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Influence of Mix of Medicinal Plants on the Course of Different Types of Hypoxia

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Abstract The experimental studies were conducted on mature white male mice weighting 18-24 g. An aqueous solution of MMP at doses of 10, 25 and 50 mg/kg, and piracetam - 100 mg/kg were intragastrically administered into the animals of the experimental groups one day and one hour before modeling of the hemic, histotoxic and normobaric hypoxia with hypercapnia. Thus, under the influence of mix of medicinal plants at a dose of 10 mg/kg, the lifetime of animals increased by 37.5% compared with the control group in hemic hypoxia. The increase of the dose by 2.5 times led to a lengthening of the lifetime of mice by 141.4%. The obtained results showed that the mix of extracts of medicinal plants had a distinct antihypoxant activity in various models of hypoxia, such ashistotoxic, hemic and normobaric with hypercapnic hypoxia. The activity of preparationis not inferior to the reference antihypoxant - piracetam. It is noteworthy that the investigated new mix of extracts of medicinal plants has actoprotective activity, which manifests itself in the lengthening of the resistance of animals in conditions of development of fatigue from forced muscle load. It is believed that the mix of extracts of medicinal plants can be introduced into medical practice as a new antihypoxant.

Keywords Hypoxia, Antihypoxants, Actoprotectors, Medicinal plants

1. Introduction

The leading factor in the pathogenesis of critical conditions is hypoxia, which initiates the development of a complex set of pathological and compensatory-adaptive reactions [1]. Based on this, in recent years, antihypoxants have been widely used in medical practice for the prevention and treatment of various pathological conditions [2]. As a result, excessive physical activity that exceeds the adaptive capabilities of the body leads to exhaustion. As a result, lipid peroxidation processes significantly increase in the body. The latter serve as triggers for the body's response to stressful influences [3]. Pharmacotherapy of pathological conditions of various etiologies, accompanied by the development of local or generalized hypoxia, requires the rational use of agents that reduce metabolic changes in the body or prevent these disorders in the post-hypoxic period, the so-called antihypoxants [4,5]. In the last decade, much attention has been paid to the development of new drugs based on substances of natural origin. Interest in such compounds is due to their relatively high biological activity and low toxicity to the human body [6]. The identification and experimental proof of new properties of natural effectors is an important part of pharmacological research [7].

The above given data determined the purpose of this work: to study the effectiveness of a new mix of medicinal plants (MMP) in various types of hypoxia models.

2. Material and Methods

2.1. Preparation of a Dry Extract

The extract of medicinal plants was obtained as follows. Aerial parts of Hypericum perforatum L., Ziziphora pedicellata Pazij et Vved. and Mediazia macrophylla were collected in the phase of budding and the beginning of flowering in the mountainous part of the Tashkent region. The roots of Glycirhiza glabra L. are harvested in September, after the fruiting phase of the plants. Plant material was dried under dark conditions at room temperature for 10 days. Taking into account that the soil contains various spores of bacteria, fumigation was carried out by special fumigation methods, then the dry raw material was separately milled till 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℃ 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 in dryer apparatus

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at 60℃ temperature.

2.2. Experiments

The model of histotoxic hypoxia wasreproduced by injection of sodium nitroprusside at a dose of 20 mg/kg intraperitoneally andhemic hypoxia was reproduced subcutaneous injection of sodium nitrate at a dose of 200 mg/kg [8,9]. Normobaric hypoxia with hypercapniawas simulated by placing animals in a hermetic chamber with a volume of 250 cm^3 [10]. An aqueous solution of MMP at doses of 10, 25 and 50 mg/kg, and piracetam - 100 mg/kg were intragastrically administered into the animals of the experimental groups one day and one hour before modeling of the hemic, histotoxic and normobaric hypoxia with hypercapnia. The criterion for the antihypoxic activity of the preparation was the life expectancy of mice in the experiment compared with the control. The counting of the lifetime of the animals was started immediately from the moment of reproduction of the hypoxia model.

The actoprotective activity of MMP was studied in a separate series of experiments on white mice weighing 19-23 g, which were subjected to forced swimming until the developing obvious signs of fatigue. In this series of experiments, the above-mentioned doses of MMP were also administered preliminary intragastrically.

The experiments were carried out in accordance with the rules of a good laboratory practice (GLP) for preclinical research, as well as the rules and International Recommendations of the European Convention for the Protection of Vertebrate Animals used in Experimental Research (1986). The approval of Ethic Committee of Republic of Uzbekistan was taken before beginning of the experiment.

2.3. Statistical Analysis

The data obtained were processed by the method of variation statistics using the paired Student's test and one-way analysis of variance using the standard software package BIOSTAT 2009 with an assessment of the significance of indicators (Mean±Std error). Differences in the compared groups were considered significant at a significance level of 95% $p < 0.05$.

3. Results and Discussion

The development of hypoxia in clinical practice is quite often induced as a result of disturbances of hemodynamics or the gas transport function of the blood (carbon monoxide poisoning, hemolysis of erythrocytes, etc.). In this regard, it was of great interest to study the effect of MMP on the lifetime of mice under conditions of hemic hypoxia. An analysis of the results of the carried out experimental studies indicates the presence of the antihypoxant property of studied preparations. Thus, under the influence of the MMP at a dose of 10 mg/kg, the lifetime of animals increased by 37.5% compared with the control group in hemic hypoxia. The increase of the dose by 2.5 times led to a lengthening of the lifetime of mice by 141.4%. A further increase the dose of the preparation (up to 50 mg/kg) did not lead to an increase the determined effect. However, the lifetime of mice was extended by 2 times under its influence. We observed nearly the same effect in the well-known antihypoxant piracetam [11].

Therefore, the investigated MMP has a distinct antihypoxic effect in conditions of hemic hypoxia.

The current findings were confirmed in next experiments on a model of histotoxic hypoxia. It is known that a number of pathologies are accompanied by a significant change in the internal environment of the body. The utilization of oxygen is disturbed as a result of the dysfunction or inhibition of membrane-bound polyenzymatic cell systems. Hypoxia reproduced with the injection of sodium nitroprusside simulates histotoxic hypoxia [8]. The preventive administration of MMP at doses of 10, 25, and 50 mg/kg increased the lifetime of mice with histotoxic hypoxia by 24.4, 65.9, and 55.3%, respectively. It is noteworthy that the pharmacological effect of the MMP at a dose of 25 mg/kg was somewhat superior to piracetam used at four times high dose. The presented results indicate the effectiveness of MMP in those types of hypoxia that are directly related to the organs and systems of the animal body, that is, in hypoxia caused by the pathology of internal organs and systems (table 1).

Table 1. Study of the antihypoxant effect of the mix of medicinal plants in mice (M ± std error, n = 6)

Types of hypoxia	Groups (in seconds)				
	Control	MMP, 10 mg/kg	MMP, 25 mg/kg	MMP, 50 mg/kg	Piracetam 100 mg/kg
hemic P	560,0±44,1	770,0±52,8 <0,05	1350,0±68,3 <0,001	1120,0±61,2 <0,001	1230,0±49,2 <0,001
Histotoxic P	470,0±34,9	580,54±46,6 >0,05	780,0±42,4 <0,01	730,0±34,9 <0,01	750,0±44,4 <0,01
Normabaric P	2250,0±24,8	2530,0±56,9 <0,01	3390,0±141,3 <0,001	2920,0±51,2 <0,001	3080,0±75,9 <0,001
Actoprotective activity P	12630,0±701,7	13810,0±852,27 >0,05	18190,0±561,9 <0,002	16690,0±469,6 <0,01	17310,0±548,4 <0,01

Hypoxia, developing as a result of insufficient oxygen supply, is quite often noted. In a number of professions, the performance of official duties is carried out in conditions of scarce air or poor oxygenation (miners, sailors of submarines, etc.). Based on this, we conducted studies to establish the effectiveness of MMP on the model of hypoxia with hypercapnia in a separate series of experiments.

Thus, the lifetime of mice increased statistically significant under the influence of MMP at a dose of 10 mg/kg. The value of which reached more than three times when the dose was increased to 25 mg/kg. Although an increase in the dose of MMP to 50 mg/kg rose the lifetime of mice by 30%, this value was less than the value from the previous dose. In this model of hypoxia, the lifetime of mice was lengthened by 36.9% when piracetam was used as a reference drug.

Thus, the new mix of medicinal plants exhibits a distinct antihypoxic effect in the studied models of hypoxia. It is noteworthy that the studied MMPs, in terms of their pharmacological activity, are not inferior to the well-known antihypoxant, piracetam.

It should be noted that the effect of MMP was greater on models of tissue hypoxia and not on a lack of oxygen in the inhaled air. Based on this, it could be assumed that the MMP has a beneficial effect on the course of metabolic processes occurring in subcellular structures. It is known that the lack of oxygen causes the development of oxidative stress, leading to the intensification of free radical processes. The investigated mix of medicinal plants in this work contains flavonoids with a distinct antioxidant property. We have previously shown that the mix of extracts of medicinal plants containing: Glycyrrhiza glabra L., Ziziphora pedicellata Pazij Vved., Mediazia macrophylla and Hypericum scabrum L. inhibits the formation of initial and intermediate products of lipid peroxidation in rats with acute toxic hepatitis induced by carbon tetrachloride [12]. In our opinion, the suppression of the intensity of free radical processes is one of the important links in the mechanism of the antihypoxic effect of the studied MMP.

During heavy physical exertion, hypoxia plays a significant role in the development of fatigue and significantly limits the performance of the body. The above positive effect of the studied MMP, i.e., an increase in the survival of biological objects under conditions of various types of hypoxia, should ensure the actoprotective activity of the studied preparation. Indeed, the swimming duration of mice pretreated with studing MMP 10 and 25 mg/kg increased swimming duration by 9.3% and 44.0% compared to the control group, respectively. A twofold increase the dose of the MMP (up to 50 mg/kg) did not lead to increase the effect, however, it provided a statistically significant increase the performance of animals by 32.1% compared to the control group. In our experiments, piracetam increased the performance of mice by 37.0%.

According to most researchers, pharmacological correction of energy metabolism during hypoxia is the main task [13,14,15]. It is known that physical activity leads to the significant consumption of energy reserves, primarily glucose. In our opinion, MMP contributed to the efficient utilization of glycogen in skeletal muscles and a more pronounced intensification of gluconeogenesis. This assumption is in good agreement with the results of the study, which showed the restoration of glycogen content in the liver in acute toxic hepatitis treated with Lesbokhol. At the same time, under the influence of the latter, the concentration of lactic acid decreased [12]. The latter probably indicates the resynthesis of glucose from lactate.

Thus, the new mix of extracts of medicinal plants has a distinct antihypoxic, antioxidant, and actoprotective effect. As a result, it induces a number of positive biochemical and functional changes in the bodies of mammals due to the more favorable course of metabolic processes directed at maintaining homeostasis of energy production in conditions of oxygen deficiency.

4. Conclusions

1. In preliminary administration, the mix of extracts from medicinal plants *Glycirrhiza glabra L., Ziziphora pedicellata Pazij Vved., Mediazia macrophylla and Hypericum scabrum L.,* prolongs the lifespan of mice under various types of hypoxia indicating that this preparation has antihypoxic activity.
2. A new mix of medicinal plants increases the performance of animals, which is associated with an increase in the body's resistance to oxygen starvation and an increase in the functional reserves of tissues, especially the reserves of energy.
3. The mix of medicinal plants can be recommended as a new antihypoxic and actoprotective medicine.

REFERENCES

[1] Bayburina G.A., Nurgaleeva E.A., Samigullina A.F., Agletdinov E.F., 2019, Features of free radical oxidation and dynamics of the content of corticosteroid receptors in the lungs in animals with different sensitivity of hypoxia in the postresuscitation period. Pathological Physiology and Experimental Therapy, 63, 4, 56-63.

[2] Litvinova S.A., Voronina T.A., Kutepova I.S., Avdyunina N.M., Pyatin B.M., 2018, Study of the anticonvulsant and antihypoxic properties of 2-ethyl-6-methyl-3-gyrorthoxypyri dine hemisuccinate. Experimental and Clinical Pharmacology, 81, 3, 3-6.

[3] Voronkov A.V., Gerashchenko A.F., Efremova M.P., Voronkova M.P., 2020, Antioxidant activity of a cinnamic acid derivative under conditions of debilitating physical exertion in the experiment. Experimental and Clinical Pharmacology, 83, 1, 19-23.

[4] Lukyanchuk V.D.,. Savchenkova L.V., 1998, Antihypoxants: state and prospects. Experimental and Clinical Pharmacology, 61, 4, 72-79.

[5] Voronina T.A., 2016, The role of hypoxia in the development of stroke and convulsive conditions. Antihypoxants. Reviews on clinical pharmacology and drug therapy, 14, 1, 63-70.

[6] Khakimov Z.Z., Rakhmanov A.Kh., Mavlanov Sh.R., The effectiveness of a mixture of extracts of medicinal plants in the correction of violations of the functional state of the liver in its lesions of various etiologies. Tashkent.: "ozkitobsavdonashriyoti", 2019, 156.

[7] Talalaeva O.S., Mishchenko V.M., Zverev Ya.F., 2012, The influence of histochrome on the exudative and proliferative phases of experimental inflammation. Bulletin of the Russian Academy of Medical Sciences, 32, 4, 28-31.

[8] Karkishchenko N.N., Karkishchenko V.N., Biomedical (preclinical) study of the antihypoxic activity of drugs. Methodological recommendations, ed., Moscow, 2017. -98 p.

[9] Mironov A.N. Guidelines for conducting preclinical studies of drugs. Part one. -M.: Grif and K, 2012. 944.

[10] Khakimov Z.Z., Rakhmanov A.Kh., Rakhimbaev S.D., 2018, Comparative study of antihipoxic and actoprotective activity of lesbokhol and fitin, Sciences of Europe (Praha, Czech Republic), 1, 32, 35-38.

[11] Vostrikov V.V., 2017, The place of piracetam in modern practical medicine // Reviews of clinical pharmacology and drug therapy, 15, 1, 14-25.

[12] Mavlanov Sh.R., Khakimov Z.Z., Rakhmanov A.Kh., 2017, Influence of lesbochol on the content of glycogen in the liver during its acute toxic damage, Infection, immunity and pharmacology, 1, 129-134.

[13] Danchenko E.O., Chirkin A.A., 2010, A new methodological approach to determining the concentration of glycogen in tissues and some comments on the interpretation of the results. Forensic Medical Expertise, 3, 25-28.

[14] Usenko L.V., Muslin V.P., Mosentsev N.F., Mosentsev N.N., 2013, A method for leveling stress-induced hyperglycemia in severe critical conditions. Emergency Medicine, 1, 48, 103-114.

[15] Chelnokov S.B., Pudina N.A., 2001, The level of blood lactate in newborns born in asphyxia, Bulletin of Intensive Care, 4, 23-25.