence of KB-28 in the complicated conditions of prolonged hypokinesia on the model of chronic immobilization stress (CIS).

The purpose of the study was to evaluate the effectiveness of sodium 2-(tetrazolo[1,5-c]quinazoline-5-ylthio)acetate (KB-28 compound) under CIS conditions.

Materials and methods. The experiments were carried out on non-pedigree white rats weighing 200–220 g obtained from the vivarium of National Pirogov Memorial Medical University, Vinnytsya. To eliminate the impact of fluctuations of the hormonal profile, the experiments were run on male rats. The animals were kept under standard conditions with the natural day/night light regime. Food and water were received ad libitum. All interventions were carried out observing the general ethical principles of

experiments on animals according to the First National Congress on Bioethics (Kyiv, 2001) and "European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes" (Strasbourg, 1986). CIS was modeled by keeping the rats in individual wooden cases for 16 h/day for 18 days [2, 14]. The duration of the experiment is in line with the stages of development of the general adaptation syndrome (GAS) [15].

The animals were divided into 4 groups of 6 animals in each: I – intact animals; II – rats in CIS conditions without pharmacological treatment (control); III and IV – animals in CIS conditions that were intraperitoneally injected KB-28 (1.7 mg/kg) and 2-ETBI (32.0 mg/kg) once daily for 18 days. These substances were used in mean effective doses (ED₅₀). ED₅₀ were calculated graphically by Litchfield-Wilcoxon method based on the results of the swimming test in the normothermia conditions [6]. Control and intact rats were injected equal volumes of isotonic solution of sodium chloride. Test compound, reference substance and pure solvent were injected to rats prior to placement in cases.

The exercise performance of animals was evaluated according to the treadmill run test. This technique allows to adjust the intensity of work [9]. The rats were loaded with the run at the treadmill speed of 42 m/min and the treadmill angle of 10°. This mode, according to the literature, is considered to be the most optimal for small laboratory animals [9]. Running time (min) of the rats until failure, as evidenced by the lack of response to electrical stimulation (40 V) at the starting line of the treadmill was recorded. The animals were previously adapted to the specified load by running for 5 min at the treadmill speed of 25 m/min and treadmill angle of 10° on the 1st and 3rd day of the experiment. The study was carried out in the appropriate phases of the general adaptation syndrome: day 4 (alert phase), day 12 (resistance phase), day 18 (exhaustion phase) [15].

We processed the digital data obtained from the study by variation statistics technique using IBM SPSS Statistic 22 software, calculated mean value M , the arithmetic mean error m , t-Student's criterion for normal distribution, White nonparametric criterion – if the latter was not available, and Wilcoxon (paired samples) criterion – in order to determine changes in the trend within the group. The changes of parameters were considered significant at $p < 0.05$.

Results and discussion. The average running time of rats of the intact group according to the phases of the experiment was 6.25; 5.95 and 6.43 min, respectively. In the course of the study, a negative effect of CIS on the physical endurance of the rats was established. The most distinct changes were observed in the control group. The sign of deteriorated performance was significant decrease in the running time in the control rats at all phases of the study (Fig.).

In the alert phase (4th day), the performance of animals without pharmacological treatment in the experimental conditions was significantly decreased by 24.0 %, respectively. On the 12th day (resistance phase), the decrease of this value was 38.2 %. The most significant deterioration of dynamic endurance in the control group was observed on the 18th day of the experiment, which corresponds to the exhaustion phase of GAS. In this period, the running time was reduced by 46.5 % compared with that in the intact group. Such dynamics of physical endurance of the control rats describes CIS as a negative body influence factor. Daily administration to animals of sodium 2-(tetrazolo[1,5-c]quinazoline-5-ylthio)acetate under CIS conditions contributed to the maintenance of the values of dynamic body endurance almost at the level of the relevant values of the intact group throughout all GAS phases. The only exception were the results obtained on the 18th day of the study (exhaustion phase), when the endurance of rats significantly decreased compared to the values of the intact animals by 16.5 % (see Fig.). The injection of KB-28 compound to rats under the experimental conditions contributed to the increase in the running time according to the GAS phases by 57.5, 59.5 and 55.7 %, respectively.

Positive dynamics of physical endurance of rats in CIS conditions was also noted with the injection of 2-ETBI. This was evidenced by the increase in treadmill running values by 52.0, 43.2 and 39.5 %, which corresponds to the alert, resistance and exhaustion phases of GAS. However, these values only reached the level of intact animals in the alert phase, and on the 12th and 18th day of the study they were significantly lower ($p < 0.05$) (Fig.). The data obtained confirm the presence of actoprotective activity in sodium 2-(tetrazolo[1,5-c]quinazoline-5-ylthio)acetate. This was manifested in a significant increase at all phases of investigation of dynamic endurance of the rats that received pharmacological treatment with KB-28 compound. At the same time, we can assume that KB-28 compound is also characterized by a stress-protective action. This effect was evidenced by the increase in the animal resistance to stress. This assumption is consistent with the results of our previous studies [7, 8].

The effectiveness of sodium 2-(tetrazolo[1,5-c]quinazoline-5-ylthio)acetate (KB-28) was expressed to the most in the alert phase and resistance phase of GAS ($p > 0.05$ relative to the intact group), whereas 2-ETBI – mostly in the alert phase ($p > 0.05$ relative to the intact group). It should be

noted that by the level of actoprotective activity, KB-28 compound, under the experimental conditions, was significantly superior to the reference substance in the resistance and exhaustion phases (12th and 18th days, respectively) of the general adaptation syndrome.

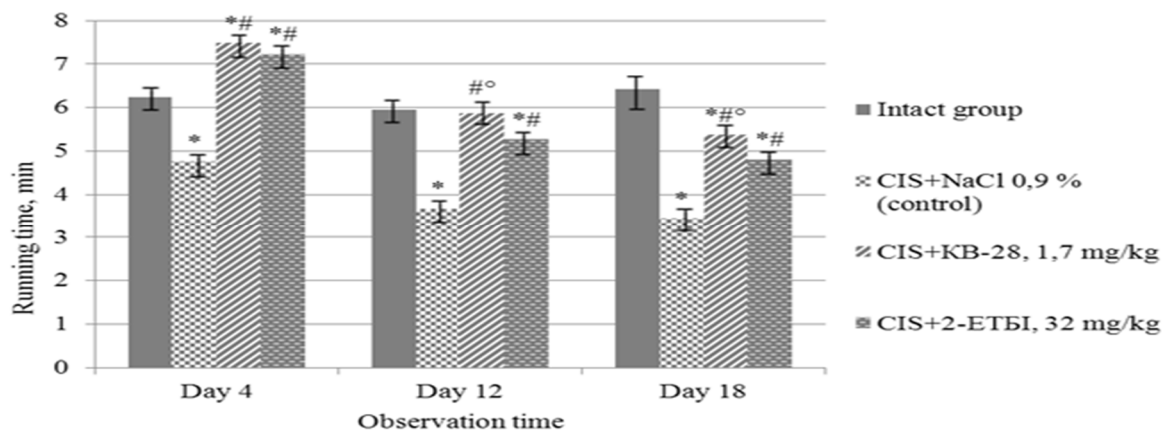


Figure. Influence of sodium 2-(tetrazolo[1,5-c]quinazoline-5-ylthio)acetate (KB-28) and 2-ethylthiobenzimidazole on the duration of the treadmill running time in rats in CIS conditions. Notes: 1. * – significant compared to the corresponding value of the intact group, $p < 0.05$; 2. # – significant compared to the corresponding value of the control group, $p < 0.05$; 3. ° – significant compared to the corresponding value of 2-ETBI group, $p < 0.05$.

The question arises about possible mechanisms for the implementation of KB-28 actoprotective effect under the CIS conditions. It is known from the literature that catabolic processes are initiated in the body in the alert and exhaustion phases of the general adaptation syndrome [15]. It can be assumed that the effects of KB-28 compound are implemented by its organ-protective action and maintaining a high level of metabolic processes [7, 16].

Conclusions

1. Chronic immobilization stress causes progressive decrease in physical endurance of rats.
2. Sodium 2-(tetrazolo[1,5-c]quinazoline-5-ylthio)acetate (KB-28 compound) shows an expressive actoprotective and stress-protective actions in the conditions of chronic immobilization stress.
3. The effectiveness of the test substance was significantly superior to 2-ETBI on the 12th and 18th day of the study.

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Реферати

ФАРМАКОЛОГІЧНІ ЕФЕКТИ СПОЛУКИ KB-28 ЗА УМОВ ХРОНІЧНОГО ІММОБІЛІЗАЦІЙНОГО СТРЕСУ

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Натрій 2-(тетразоло[1,5-с]хіназолін-5-ілтїо)ацетат (сполука KB-28) за даними експериментальних досліджень виявляє виразну актопротекторну дію у звичайних умовах. У роботі досліджено вплив сполуки KB-28 за умов хронічного іммобілізаційного стресу. Виявлено, що введення даної речовини підтримує високий рівень працездатності щурів. Це підтверджує наявність у KB-28 актопротекторного ефекту. Доведено, що вказана дія досліджуваної речовини зберігається в ускладнених умовах експерименту. Також встановлено, що натрію 2-(тетразоло[1,5-с]хіназолін-5-ілтїо)ацетату притаманна стреспротекторна дія, що проявилось швидкою адаптацією тварин до умов хронічного іммобілізаційного стресу. За ефективністю сполука KB-28 вірогідно переважала речовину порівняння на 12 та 18-ту добу дослідження.

Ключові слова: натрій-2- (тетразоло [1,5-с] хіназолін-5-ілтїо) ацетат, гідробромід 2-етілтїобензимидазола, хронічний іммобілізаційний стрес.

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ФАРМАКОЛОГІЧЕСКИЕ ЭФФЕКТЫ СОЕДИНЕНИЯ KB-28 В УСЛОВИЯХ ХРОНИЧЕСКОГО ИММОБИЛИЗАЦИОННОГО СТРЕССА

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Натрій 2-(тетразоло[1,5-с]хіназолін-5-ілтїо)ацетат (соединение KB-28) по данным экспериментальных исследований оказывает выразительное актопротекторное действие в обычных условиях. В работе исследовано влияние соединения KB-28 в условиях хронического иммобилизационного стресса. Виявлено, что введение данного вещества поддерживает высокий уровень работоспособности крыс. Это подтверждает наличие у KB-28 актопротекторного эффекта. Доказано, что ука-занное действие исследуемого вещества сохраняется в осложненных условиях эксперимента. Также установлено, что натрію 2-(тетразоло[1,5-с]хіназолін-5-ілтїо)ацетату присуще стреспротекторное действие, на что указывала быстрая адаптация животных к условиям хронического иммобилизационного стресса. По эффективности соединения KB-28 достоверно преобладало над веществом сравнения на 12 и 18-е сутки исследования.

Ключевые слова: натрий-2- (тетразоло [1,5-с] хиназолін-5-ілтїо) ацетат, гидробромид 2-этилтиобензимидазола, хронический иммобилизационный стресс.

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BONE STUMP FORMATION IN RELATION TO THE MUSCLE TENSION VALUE AT AMPUTATION PLASTIC SURGERY

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Three series of experiments on 41 dogs with amputation in the medium third thigh and muscular plasty with muscle tension 916-962 μH (experimental group), 980-1100 μH and 650-800 μH (control groups). The monitoring lasted 1 and 3 months. In the 1st series of experiments with muscular tension 916-962 μH , already within one month we observed the formation of the bone cortical endplate, the normalization of intraosseous circulation, with the retention of acylindrical bone stump, the structure of cortical diaphysis plate and the content of the bone marrow channel. During the 2nd series of experiments, 17 out of 19 cases showed the stump formation different from the normal diaphysis: asymmetric axes curvature of the amputated bone, conic thinning or bulbous thickening of the end section, reduction in the diameter through periosteal bone formation (osteogenesis). The 3rd series due to insufficient muscular tension showed incomplete bone marrow closure, abrupt microcirculation distortion and reparatory regeneration failure. Complete (within biological abilities of the bone tissue) stump formation is possible through muscular tension at amputation plasty 916-962 μH . Such stump tends to show fast healing processes and normalization of intraosseous circulation with the formation within 1 month after the amputation of a bone end plate. Muscle plasty with tension 980-1100 μH in most cases leads to distortions in intraosseous circulation, formation of cone-like or through periosteal regenerates, thickened stumps with axis deflation, resorption and fracture of cortical diaphysis plate. Muscular plasty with muscular tension 650-800 μH prevents from occlusion of the bone marrow cavity leading to distortions in microcirculation and reparatory regeneration, with stump formation entirely different from the normal diaphysis.

Key words: amputation, reparatory regeneration, muscle tension, intraosseous circulation.

The research of the issue of extremities amputation is prolific including the recent research devoted to the problems of wound healing prognosis [10], pain syndrome [5-7], amputation techniques in various modifications [1-3, 5]. However, such important issues as healing the bone-saw-line, muscle state, microcirculatory distortion have not been given proper consideration. According to the data [9]