

STUDY OF THE EFFECTIVENESS OF THE BIOLOGICALLY ACTIVE SUPPLEMENT "SOMNIUM" BASED ON MELATONIN

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ABSTRACT

Among the numerous environmental factors that constantly affect the body, proper rational nutrition is one of the most important, as it ensures the preservation of life, health and human performance. The problem of rational nutrition is of particular importance in cases of various physiological and pathological overloads of the body. Unhealthy diet, both quantitatively and qualitatively, leads to the emergence of a number of different complications, such as at least 50% of cases of cardiovascular diseases, about 40% of cases of lung cancer, colon and rectum, kidneys, prostate, bladder in men and about 60% of cases of breast cancer, uterus, kidneys, intestines in women.

INTRODUCTION

Sleep is one of the most important and vital physiological processes occurring in the human body. It is known that people spend about one third of their lives sleeping. The main functions of sleep include: maintaining cellular homeostasis; energy conservation of the body; regulation of immune processes; maintaining an adequate level of excitability of cortical neurons and functioning of the central nervous system (CNS) [1,2]. It has been shown that high-quality and sufficiently long sleep normalizes or improves the functioning of the central nervous system, including cognitive functions, thinking, emotions, stress resistance, and attention [3,4,5,6]. Adult sleep has two phases: slow sleep or sleep without rapid eye movements (Non-rapid eye movement - NREM); fast sleep or sleep with rapid eye movements (Rapid eye movement - REM). NREM sleep consists of 4 stages: Stage 1 - superficial sleep stage, lasting from 1 to 5 minutes; Stage 2 - appearance of sleep spindles and single long delta waves; Stages 3 and 4 - slow-wave sleep. However, a number of researchers suggest combining stages 3 and 4 into one stage of slow-wave sleep. REM sleep is characterized by irregular rapid eye movements, decreased muscle tone, and a predominance of low-amplitude high-frequency bioelectrical activity in the brain compared to NREM sleep. Both phases of sleep (NREM and REM) perform a

neuroprotective function by limiting oxidative damage to neurons and, as a consequence, reducing their apoptosis and reducing the risk of premature initiation of neurodegeneration processes [7, 8, 9, 10, 11]. There are several types of sleep disorders, the most significant of which are: insomnia; sleep apnea syndrome; circadian rhythm sleep/wake disorders. Various types of sleep disorders have become a global and steadily growing problem in the world as a whole, both among children and (especially) among adults. This is due to the fact that various sleep disorders not only reduce the quality of life and the efficiency of the central nervous system and the entire human body as a whole, but can also clinically significantly worsen the physical and mental health of people. Insufficient sleep is a risk factor for the development of many diseases, including neurological, mental, somatic: cardiovascular and endocrinological [12,13, 14,15,16,17,18].

Objective of the research. The faculty of the Tashkent Pharmaceutical Institute, Department of Pharmaceutical Technology, developed a biologically active food supplement in the form of drops "Somnium", containing melatonin. The main objective of the study is to determine the average lethal dose and assess the effectiveness of the

biologically active food supplement in the form of drops for drinking "Somnium".

Materials and methods. Study of acute toxicity of biologically active food supplement in the form of drops "Somnium". Under experimental conditions, the ascertainment of acute toxicity of the studied biologically active food supplement in the form of drops "Somnium" was carried out on 2 types of laboratory animals (white outbred rats and mice) with a single intragastric administration of the studied sample in doses of 2000, 3500 and 5000 mg/kg of animal weight. No deaths of experimental animals were observed during the 14 days following a single administration. The maximum dose of the biologically active food supplement in the form of drops "Somnium" administered into the stomach of laboratory

animals was more than 8 times higher than the maximum daily dose recommended for humans.

During the following days of observation, the animals gained weight, maintained a normal reaction to external stimuli, the general condition and behavior of the animals in both experimental groups was satisfactory. All animals were active and readily ate food, the fur and visible mucous membranes did not change. No deaths of animals were observed during the entire observation period. Thus, the average lethal dose of the studied biologically active food supplement in the form of drops "Somnium" for animals taken in the experiment has not been determined. No differences in the sensitivity of mice and rats to the drug depending on the species and sex have been ascertained.

Table 1
Acute toxicity of the biologically active additive in the form of drops "Somnium" when administered intragastric to laboratory animals of both sexes

Biologically active supplement	Dose mg/kg	Number of animals in the group/number of dead animals	LD ₅₀
"Somnium"	2000	6/0	Not defined
	3500	6/0	
	5000	6/0	

When registering a biologically active supplement, the scope of research is expanded and includes mandatory experimental research, due to the fact that the standards for the quantitative content of the active substances of the biologically active supplement "Somnium" in the body.

When designing the study of the effectiveness of the biologically active supplement in the form of drops "Somnium", the properties of the constituent components were taken into account, which help maintain the functional activity of the body's organs and systems within physiological limits. The studied biologically active supplement in the form of drops "Somnium" is intended for the prevention of sleep disorders. Thus, the biologically active food supplement "Somnium" regulates the functions of vital organs and systems at the physiological level, which is reflected in the hematological and biochemical indicators.

The effectiveness of the biologically active supplement in the form of drops "Somnium" was studied on rats after four weeks of daily single intragastric (through a tube) administration of the biologically active food supplement in the form of drops "Somnium" in the recommended daily dose. The dose of drops was calculated based on the norm for liquid intake of the biologically active supplement in the form of drops "Somnium" intended for an average person weighing 60 kg. The experiments were carried out on white female rats in

accordance with the purpose, obtained from the zoo section of the DSES MDM (Department of Sanitary and Epidemiological Surveillance of the Main Directorate of Medicine) with an initial body weight of 120-160 g. The animals were kept under standard conditions on a general vivarium food ration.

Description of animal groups: Group 1 animals - control - animals are on a complete general vivarium diet with intragastric administration of distilled water for the purity of the experiment; Group 2 - experimental animals with the introduction of the studied drops "Somnium" into the diet in one daily dose.

The experiments were carried out in compliance with the principles of the "European Convention for the Protection of Vertebrate Animals used for Experimental and other Scientific Purposes".

Results. In terms of body weight and weight gain, no statistically significant differences were found between animals that received the test drugs and control animals that received distilled water.

When assessing the effect of the studied dietary supplement on maintaining metabolism in the body, we studied the hematological and biochemical parameters of the blood of experimental animals that received the drugs, in comparison before and after the end of the experimental administration at the recommended dose (Tables 2 and 3).

Table 2
The effect of the biologically active supplement "Somnium" on hematological parameters

Groups	Observation period	Hematological parameters				
		Hematocrit, %	Hemoglobin concentration, g/l	Thrombocrit, %	Leukocytes, - 10 ⁹ /l	Erythrocytes, - 10 ¹² /l
Control, intact	Before administration	33.73±1.8	132.6±3.76	0.46±0.03	14.53±0.48	6.69±0.26
	At the end	34.18±1.1	130.8±4.12	0.45±0.01	14.60±0.34	6.80±0.22
"Somnium"	Before administration	33.70±1.4	134.4±3.80	0.461±0.01	14.55±0.51	6.71±0.22
	At the end	34.12±1.12	132.6±4.10	0.450±0.01	14.58±0.24	6.78±0.24

The results of the hematological analysis showed that intragastric administration of the dietary supplement "Somnium" did not reveal any negative impact on peripheral blood indices and allowed maintaining an optimal physiological status throughout the entire duration of the test.

Table 3
The effect of the biologically active supplement "Somnium" on biochemical parameters

Groups	Statistician indicators	Observation period, week	Biochemical parameters			
			ALT, E/L	ALT, E/L	ALT, E/L	ALT, E/L
Control, intact	M±m	1	50.2±33.7	114.4±5.17	318.4±35.3	67.30±1.4
		4	54.2±2.5	116.0±5.26	316.2±37.5	67.83±1.2
"Somnium"	M±m	1	56.1±3.1	114.8±5.4	313.4±40.9	66.93±2.3
		4	52.0±3.7	119.8±3.6	314.8±31.6	78.42±1.89

Studies on the effect of the dietary supplement "Somnium" on biochemical markers of damage to internal organs: total protein (TP), alkaline phosphatase (ALP) activity, aspartate aminotransferase (AST) and alanine aminotransferase (ALT) activity in the venous blood serum of animals made it possible to ascertain an increase in total protein in the blood serum of experimental animals by an average of 17-20%, which indicated the activation of protein metabolism processes and, thus, an improvement in the energy supply of biochemical processes occurring in the body. The amylase enzymes (AST and ALT) in all experimental groups did not exceed the physiological norm. The alkaline phosphatase activity was also within the optimal physiological norms for this type of animal, which indicates the absence of a damaging effect of these additives and allows us to speak of a general strengthening effect. The conducted hematological and biochemical tests showed not only the harmlessness, but also the real possibility of using this biologically active food supplement in the form of drops "Somnium" as biologically active food supplements that improve metabolic processes and maintain the physiological status of the body in an optimal state. At the same time, the presence of a tendency to decrease the activity of ALT allows us to assume that the use of the tested biologically active supplement in the form of drops "Somnium" reduces the damaging effects of free radicals.

To determine the neurotrophic effects of the formulations of the biologically active supplement in the form of drops "Somnium", changes in the behavioral reactions of experimental animals of the groups that received these supplements in the OP (open field) test were assessed daily at the same time of day (from 9.00 to 11.00) before feeding for 14 days. Testing in the OP is widely used in various experimental studies, and it allows for a relatively quick assessment of the animal's overall physiological response to the

effect of the studied biologically active supplement to food. This reaction includes elements of motor, orienting-exploratory and emotional behavior. In our study, the OP test zone was an area measuring 80x90 cm, divided into 20 squares and limited by a barrier. During the experiment, conducted in a darkened, soundproof room, the field was uniformly illuminated by a 100-watt incandescent lamp located 1 m from the center. The rat was placed in the middle of the area, and the following parameters were recorded for 2 min: horizontal motor activity, vertical motor activity, and frequency of defecation. In intact rats, during the first testing in the OP, the indices of both the HMA - horizontal motor activity - (9.60±0.30) and the VMA - vertical motor activity - (2.06±0.60) had an insignificant tendency to increase compared to those in the experimental groups. Orientation-exploratory reactions were realized, as a rule, in the first seconds of testing. During repeated testing in the OP on the 14th day of the experiment, a slight decrease in the intensity of the horizontal and vertical components of motor activity was observed in the experimental groups. The results of the experiments give grounds to conclude that the use of a biologically active supplement in the form of drops "Somnium" leads to some inhibition of motor activity due to the calming effect of the recipe of this biologically active supplement to food.

At the end of the experiment, the rats of the control groups and the animals that received the studied dietary supplements to food were euthanized in a gentle manner (by deep ether anesthesia). The condition of the internal organs was assessed visually during autopsy, the mass of the organs was measured and the specific values of this indicator were calculated. Considering that no pronounced pathological changes were noted in the rats of either the control or experimental groups, a comparative assessment of the relative mass of the internal organs was carried out for completeness of perception.

Table 4
Specific gravity of internal organs after four weeks of administration of the studied biologically active supplement in the form of drops "Somnium"

Organ	Group	
	control	"Somnium"
Brain	0.80±0.04	0.72±0.01
Liver	4.17±0.20	3.70±0.26
Lungs	0.68±0.02	0.61±0.04
Kidney	0.31±0.01	0.28±0.01
Heart	0.33±0.01	0.38±0.05
Spleen	0.37±0.03	0.35±0.01

Testicle	0.53±0.05	0.54±0.05
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When determining the relative mass of organs (Table 4), no convincing data on the presence of tissue edema, impaired blood supply or hemorrhages were obtained in comparison with the control. No reliable differences between the groups in gravimetric coefficients were found.

CONCLUSION

The obtained experimental results allow us to conclude that the studied biologically active food supplement in the form of drops "Somnium" produced by OOO "HVARA", Uzbekistan - activates protein metabolism processes and improves energy supply of biochemical processes occurring in the body, which allows maintaining the physiological status of the body in an optimal state. At the same time, the biologically active food supplement in the form of drops "Somnium" has some calming effect, which allows it to be used for the purpose of normalizing sleep.

Thus, the biologically active food supplement in the form of drops "Somnium" refers to virtually non-toxic (hazard class V according to the hygienic classification) and low-hazard (hazard class IV according to SSt 12.1.007) preparations. Experimental evaluation of the biologically active food supplement in the form of drops "Somnium" allows us to classify them as effective biologically active food supplements.

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