the malate-aspartate shunt, which is depressed in ischemia [5]. Evidence of activation of transamination in the mechanism of improvement of the function of the ischemic heart is given by disappearance of this effect under the influence of hydroxyaminoacetic acid, an inhibitor of cytoplasmic and mitochondrical transaminases [3]. Under conditions of ischemia amino acids thus improve contractile function by maintaining the natural compensatory reactions of energy metabolism through preservation of amino-acid pools and subsequent activation of oxidative and substrate phosphorylation in the mitochondria, and not by lowering the ammonia level.

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EFFECT OF AN ANTIOXIDANT ON RESISTANCE OF THE UNTRAINED ANIMAL TO MAXIMAL PHYSICAL EXERCISE

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During maximal physical exertion by untrained animals and humans the ATP and creatine phosphate concentrations in the skeletal muscles fall regularly, glycolysis is activated, the lactate concentration in the blood rises considerably, and the pH of the plasma falls [1, 9]. One possible cause of the insufficient power of the system for aerobic resynthesis of ATP, which is the basis of the changes mentioned above, is damage to cellular and, in particular, mitochondrical membranes. Such injuries have in fact been demonstrated after maximal physical exertion and are manifested as the appearance of enzymes in the blood stream, due to increased liberation of cytosol enzymes through the plasma membrane into the blood plasma, and also to destruction of the outer membrane and cristae of mitochondria [2]. At least two possible causes of the disturbance of the membrane mechanisms of oxidative phosphorylation during extremal physical exertion are now known. The first is that, as a result of hypoxemia and tissue hypoxia, lipid peroxidation (LPA) and phospholipases in the mitochondria [6] are activated, so that the membrane becomes permeable for protons and, in accordance with the chemo-osmosis theory, it disturbs oxidative phosphorylation. The second cause is a fall in pH which, as has recently been shown, through the same mechanisms of activation of phospholipases and LP, switched oxidation of NADH to the so-called pathway, and thereby substantially reduces the efficiency of utilization of substrates and oxygen for ATP synthesis [8]. This means that one way of increasing the efficiency of oxidative phosphorylation during extremal physical exertion and increasing resistance to such loads is by the rational use of inhibitors of LPO and phospholipases.

The object of the present investigation was to study the effect of preliminary administration of antioxidant M-1, an inhibitor of peroxidation, on the maximal duration of standard physical exertion by untrained animals, on their blood enzyme levels, and on the blood lactate concentration.

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TABLE 1. Effect of Antioxidant on Maximal Duration of Running on Treadmill and on Blood Enzyme Activity (M ± m)

Group of animals	Experimental conditions	Maximal duration of running on treadmill, min	Enzyme activity in blood plasma, μmoles/ml	
			AlAT	LDH
1	Control (n = 10)	—	1,34±0,10	21,48±1,99
2	Control + antioxidant (n = 9)	—	1,28±0,09	20,09±1,55
3	Maximal exertion (n = 10)	66,9±1,1	3,83±0,99	34,96±2,21
4	Maximal exertion + antioxidant (n = 9)	108,1±0,10	2,10±0,10	27,96±1,59
P_{3-4}		>0,001	>0,05	>0,001

TABLE 2. Effect of Antioxidant on Plasma Lactate Concentration during Maximal Physical Exertion (76 min) (M ± m)

Group of animals	Experimental conditions (n = 10)	Plasma lactate concentration, μmoles/ml	P
1	Control	7,4±0,05	P_{1-2}, not significant
2	Antioxidant	7,3±0,06	P_{2-3}>0,001
3	Maximal exertion	19,5±2,2	P_{1-4}>0,001
4	Maximal exertion + antioxidant	11,08±0,9	P_{3-4}>0,001

EXPERIMENTAL METHODS

Experiments were carried out on 97 male Wistar rats weighing about 200 g. In the experiments of series I the animals were divided into four groups: Group 1 was the control; the animals of Group 2 received M-1 in a dose of 20 mg/kg intraperitoneally daily for 3 days; the animals of Group 3 were subjected to a single session of physical exercise of maximal duration, in the form of running on a treadmill at a speed of 16 m/min, up to the limit; the animals of group 4 received an injection of M-1 in the dose mentioned above, after which they did the same exercise. Rats of all groups were killed and activity of alanine aminotransferase (AlAT) was determined by the method of Reitman and Frankel [7] and lactate dehydrogenase (LDH) activity was determined by Natelson's method [4]. AlAT activity was expressed in micromoles pyruvic acid formed during incubation for 1 h at 37.0°C per milliliter of serum; LDH activity was expressed in micromoles pyruvic acid disappearing during incubation for 1 h at 37.0°C per milliliter serum. In series II a similar four groups of animals were distinguished, but the experimental conditions differed in that animals receiving M-1 beforehand did not run to the limit, but for a length of time which was maximal for animals not receiving M-1. Immediately after exercise all the rats were killed and the lactic acid concentration in the plasma was determined by Hahorst's method [4].

EXPERIMENTAL RESULTS

The maximal duration of running on the treadmill up to the limit, for animals not receiving the antioxidant, averaged 67 min whereas for animals receiving the antioxidant beforehand it was 108 min (Table 1). In other words, under the influenceof the antioxidant,

the endurance of the animals measured by the maximal duration of running was increased by about 60%. Under the influence of maximal exertion, in animals not receiving the antioxidant, a high blood enzyme level developed: AlAT activity increased by 2.8 times and LDH activity by almost twice. In animals receiving the inhibitor of peroxidation beforehand, the blood enzyme levels after prolonged exertion were much lower: AlAT activity increased by 65% but LDH activity by only 40%.

As Table 2 shows, the antioxidant did not affect the blood lactate concentration in animals at rest, but after exercise of equal duration the increase in the lactate concentration in animals receiving the antioxidant was many times smaller than in animals not receiving the LP inhibitor. In fact, in the control the lactate concentration after running for 70 min, up to the limit, rose from 7.4 to 19.5 μmoles/ml plasma, i.e., by 12 μmoles/ml. In animals receiving the antioxidant this parameter increased from 7.3 to 11.08 μmoles/ml, i.e., by 2.8 μmoles/ml. In other words, the increase in the blood lactate concentration under the influence of preliminary injection of the antioxidant was reduced by more than 75% and the blood lactate concentration after running was only just over half its value in animals unprotected by the antioxidant.

According to a now reasonably well established view, the blood lactate concentration limits the duration of physical work [10]. It can accordingly be postulated that in the present experiments the control animals stopped running because of fatigue, whereas animals protected by the antioxidant were able to continue running for a long time. It can be tentatively suggested that the probable mechanism of this phenomenon is that blockade of LPO by the antioxidant prevents both an increase in ionic permeability of the mitochondrial membrane and also the switching of substrate oxidation to the external pathway, unconnected with phosphorylation. Ultimately the efficiency of the system for aerobic resynthesis of ATP is increased and the blood lactate concentration rises less than in the control. The results are evidence that the antioxidant M-1 can increase the resistance of the untrained organism to physical exertion.

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