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EFFECT OF SELENIUM-CONTAINING COMPOUNDS ON ELECTRICAL

ACTIVITY OF THE ISOLATED GUINEA PIG RETINA DURING

INDUCED LIPID PEROXIDATION

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Data in the literature [5] and our own experimental observations [3] indicate that accumulation of endogenous products of lipid peroxidation (LPO) inhibits electrical activity of the isolated retina of cold-blooded animals. At the same time, LPO in the retina is known to be inhibited by various selenium compounds, among which organic compounds have proved to be most effective [4].

In connection with the facts described above it was interesting to study the possibility of regulation of electrical activity of the isolated retina of warm-blooded animals by means of selenium-containing compounds under conditions of induced lipid peroxidation.

## EXPERIMENTAL METHOD

Experiments were carried out on 120 male guinea pigs weighing 300-350 g, kept under standard vivarium conditions. The retina of dark-adapted animals (for not less than 2 h) was removed by a special surgical method from the eye in weak red light. The preparation thus obtained was placed on filter paper with the receptors facing downward and laid in a special continuous-flow chamber with two recording electrodes. The retina was perfused with Ringer's solution for warm-blooded animals, regularly saturated with oxygen. The electroretinogram (ERG) was recorded by means of the UBP 1-02 biopotentials amplifier and photographed from the screen of an S1-18 oscilloscope. Photic stimulation was applied by means of a xenon flash tube, giving flashes from 0.005 to 0.19 J in intensity. The light was focused on the light guide of the chamber by an optical system. The flash duration was 150 usec.

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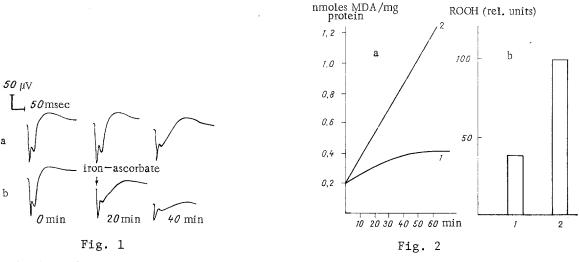


Fig. 1. Action of an iron—ascorbate system on parameters of guinea pig ERG: a) control, b) experiment.

Fig. 2. Time course of accumulation of LPO products in guinea pig retina under the influence of iron—ascorbate system. a) Time course of accumulation of MDA in control (1) and experimental (2) retinas, b) change in content of hydroperoxides in lipids of control (1) and experimental (2) retinas.

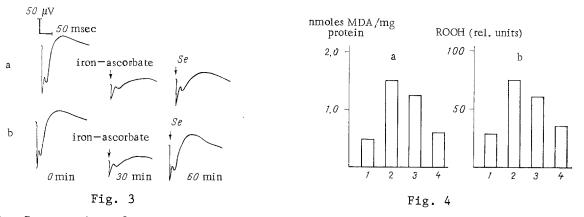


Fig. 3. Restoration of parameters of ERG by selenium-containing compounds in the presence of induced LPO. a) Treatment with p-bromphenylseleno-3-morpholinopropanol-2 hydrochloride, b) treatment with 1-phenylseleno-44-phenyl-4-hexamethyleniminobutine-2 hydrochloride.

Fig. 4. Inhibitory action of selenium-containing compounds on LPO. a) Change in MDA content, b) change in hydroperoxide content. 1) Control retina, 2) incubation in iron-ascorbate system; 3) treatment with p-bromphenylseleno-3-morpholinopropanol-2 hydrochloride; 4) treatment with 1-phenylseleno-44-phenyl-4-hexamethyleniminobutine-2 hydrochloride.

LPO was activated by the addition of FeSO<sub>4</sub> and ascorbic acid ( $10^{-5}$  M and 0.8 mM, respectively) to the Ringer's solution. Water-soluble organic compounds of selenium, namely, 1-phenylseleno-44-phenyl-4-hexamethylenimino-butine-2 hydrochloride and p-bromphenylseleno-3-morpholinopropanol-2 hydrochloride, which also were added to the Ringer's solution in concentrations of 0.03%, were used as LPO inhibitors.

The rate of LPO in the retina in the course of 60 min was estimated from changes in the concentrations of hydroperoxides and malonic dialdehyde (MDA). The MDA concentration was estimated by the reaction with thiobarbituric acid [1]. Hydroperoxides were estimated quantitatively by a polarographic method [2].

## EXPERIMENTAL RESULTS

The ERG of isolated retinas of dark-adapted guinea pigs consists of a<sub>1</sub>- and a<sub>2</sub>-waves and of a b-wave, whose amplitude remains almost unchanged for 1 h or more during perfusion with Ringer's solution. Addition of the iron-ascorbate complex to the Ringer's solution caused a rapid fall in amplitude of all ERG waves (Fig. 1). By the 40th minute of the experiment the amplitude of the ERG was depressed to a very small oscillation in response to the testing flash. Rinsing the retina with Ringer's solution did not lead even to partial recovery of the ERG, whose amplitude continued to fall until it disappeared completely. According to the results [2] of an investigation with cold-blooded animals, lowering of the amplitude of the ERG is due to the formation of LPO products. This was confirmed yet again by our own experiments on guinea pig retinas in which the content of hydroperoxides and of MDA was compared in control and experimental retinas exposed for 60 min to the action of an iron-ascorbate system (Fig. 2). It was shown that MDA is present in significant amounts in retinas incubated in the presence of an iron-ascorbate system after 40 min, with a considerable increase in its content by 60 min (Fig. 2b). Since MDA is a late conversion product of lipid peroxides, it will be evident that depression of the ERG may be due to the formation of lipid hydroperoxides, which were found under analogous conditions by polarography (Fig. 2a).

On addition of selenium compounds to the perfusion fluid, the parameters of the ERG were restored after 30 min, when the lowering of amplitude was considerable. The compound p-bromphenylseleno-3-morpholinopropanol-2 hydrochloride was shown to restore the parameters of the ERG by 15-20%, whereas 1-phenylseleno-44-phenyl-4-hexamethyleniminobutine-2 hydrochloride restored them by 80% (Fig. 3).

To prove that the parameters of the ERG are restored through the inhibitory action of selenium-containing compounds, the dark-adapted retina was transferred to incubation medium with the addition of selenium-containing compounds after preliminary stimulation of LPO for 30 min by an iron—ascorbate system. It will be clear from Fig. 4 that the effectiveness of selenium-containing compounds during depression of the isolated retina by LPO correlates with restoration of the ERG parameters during the action of these substances.

It can be asserted on the basis of these experimental results that accumulation of LPO products in the retina of warm-blooded animals leads to depression of its electrical activity in the same way as was observed in cold-blooded animals [3]. Selenium-containing compounds, by inhibiting LPO, restore electrical activity of the isolated retina.

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