

Autoprotective Activity of Glyzimed

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Abstract. The autoprotective activity of Glyzimed, which contains herbal plants *Hypericum perforatum* L., *Ziziphora pedicellata* Pazij et Vved., *Mediizia macrophylla* and rhizome parts of *Glycyrrhiza glabra* L. was studied on experimental animals. Experimental studies were carried out on male white mice weighting 18-22 g. The comparative actoprotective activity of glyzimed, piracetam, and phytin, was studied on adult white mice, which were exposed to the forced swimming until the development of obvious signs of fatigue and the grip strength of paws was tested using a grip strength system device (Ugo Basile Srl, Italy). The animals of the experimental groups were intragastrically administered an aqueous solution of glyzimed using a syringe with a metal probe at doses of 10, 25 and 50 mg/kg, piracetam - 100 mg/kg and phytin - 200 mg/kg one day and one hour before the start of the experiment. Antihypoxants statistically significantly increase the maintaining of physical performance, and activity of glyzimed is almost twice superior to piracetam. Glyzimed can be proposed as an effective actoprotective medicine.

Key words: actoprotective activity, grip strength, antihypoxants, glyzimed

Introduction

Prolonged and intense physical work leads to the development of body fatigue as a result of insufficient recovery processes for energy expenses or exposure to extreme environmental factors. The main factor causing the development of body fatigue is the depletion of the reserve capacity of the body [1,2].

At the same time, body fatigue can be characterized as a temporary reversible violation of the physiological and biochemical processes, which are compensated after working period [2, 3]. Deficiency of energy strongly suppresses various processes of synthesis processes, including enzymes, proteins, phospholipids, glycogen, hormones and others, which are necessary for the functioning of body [4]. To ensure the normal functioning of the body, it is necessary to restore the energy potential as soon as possible by enhancing the processes of oxidative phosphorylation and suppressing the intensity of free radical oxidation processes increasing during hypoxia. It is believed that in order to increase efficiency in conditions of oxygen deficiency, it is necessary to use membrane stabilizers, which reduce heat production and increase the formation of macroergic molecules. In this regard, the use of antihypoxants is the most justified [5,6,7,8].

Previously, we have established a high antihypoxant activity of the medicinal plants mixture - Glyzimed, but its actoprotective activity has not been studied in depth [9].

Aim of study. The purpose of this work was to evaluate the actoprotective activity of Glyzimed.

Materials and methods

Experimental studies were carried out on male white mice weighting 18-22 g, obtained from vivarium of the Department of Sanitary and Epidemiological Surveillance of the Main Medical Department under the Administration of the President of the Republic of Uzbekistan. After quarantine for two weeks, all laboratory animals were carefully examined, weighed and their age, sex, and motor activity were taken into account. During the entire period of experiment, laboratory animals were kept in a vivarium at a temperature of 20-24°C, humidity of at least 50%, in a well-ventilated room and day/night light regimen, in standard plastic cages by 6-8 individuals in each, with a standard diet.

Plant material and preparation of dried extract. Aerial parts of *Hypericum perforatum L.*, *Ziziphora pedicellata Pazij et Vved.* and *Mediizia macrophylla* as well as root and rhizome parts of *Glycirhiza glabra L.* were obtained in summer of 2017 from foothills to medium zones of mountains of Tashkent region, Fergana, Samarkand and Surkhandaryo regions of Uzbekistan. Plant material was dried under dark conditions at room temperature for 10 days. The dry material was milled, obtaining 4-6 mm particles and mixed in proportion 1,25:1,0:1,25:1,5 (productivity of dried extract was higher than other proportions) then extracted by water at 93-95 °C temperature for 3 hours. The extract was then separated from the sample residue by filtration through filter paper. The resulting extracts were concentrated in vacuum until remaining a crude solid extract, which then was dried at 60 °C.

The comparative actoprotective activity of glyzimed, piracetam, and phytin, was studied on adult white mice, which were exposed to the forced swimming until the development of obvious signs of fatigue [2, 10]. The static power characteristics of animals were studied with the paw grip strength test, and retention of animals on a slippery vertical rod. The grip strength of paws was tested using a Grip strength system device (Ugo Basile Srl, Italy) with the special gratings that animals cling to it with paw toes. According to the dynamometer readings, the force parameters required for each animal were recorded. The test of keeping an animal on a slippery vertical rod was used to assess the physical performance of laboratory animals under pharmacological exposure. For this test, the animals were placed head up in the middle of slippery glass rod, mounted on a tripod at a height of at least 1 meter above the floor. The time of retention of mice on the rod was recorded in seconds. The preservation of physical performance under the pharmacological influence of drugs was judged by the absence of significant changes of the indicator in comparison with the placebo control group. The animals of the experimental groups were intragastrically administered an aqueous solution of glyzimed using a syringe with a metal probe at doses of 10, 25 and 50 mg/kg, piracetam - 100 mg/kg and phytin - 200 mg/kg one day and one hour before the start of the experiment. All experiments were performed in compliance with the requirements of the European Convention "On Protection of vertebrate animals used for experimental and other scientific purposes" (Strasbourg 1986) and in accordance with the Russian Federal Law "On protection of animals from cruel treatment".

The results of the study were statistically processed using the Biostat 2009 software package. The data are presented as the mean (M) and standard error of the mean value (m). Student's t-tests were used to test statistical hypotheses about the difference between the study groups. Statically significant changes were taken at a probability level of 95% or more ($p < 0.05$).

Results

The hypoxia plays a significant role in the development of fatigue and significantly limits the body's performance during heavy physical activity. The positive effect of glyzimed, so an increase in the survival of biological objects under conditions of various types of hypoxia should probably contribute to an increase in its actoprotective activity. Indeed, the duration of forced swimming time after the administration test compound at a dose of 10 and 25 mg/kg increased by 9.3 and 44.0% compared to the control, respectively. A twofold increase in the dose of the preparation (up to 50 mg/kg) did not lead to an increase in the effect, however, it provided a statistically significant increase in the working capacity of the animals by 34.5% compared to the control. In our experiments, phytin increased the working capacity of mice by 37.0%, and piracetam by 34.0%.

Thus, glyzimed- the new collection of extracts of medicinal plants has a distinct antihypoxant and actoprotective effect, probably its effect is a result of the development of a number of positive biochemical and functional changes in the body of mammals due to the more favorable course of metabolic processes which are directed for maintaining energy production in conditions of oxygen deficiency.

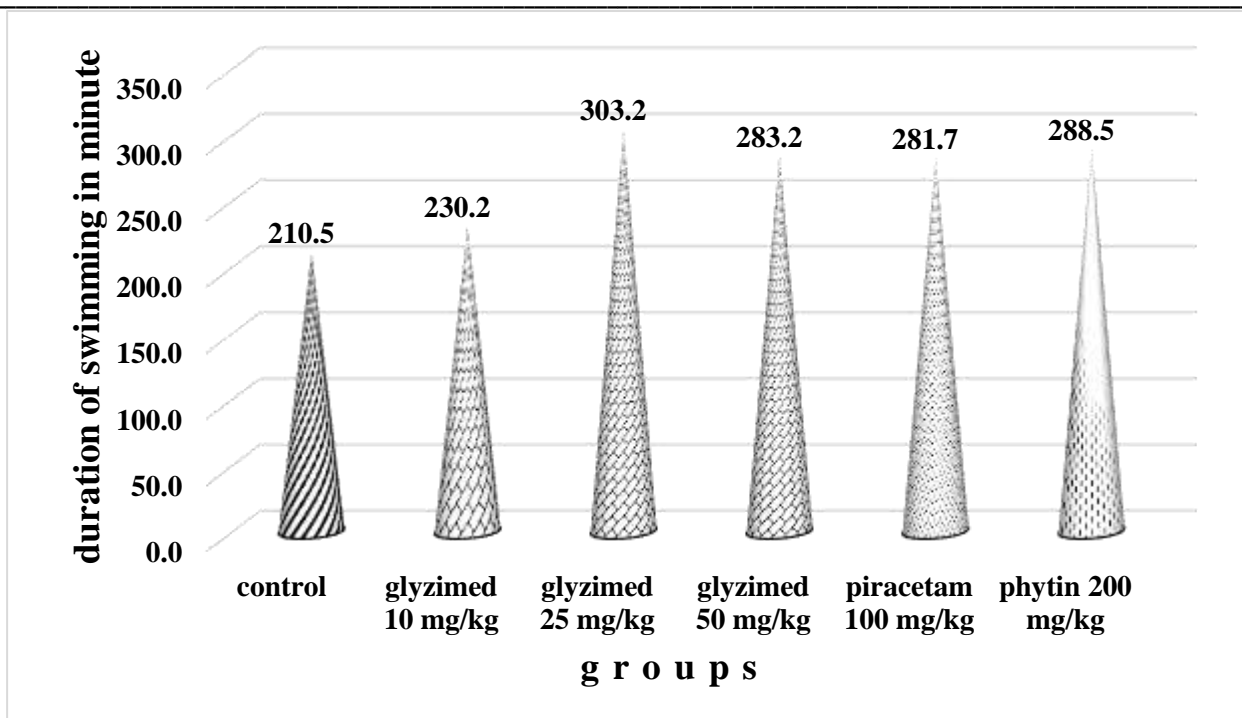


Figure 1. Study influence of glyzimed, piracetam, and phytin on the forced swimming duration of mice.

It is known that only a small proportion of their physical ability and performance is involved in everyday life and professional activities of most people, which is one of the main components of the quality of life. At the same time, almost all diseases, due to various reasons, lead to a decrease in working capacity. Pharmacological agents that increase physical activity can significantly speed up the process of complete recovery of the body after a disease [2]. Based on this, in a separate series of experiments, we comparatively studied the effect of glyzimed, piracetam and phytin on the physical performance of white mice in the test of retention of the animal on a slippery vertical rod, which also allows us to assess the maintaining physical performance.

As shown by the results of the studies, the length of retention time of the intact animals (control group) on the slippery rod were mean 5.27 ± 0.10 seconds, which remained unchanged for the next 60 minutes after intragastric administration of drinking water of the appropriate volume. The preventive administration of piracetam led to an increase in the duration of the retention time of mice by 32.5%, phytin - 61.2%, and glyzimed - 78.0%.

Consequently, the studied antihypoxant agents increased not only physical performance, but also maintaining of it. In this regard, as it is clear from the above

On the assessment of physical performance, an important place is given to the stable force characteristics of the body in experimental studies. For these purposes, the test for assessing the strength of the grip of small laboratory animals is most widely used [11]. The method based on that the animal clings the grate which is connected to the dynamometer and the animal is carefully pulled back until detaching it from the grate. The dynamometer records the force required for the animal to unclench the grate. This equipment allows to automatically register all the necessary parameters.

The results of in-depth pharmacological studies showed that the grip force in healthy mice (control group) ranged from 106.0 to 122.0 g and mean 111.67 ± 2.65 g, which did not change significantly even after one hour after the administration of an appropriate volume of drinking water. The preliminary administration of piracetam (at a dose of 100 mg/kg) after 1 hour led to an increase in paw grip strength by 30.6%. It can be seen from the data in the table 1 that phytin and glizimed also increased the grip strength of the paws of mice. So, before the administration of the drug, the paw grip strength was 117.30 ± 4.73 g in the group of animals which preventively received phytin (at a dose of 200 mg/kg). One hour after the intragastric administration of the drug it increased to 162.50 ± 5.14 g. The grip strength under the influence of the drug increased by 38.8%. We noted a somewhat higher results in the group of animals previously

treated with glyzimed (at a dose of 25 mg/kg). As can be seen from the data in the table, the grip strength increased by 44.3%.

Consequently, the studied antihypoxants increase the working capacity of animals, its maintaining, as well as muscle strength. In this regard, the activity of phytin is superior than piracetam, and activity of glyzimed is superior both of these drugs.

Table 1

Study of the effect of glyzimed, piracetam and phytin on the grip strength of the paws of mice ($M \pm m$, $n=6$)

groups \ indicators	the grip strength in gramms	
	Initial	After 1 hour
Intact P	111,67 ± 2,65	115,10 ± 2,26 >0,05
Piracetam P	109,73 ± 6,77	142,75 ± 7,06 <0,02
Phytin P	117,28 ± 4,73	162,50 ± 5,14 <0,002
Glyzimed P	118,05 ± 5,78 <0,01	170,10 ± 9,50 <0,01

Note: P - a significant difference in comparison with the initial indicators of the corresponding groups.

Conclusion

1. A mixture of extracts of medicinal plants has a distinct actoprotective activity.
2. The increase in physical performance of experimental animals under the influence of glyzimed is accompanied by a distinct increase in the grip strength.
3. In animals, antihypoxants statistically significantly increase the maintaining of physical performance, and activity of glyzimed is almost twice superior to piracetam.
4. Glyzimed can be proposed as an effective actoprotective medicine.

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