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CLARIFICATION TOLERANTMONEY ACTIVITY IN DIFFERENT GROUPS OF HYPOMETABOLISM AGENTS

Abstract: *There were studied three groups of hipometabolics: a). serotonin and katacine block the different substrate oxidation in mitoxondria; b). halotame and aminooxacetate block the NADH-dapendent substrates; c). snake venoms block the all substrate oxidation and uncouple the oxidative phosphorilation process.*

Tolerantogenic agents (serotonin and katacin) decrease the enzyme activity of main respiratory chain and ATFase of mitochondria diminish the gas-oxygen metabolism of organism.

Key words: *serotonin, catacin, respiratory chain, hypometabolism, oxidation, mitochondria, gyurza venom.*

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Introduction

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The question of increasing the life stability of the body is one of the most important medical and biochemical problems.

Currently, the theoretical aspects of this problem are insufficiently studied and therefore further research in this direction is needed.

A more developed aspect of this direction is the analysis of hypoxic effects and the search for antihypoxants to increase the viability of the body in these conditions [1-3]. The analysis of the available literature data in most cases States inhibition of the intensity of metabolism of antihypoxic [2,3] although other mechanisms of action of these substances on metabolic processes are possible [1,4].

The antihypoxic nature of the influence of drugs is most often judged in the literature by their ability to increase the life expectancy of an animal in a hypoxic chamber but at the same time the cellular mechanisms of this process are known.

In this regard, in the experiments we used a number of hypometabolic environment which are hypoxic. These hypometabolic are divided into three groups: a). overwhelming the oxidation of many substrates in the mitochondria of serotonin, katcin [3,5]; b). suppress the oxidation NAD-dependent substrates of aminooxyacetic [6,7]; c). suppressing breathing along with the uncoupling the process of oxidative phosphorylation I Viper [5,8].

We considered it necessary to study the influence of these groups of hypometabolics on the hypoxic stability of animals and enzymes of the respiratory chain of mitochondria of the rat liver in order to find a connection between the effect of increasing the physical stability of the body and the nature of the influence of these substances on the energy links of the mitochondria.

Method of research.

The experiments were carried out on laboratory mice in a sealed hypoxic chamber with a volume of 500 ml. Two mice were placed in the chamber, one of

which was experimental (with ink) and the other - control (with an injection of saline solution).

The study of the activity of respiratory enzymes, tseni and ATFaza was carried out on isolated mitochondria of rat liver which were isolated by the conventional method of differential centrifugation [9]. The isolation medium contained 0.3 M sucrose and 10 mm Gris HCI (pH 7.5). The isolated mitochondria were frozen and thawed before the experiments to test the effects of hypometabolics.

The study of enzyme activity of frozen – thawed mitochondria was performed by paleographic method [10]. At the same time, the nature of the influence of different hypometabolics on the activity of NADH oxidase, succinite oxidase was determined. In another series of experiments, different mitochondrial ATF activity was studied [11].

The mitochondrial protein was determined by Lowry [12].

Results and discussion.

Initially, we have identified different groups of hypometabolism on the lifespan of mice in hypoxic conditions. From the data of the table it can be seen the multidirectional effect of these agents on the life of these animals. Among them, serotonias and actations, known previously as antihypoxants [2,3], cause an increase in life expectancy by more than three times. Of these substances, actin is the most effective. This drug is isolated from oak bark and contains many alcohol groups in contrast to serotonin molecule which contains only one alcohol group. Another hypometabolic AOA is considerably less in comparison to the serotonin and cation changes lives animals ' resistance indicating weak expression of the antihypoxic effect of AOA.

The effect of Gyurza venom on the hypoxic resistance of mice has also been studied. There are several reports in the literature [5,13] about the positive metabolic effect of snake venoms on the body, and in mitochondria they show a dissociating effect in combination with inhibition [5, 8]. In our experiments, it was found that the poison of Gyurza negatively affects the life of mice, reducing it by 30-40% (table 1).

Table 1. The effect of different drugs on the hypoxic resistance of mice with normobaric hypoxin (non-lethal doses)

Conditions of experience	Dose	Number animals	Life span min	Changes in %
The control	-	8	18,3 ± 2,3	0
Catacin	40 мг/кг	11	59,2 ± 6,5	361,1
Serotonin	80 мг/кг	9	52,4 ± 3,6	322,2
AOA	0,3 м М	8	27,6 ± 2,8	150,4
Gyurza venom	2 мг/кг	6	13,8 ± 2,3	-72,2

Next, we conducted the study in a wind, the effect of the above hypometabolic on the activity of enzymes of the respiratory chain and ATF the basics of isolated frozen - thawed rat liver mitochondria.

The results of these experiments made it possible to find certain regularity in the nature of hypometabolic (table 2). So actin and serotonin inhibit the activity of NADH and succinite oxidases.

Table 2. The effect of hypometabolics and snake venom on the activity of rat mitochondrial respiratory chain enzymes (n = 6 - 12).

Experience options	Dose	n-at 0 min kg protein	
		NADH oxidase NADH + cyt C	Succinate oxidase succinate
The control	-	72,3 ± 6,3	149,4 ± 8,9
Catacin	100 мкг/мл	21,6 ± 3,2	36,9 ± 3,1
Serotonin	5 мм	23,3 ± 2,1	33,8 ± 2,8
AOA	1мм	68,9 ± 2,8	139,1 ± 7,8
Gyurza venom	80 мкг/мл	18,2 ± 2,7	48,5 ± 6,4

In parentheses are the substrates of oxidation (succinate 5 mM; NADH 1 mM + 200 mkg of cytochrome C.

Use another pair of hypometabolic showed that gallivan suppresses NADH oxidase do not influence the enzymes of the respiratory chain. Aminooxyacetate does not significantly affect mitochondrial respiratory chain enzymes, and according to the literature it inhibits the oxidation of

OVER-dependent strathonglugamate and mulatto without oblique oxidation of other substrates [14].

As for the poison of Gyurza it quite sharply suppresses the activity of NADH and succinite oxidases which indicates a high means of poison to respiratory enzymes of mitochondria.

The study of the effect of the different hypo metabolic ATF different activity of rat liver mitochondria showed (table 3) that anjali and serotonin have a certain inhibitory effect on initial ATFaza (in the conditions without additives resubmit); AOA, this effect is not observed and the Viper's poison unlike other agents activate ATFaza. The effects of the first two agents can be explained by direct inhibition of ATFaza, and the venom effect by increased proton conductivity of mitochondria, increasing ATP hydrolysis.

Clearer results were obtained by studying the DNF of ATFaza - stimulated (table 3). In this case, there are significant changes in ATFaza under the influence of hypo metabolics action and serotonin, as well as poison Gyurza plant its activity almost three times, but with the action of glodan and AOA, it changes little. As can be seen, the effect of anjali and serotonin similar to that of Viper's poison, however, you should note that snake venom has a more divisive form of action on mitochondria.

Table 3. The level of DNF-stimulated ATPase activity (mkm N/min mg of mitochondrial protein) when the liver has various hypometabolics

Preparations	ATF without disconnection	The same + ATP + disconnect
The control	3,8 ± 0,21	91,2 ± 3,13
Catacin	1,4 ± 0,12	29,4 ± 2,46
Serotonin	1,6 ± 0,12	36,6 ± 2,33
AOA	3,5 ± 0,71	86,9 ± 2,26
Gyurza venom	24,3 ± 2,6	36, 4 ± 3,15

Disconnect uncoupler - 2.4-dinitrophenol (DNF) 50 mkM.

Thus the obtained results suggest that agents poveschayuschie life resistance to hypoxia should have certain properties in particular to understand the consumption of oxygen by the body to suppress the activity of enzymes of the respiratory chain ATFaza mitochondria and not cause disconnection of the oxidative phosphorylation process. According to our data, only actin and serotonin meet these requirements. These results may be prerequisites for the search for effective tolerant drugs for medical and biochemical purposes.

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