most muscle fibers. Under the electron microscope, against the background of a translucent sarcoplasm, preserved mitochondria with an electron-dense matrix and parallel arrangement of the cristae could be seen. No changes were observed in the nuclei.

The experiments thus showed that cardioplegia followed by restoration of cardiac activity can be produced with the aid of 0.25% formalin solution. Formaldehyde, by blocking processes of cell metabolism, inhibits proteolysis and promotes preservation of the structure and viability of the heart under ischemic conditions.

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EFFECT OF HYPOXIA AND FENIGIDIN ON ACTION POTENTIAL DURATION AND CONTRACTILITY OF THE FROG MYOCARDIUM

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UDC 612.172.4-06:612.273.2

Under hypoxic conditions a reduction in the force of contraction of the myocardial fibers is accompanied by a decrease in the duration of action potentials, which is determined by the inward current through the slow calcium channels and the outward potassium current [2, 5-7].

However, changes in which of these two currents lead to a decrease in the duration of the action potentials is not clear.

Accordingly, the aim of the investigation described below was to identify the principal factors determining the duration of action potentials during hypoxia. To examine this problem the action of hypoxia and of the specific calcium channel blocker fenigidin (known in the literature as BAU-1040, nifedipine, and adalat) [1, 3, 4], on the duration of action potentials and the force of contraction of a strip of the frog ventricle was studied.

Experiments were carried out in strips of frog ventricle 3-5 mm long, placed in a continuous flow chamber 10 ml in volume. Mechanical activity of the strip was recorded by means of the 6M × 2B mechanotron and N-338-2 automatic writer; square pulses 15-30 msec in duration and with a frequency of 0.2-0.3 Hz, generated by an ÉSL-1 stimulator, were applied; the intensity of the stimuli was 3 to 4 times greater than the threshold. The transmembrane action potentials were recorded by glass microelectrodes. The duration of the action potentials

KEY WORDS: hypoxia; fenigidin; duration of action potential; contractility; myocardium.

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(Presented by Academician of the Academy of Medical Sciences of the USSR Z. I. Yanushkevichus.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 91, No. 4, pp. 403-404, April, 1981. Original article submitted October 17, 1980.

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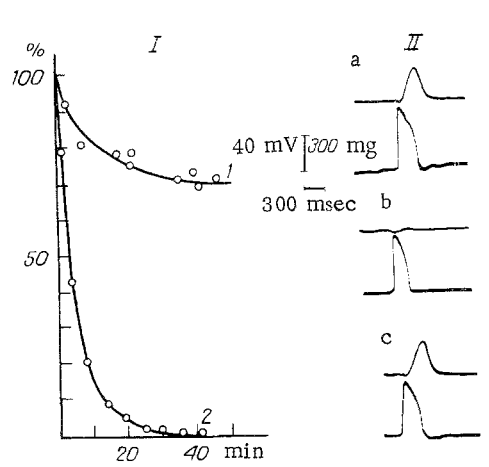

Fig. 1

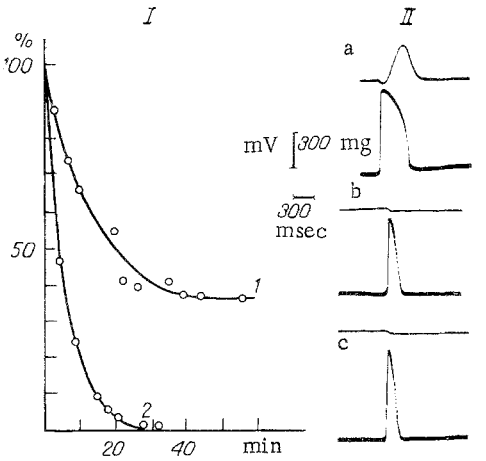

Fig. 2

Fig. 1. Effect of hypoxia on duration of action potentials and force of contraction of strip of frog ventricle. I) Change in duration of action potentials (1) and force of contraction (2) during perfusion with hypoxic Ringer's solution (curve 2 plotted exponentially, τ = 6 min, points on curve correspond to experimental values); II) simultaneous recording of action potentials and contraction; a) under normal conditions; b) after perfusion for 40 min with hypoxic Ringer's solution; c) after rinsing for 1 h with Ringer's solution containing oxygen. Top traces — contraction, bottom traces — action potentials. Abscissa, time of perfusion with hypoxic Ringer's solution (in min); ordinate, change in duration of action potentials and force of contraction (in % of initial level taken as 100).

Fig. 2. Effect of fenigidin on duration of action potentials and force of contraction of muscle strip of frog ventricle. I) Change in duration of action potentials (1) and force of contraction (2) during perfusion with physiological saline containing 3.5×10^{-5} M fenigidin; II) simultaneous recording of action potentials and contraction (a): normally; b) after action of fenigidin (3.5×10^{-5} M) for 40 min; c) after rinsing for 1 h with physiological Ringer's solution. Remainder of legend as in Fig. 1.

was measured at half-amplitude level. The initial physiological saline contained (in mM): NaCl 110, KCl 2.5, $CaCl_2$ 1.08, $C_6H_{12}O_6$ 5.5, Tris-Cl 10; pH 7.4-7.5. Hypoxic solutions were made up by displacing oxygen from the solutions with nitrogen. The action of fenigidin was studied in a concentration of $3.5 \cdot 10^{-5}$ M, for which the necessary quantity of fenigidin was dissolved in 0.5 ml ethyl alcohol and added to physiological Ringer's solution. At the end of the experiment the preparation was rinsed for 60 min with physiological Ringer's solution. All experiments were carried out at room temperature (18-22°C).

EXPERIMENTAL RESULTS

Graphs showing changes in the duration of action potentials and force of contraction (I) and examples of experimental traces (II) during perfusion of the muscle strip with hypoxic Ringer's solution are given in Fig. 1. After perfusion of the preparation for 40 min with hypoxic Ringer's solution the duration of the action potentials was reduced by 30% (curve 1 in Fig. 1, I), and contractility was completely suppressed. The dependence of the diminishing force of contraction on time can be described by an exponential curve (the continuous curve in Fig. 1, I, 2) with a time constant τ = 6 min. The action of hypoxia was reversible in character; on rinsing the preparation with oxygen-containing Ringer's solution the duration of the action potentials and the force of contraction were completely restored (Fig. 1, II, c). Similar results also were obtained in other experiments. The duration of the action potentials based on the results of 24 experiments was reduced by 37 ± 10%, whereas the time constant of the exponential decline in the force of contraction was 8 ± 2 min. In all experiments the effect of hypoxia was reversible.

Since the duration of the action potentials is partly determined by the inward current carried through calcium channels, their blocking could be one cause of its decrease during hypoxia. It was accordingly interesting to compare the action of hypoxia with that of fenigidin, a specific blocker of calcium channels, on the duration of the action potentials.

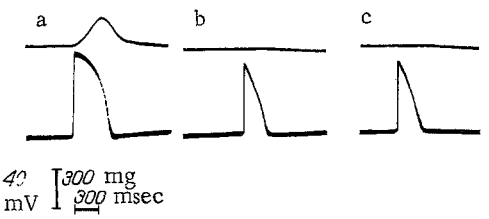

Fig. 3. Simultaneous recording of action potentials and force of contraction under normal conditions (a), after exposure to fenigidin ($3.5 \cdot 10^{-5}$ M) for 1 h (b), and after perfusion for 30 min with hypoxic Ringer's solution not containing fenigidin (c). Top traces — contraction; bottom traces — action potentials.

Changes in the duration of action potentials and the force of contraction (I) and examples of experimental traces (II) during perfusion of the preparation with physiological Ringer's solution containing $3.5 \cdot 10^{-5}$ M fenigidin are given in Fig. 2. This concentration virtually completely suppresses the inward current through calcium channels [1, 4].

The duration of the action potentials after exposure to fenigidin for 40 min, in the example given, was reduced by 64% (curve 1 in Fig. 2, I). The mean value for 10 experiments was 62 ± 2%. During this period contractility was totally suppressed (continuous curve 2 in Fig. 2, I plotted for τ = 6 min). The time for total suppression of contraction of the muscle strip, it will be noted, was the same as the time during which the duration of the action potentials reached a steady level. Subsequent rinsing of the preparation with physiological Ringer's solution affected neither the duration of the action potentials nor the force of contraction (Fig. 2, II, c), i.e., the action of $3.5 \cdot 10^{-5}$ M fenigidin was reversible.

Rinsing the preparation with hypoxic Ringer's solution not containing fenigidin, after preliminary blocking of the calcium channels with fenigidin ($3.5 \cdot 10^{-5}$ M), also caused practically no change in the duration of the action potential of the muscle strip (Fig. 3). This largely ruled out the possibility that the decrease in the duration of the action potential during hypoxia took place on account of an increase in potassium conductance.

The results thus indicate that the main factor shortening action potentials during hypoxia is blocking of the inward current through the calcium channels. Total suppression of contraction of the frog ventricle during hypoxia evidently cannot be attributed entirely to blocking of the calcium channels.

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