

Review Article**Research Of a Magnesium-Containing Biocomplex in Experimental Animalson the Ultrasonic Stress Model**Bagdasarova E.S¹, Yokubova N.B.²¹Pharmaceutical Institute of Education and Research, Tashkent, Republic of Uzbekistan**ABSTRACT:**

The article presents the results of a study of a Mg-containing biocomplex on the effect of ultrasonic stress and cognitive impairment with the reference drug glycine on the elevated plus maze (EPM) model with open and closed arms.

Keywords: *Ultrasound, Stress, Magnesium-Kurglycine, Glycine, Elevated Plus Maze, Cognitive Abilities.*

INTRODUCTION:

Stress is the body's physiological and psychological response to various negative environmental factors or internal conflicts. In modern society, it has become an integral part of many people's lives and can have a significant impact on their cognitive abilities.

Cognitive functions, in turn, comprise a broad range of mental processes, including perception, attention, memory, reasoning, problem-solving, planning, and decision-making. These functions play a key role in everyday life, enabling a person to adapt to a changing environment, learn, solve problems, and interact with the world around them.

According to E.E. Vasenina, the effects of stress, especially prolonged stress, significantly impact human cognitive functions. Research in neuropsychology and neuroscience demonstrates that stress has a significant impact on cognitive function. Prolonged or intense exposure to stress can lead to various changes in mental processes, which impact behavior and overall functioning of the body [1].

There is currently no doubt that stress plays a significant role in the pathogenesis of psychosomatic illnesses [2; 3]. Although everyone is exposed to a variety of stressors from early childhood, stress-related illnesses do not develop in everyone, but only in individuals with low stress tolerance. Stress tolerance is an integral personality

trait that underlies successful social interaction and is characterized by emotional stability, low anxiety, high levels of self-regulation, and psychological preparedness for stress [4].

Since millions of people around the world require sedatives daily, scientists are trying to create new, effective anti-anxiety medications that do not cause side effects and are suitable for children, pregnant women, and the elderly.

In connection with the above, there is a need to create new drugs that improve the cognitive properties of the body under stress.

Purpose of the study: Study of the effect of ultrasonic stress on

cognitive abilities of laboratory animals and their pharmacocorrection with a magnesium-containing biocomplex.

MATERIALS AND METHODS OF RESEARCH:

The object of the experimental study is a Mg-containing biocomplex synthesized at the Pharmaceutical Institute of Education and Research under the guidance of the scientific adviser of the Institute, Doctor of Philosophy, Professor Yunuskhodzhaev A.N. and Master Romatova Sh. Sh.[5]. The magnesium-containing biocomplex we studied contains magnesium, curcumin, and glycine—substances known to possess

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neuroprotective, antidepressant, and antioxidant properties. Glycine was used as a comparative agent.

The studies were carried out in accordance with the requirements of the regional GLP standard – “Good Laboratory Practice” [6] and in accordance with the rules of the “European Convention on Vertebrate Animals for Experimental and Scientific Purposes” [7].

One of the most common causes of anxiety is environmental novelty and uncertainty. The elevated plus maze (EPM) test is based on the same natural stimuli that can induce anxiety in humans. It is believed that the EPM method successfully balances two motivations: animals' natural fear of the novelty and openness of a space, and the desire to explore this new space. The elevated plus maze was described by File and colleagues as a simple method for assessing anxiety responses in rodents. Experiments with animals in an elevated plus maze with four arms (two open and two closed) were also described by Hendley and Mitani. The EPM apparatus consists of four arms shaped like a plus sign, raised above the ground to a height of 50 cm to 100 cm. Two opposite arms are open, and two more opposite arms are usually closed by walls 15-50 cm high. In the center of the cross is a central square platform, usually 10 x 10 cm in size, for rats, which allows access to all four arms.

The elevated plus maze (EPM) is a widely used behavioral assay for rodents and has been validated to assess the anti-anxiety effects of drugs, steroid hormones, and to identify brain regions and mechanisms underlying anxiety-related behavior.

The elevated plus maze test is designed to study the behavior of rodents under variable stress conditions (with free choice of comfortable conditions) and allows for the assessment of: the animal's anxiety level (based on dark/light preference, fear of heights, and the severity and dynamics of peeking behavior); symptoms of neurological deficit; and habituation. According to the guidelines for preclinical studies of new pharmacological substances, assessing the behavior of rats and mice in the elevated plus maze is included in the list of studies investigating the tranquilizing (anxiolytic) effect of the compound under study (basic tests).

The setup consists of two open and two closed arms, and animals tend to spend more time in the closed arms due to anxiety. The anxiolytic effect of the drug is assessed by increasing the number of entries into the open (light) arms and the time spent in them, without increasing overall motor activity.

Testing time: 5 min. Recorded parameters: time spent in closed and open arms, number of entries into open and closed arms, number of stands, and number of hangings from the arm.

RESEARCH RESULTS:

The experiments were conducted on white mice of both sexes weighing 18-22 g, in groups of 6 animals, for a total of 24 animals. The laboratory animals were divided into 4 groups:

Group 1 – control group

Group 2 – intact group – creation of stress using ultrasound

Group 3 – magnesium-containing biocomplex – per os at a dose of 250 mg/kg

Group 4 – glycine – per os at a dose of 30 mg/kg

Ultrasound (500 Hz) was used as a stress model for 3 days in all mice except the control group. In the plus-maze test, the number of entries into the open arm (OA) and closed arm (CA), the time spent in the OA and CA, the number of downward glances, and backward movements over 5 minutes were recorded. The results were processed using the Student's t-test at $p=0.05$ [8]. The results of the experimental study of the emotional behavioral state of animals in the plus-maze test are presented in Table 1.

During the experiment, we found that ultrasonic stress caused a 54.2% decrease in the number of entries into the OR in intact animals compared to control data; and also a 45.6% decrease in the time spent in the OR. The experimental preparations Mg-kurglycin (250 mg/kg) and glycine (30 mg/kg), on the contrary, caused an increase in this indicator in the OR by 14.6% and 17.6%, respectively (Fig. 1).

Moreover, the stress factor caused an increase in the number of entries into the closed arm (CA) in intact animals by 64.7% compared to the control group; the time spent in the CA increased by 79.3%. The administration of the test drug Mg-kurglycin (250 mg/kg) and glycine (30 mg/kg) reduced the time spent by animals in the CA by the 20th day of observation by 204% and 192%, respectively (Fig. 2).

Table 1. Pharmacocorrection of ultrasound stress with magnesium-curglycin in the plus-maze test

Таблица 2.
Фармакокоррекция ультразвукового стресса Магний-курглицином в тесте «Крестообразный лабиринт»

	Число входов в ОР		Время нахождения в ОР		Число входов с ЗР		Время нахождения в ЗР		Число заглядываний вниз		Задний ход	
	1 день	20 день	1 день	20 день	1 день	20 день	1 день	20 день	1 день	20 день	1 день	20 день
Контрольная группа	6.17	5.67	92.50	112.50	12.67	15.00	207.50	187.50	1.17	1.00	1.17	0.83
Интактная группа	2.83	4.83	50.33	63.67	20.67	23.17	249.67	236.33	0.17	1.33	1.17	0.83
Опытная гр Mg-курглицин 250мг/кг	2.33	6.50	84.00	100.33	8.17	7.33	216.00	166.67	00	1.33	0.67	1.00
Опытная гр Глицин 30мг/кг	2.33	6.67	84.50	83.50	8.50	8.50	215.50	216.50	00	0.67	0.83	0.67

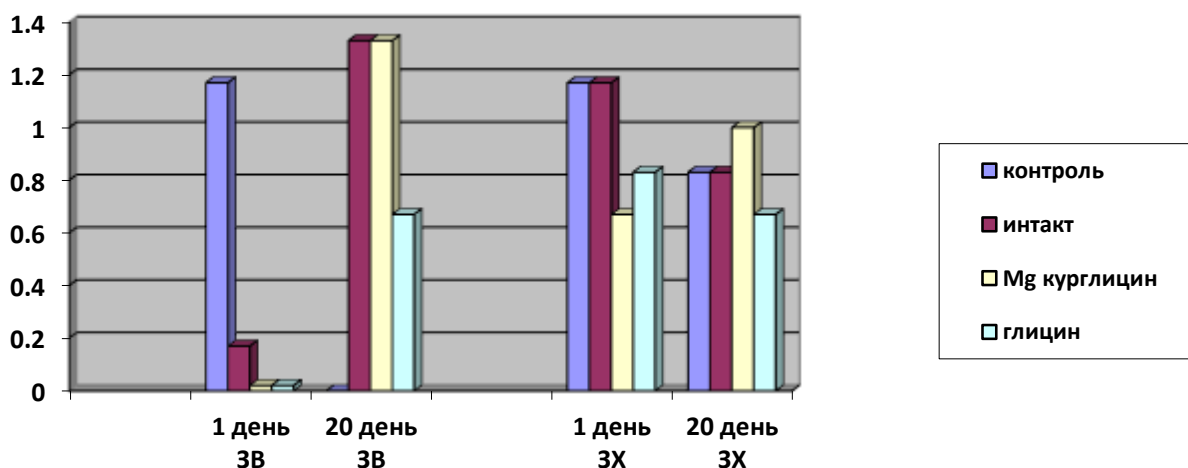


Fig. 1 Number of inputs to OR (A) and ZR (B)

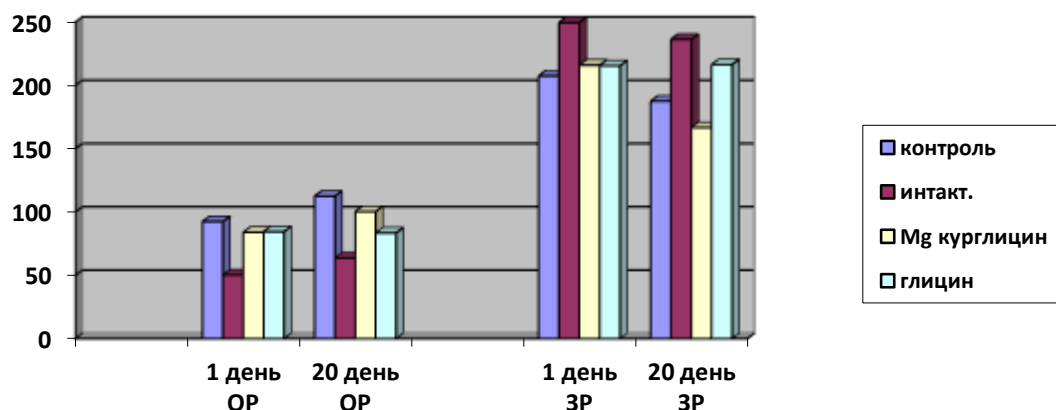


Fig. 2 Time spent in OR (A) and ZR (B)

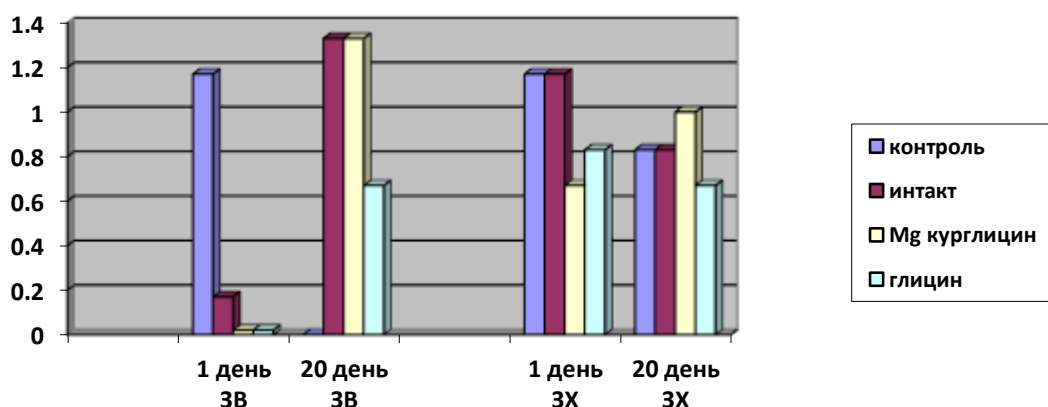


Fig.3 Number of looks down (ZV - A) and reverse (ZH - B)

Mg-kurglycin (250 mg/kg) also caused a significant increase of 17% in the “reverse” index in mice (Fig. 3).

Thus, we can note a pronounced correlation effect of the study drug Mg-kurglycin (250 mg/kg) against the background of disorders caused by the stress factor ultrasound. Moreover, by this criterion, it is superior to the reference drug, glycine.

CONCLUSIONS:

During the study, it was found that a 3-day ultrasound exposure leads to a decrease in the time

spent in the open arm (OA) and an increase in the time spent in the closed arm (CA) during the Plus Maze test, compared to the group not exposed to the stress factor, which certainly indicates the development of a stress response in animals. Administration of the test drug magnesium-kurglycin (250 mg/kg) to animals initially causes a minor effect, but by the 20th day of observation, a pronounced leveling effect occurs; the time spent in the OA (OR) in the Plus Maze test is comparable to the results in control mice.

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