ml for EDTA-S1, $p < 0.001$). Meanwhile, preservation of the adhesiveness of the monocytes and platelets did not cause any significant impairment of the filterability of the suspensions: that of HS1 was only 21% below that of EDTA-S1 (9.47 ± 0.78 ml and 11.46 ± 0.82 ml respectively, $p > 0.05$), whereas the adhesion index of monocytes and, in particular, of platelets in HS1 was significantly higher than in EDTA-S1 (Table 2). In the presence of polymorphs (suspension 2), however, filterability of the heparinized suspension was 5.5 times less than that of the EDTA suspension. The presence of adhesive activity evidently sharply increases the ability of polymorphs to jam the capillaries of the filter and makes their role in this process without doubt of supreme importance among other cells.

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EFFECT OF PAGINOL S-2000 ON RESPIRATION AND OXIDATIVE PHOSPHORYLATION OF LIVER MITOCHONDRIA OF RATS POISONED WITH BUTYLCAPTAX

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The massive use of pesticides in agriculture necessitates the study of their effect on structural, functional, and biochemical processes in man and animals. The study of the effect of pesticides on cell metabolism is an important aspect of the study of the mechanism of the toxic action of these compounds and the creation of new methods of protection and correction of the pathological processes for which they are responsible, on this basis.

Despite the availability of a wide range of substances and methods of treatment, the search for effective ways of correcting structural and functional disturbances of the liver in diseases of chemical etiology still continues. The search for new therapeutic substances is aimed primarily at the search for and use of new inhibitors of free-radical reactions in biomembranes. Besides natural antioxidants, an important place is occupied by the synthesis and use of new compounds which possess these properties [3, 7]. The writers showed previously that if butylcaptax is given to animals, free-radical lipid peroxidation (LPO) in rat liver mitochondrial membranes is intensified [6].

It was accordingly decided to study the effect of paginol S-2000 on respiration and oxidative phosphorylation of liver mitochondrial membranes of rats poisoned with butylcaptax.

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TABLE 1. Action of Paginol S-2000 on Respiration and Oxidative Phosphorylation (in activity units) of Liver Mitochondria of Rats Poisoned with Butylcaptax (oxidation substrate – succinate) (M ± m)

Parameters	Control	Butylcaptax	Butylcaptax + paginol S-2000
V_2	40±2	34±1	38±3
V_3	120±4	98±3	108±8
V_4	41±2	35±2	37±4
V_{DMP}	160±6	126±5	152±9
RC	2,93±0,08	2,80±0,07	2,92±0,09
ADP/O	1,94±0,05	1,78±0,04	1,89±0,08

TABLE 2. Action of Paginol S-2000 on Respiration and Oxidative Phosphorylation (in activity units) of Liver Mitochondria of Rats Poisoned with Butylcaptax (oxidation substrate – α-ketoglutarate) (M ± m)

Parameters	Control	Butylcaptax	Butylcaptax + paginol S-2000
V_2	24±1	20±1	20±1
V_3	65±2	54±3	46±4
V_4	24±1	21±1	19±2
V_{DMP}	66±3	54±4	42±5
RC	2,71±0,07	2,57±0,09	2,42±0,07
ADP/O	2,75±0,08	2,42±0,07	2,24±0,06

EXPERIMENTAL METHOD

Butylcaptax is a benzisothiazole derivative used in agriculture as a cotton defoliant. Paginol S-2000 is a synthetic water-soluble antioxidant, synthesized at the Institute of Chemical Physics, Academy of Sciences of the USSR [1].

Experiments were carried out on male Wistar albino rats weighing 180-200 g. The animals were divided into three groups: 1) control group, animals receiving distilled water; 2) a group receiving butylcaptax only for 5 days (daily dose 0.1 LD_{50}), 3) animals receiving butylcaptax and, in addition, the antioxidant paginol S-2000 1 h after poisoning (daily dose 30 mg/kg).

Butylcaptax was introduced by the intragastric route, using a special tube. The respiration rate of mitochondria isolated from the liver [9] was recorded by a polarographic method [5]. The medium in which the measurements were made contained 0.15 M sucrose, 10 mM Tris-HCl, pH 7.4, and 5 mM KH_2PO_4. Succinate and α-ketoglutarate (each 10 mM), pH 7.4, were used as oxidation substrates. The reaction was started by addition of the mitochondrial suspension. The final concentration of ADP was 200 μM and of 2,4-dinitrophenol (DMP) 50 μM.

EXPERIMENTAL RESULTS

Administration of butylcaptax to the animals in a dose of 0.1 LD_{50} led to a significant decrease in the rate of oxidation of succinate and α-ketoglutarate in the liver mitochondria of the poisoned rats.

The rate of oxidation of succinate in state V_2, V_3, V_4, and V_{DNP} was reduced by 15, 17.3, 15.6, and 21.3% respectively compared with the control. As a result of these changes, the degree of coupling of the mitochondrial preparations, estimated from the value of the respiratory control (RC), was observed, and the ADP/O ratio also was lowered (Table 1).

When α-ketoglutarate was used as the substrate, under the influence of butylcaptax the velocity of electron transfer along the respiratory chain (by 12.5-18.2%) and the efficiency of oxidative phosphorylation, estimated from the ratio ADP/0, both decreased (Table 2).

The experimental results showed that 24 h after daily administration of butylcaptax for 5 days, oxidation of the substrates along the NADH-dependent pathway in the liver mitochondria was reduced. The decrease in the respiration rate in state V_3 and after addition of the uncoupler indicates that butylcaptax has a direct action on the respiratory chain. Inhibition of phosphorylating respiration of the liver mitochondria in media with succinate and α-ketoglutarate was evidently connected with lowering of the metabolic reserves of intramitochondrial adenine-nucleotides or of their transport.

Inhibition of oxidative phosphorylation of the liver mitochondria is observed [4] in animals in certain physiological and pathological states at the level of adenine-nucleotide translocase, a mitochondrial carrier of ADP and ATP, which plays a key role in the general mechanism of oxidative phosphorylation.

In the next series of experiments the effect of paginol S-200 on oxidative phosphorylation of the liver mitochondria was studied in rats poisoned with butylcaptax. The results showed that paginol S-200 restores the succinate path or oxidative phosphorylation of the liver mitochondria almost completely. However, if α-ketoglutarate was used as the substrate, the values of the parameters of measured were lower than those in the liver mitochondria of the control rats. For instance, whereas under the influence of butylcaptax alone the oxidation rate of α-ketoglutarate in states V_3, V_4, and V_{DNP} was reduced by 17, 12.5, and 18.2%, if paginol S-2000 also was given, it fell by 29.3, 20.8, and 36.4% respectively. Under these circumstances the value of RC and of the ADP/0 ratio fell with butylcaptax by only 5.2 and 11.2%, with butylcaptax + paginol it fell by 10.7 and 18.6% respectively.

In our view, under the influence of paginol switching of the respiratory chain takes place from oxidation via the NADH-dependent path to the succinate part [2, 8]. Advantages of succinate from the energy point of view have several important biological consequences: a high oxidation rate, the supply of high-energy compounds and hydrogen to the respiratory chain, and also the specific role of succinic acid in the mechanism of several biosynthetic processes, including synthesis of fatty acids, corticosteroids, porphyrins, etc. [2].

It can thus be concluded from these results that there are certain particular features of compensatory and adaptive processes taking place in the liver mitochondria under the influence of butylcaptax and paginol S-2000: whereas butylcaptax inhibited mitochondrial respiration and oxidative phosphorylation when succinate and α-ketoglutarate were used as oxidation substrates, if the poisoned animals were given paginol S-2000, the succinate path was restored, thereby leading to a normal level of function of the mitochondrial ATP-synthesizing system.

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