EFFECT OF ELEUTHEROCOCCUS ON SUBCELLULAR STRUCTURES OF THE HEART IN EXPERIMENTAL MYOCARDIAL INFARCTION

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Liquid extract of eleutherococcus (EL), like ginseng, is one of the group of adaptogens. It has a stimulating action, a tonic action if given for a long period, and it increases physical and mental working capacity and strengthens the nonspecific resistance of the body [7, 8]. Experiments have shown the positive effect of EL, whether given prophylactically, therapeutically, or for both purposes, on the time course of the electrocardiographic disturbances in myocardial infarction (MI) and on the size of the lesion, and if given therapeutically, on intensification of nucleic acid and protein synthesis in the zone of acute focal ischemia, it reduces the intensity of free-radical lipid oxidation, stabilizes membranes of subcellular structures, and increases tolerance to physical exertion [1-6]. The aim of this investigation was to determine the role of subcellular structures in the mechanism of action of EL on the heart muscle of animals with and without MI, using electron microscopy.

EXPERIMENTAL METHOD

Experiments were carried out on 95 random-bred conventional albino rats weighing 180-250 g. Of this number 8 intact animals served as the control (group 1), 32 received EL (group 2), MI

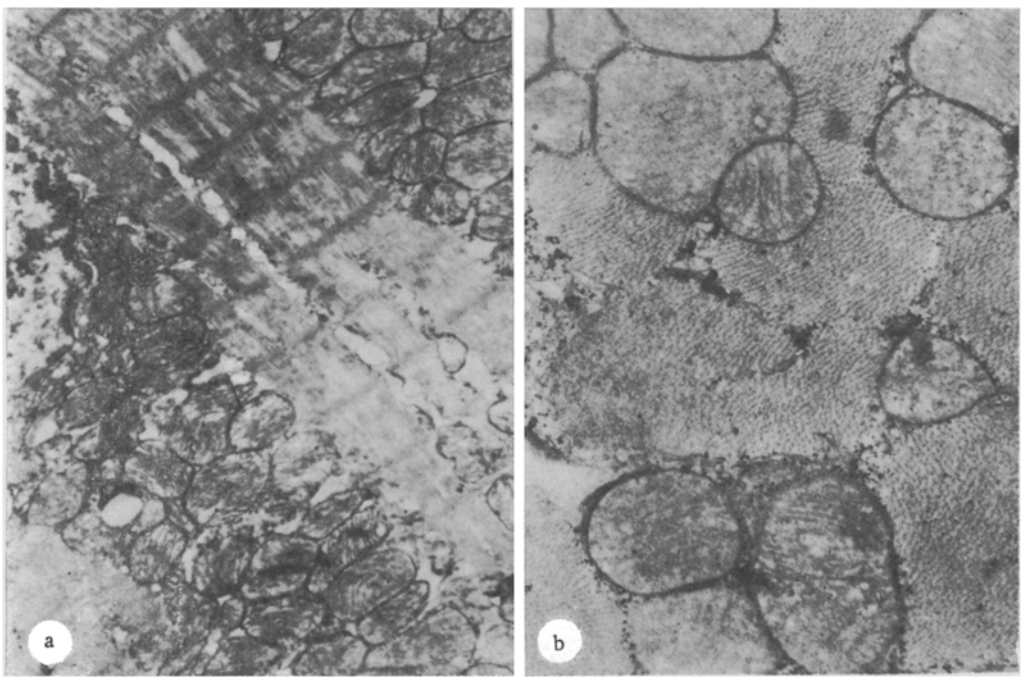

Fig. 1. Cardiomyocyte of intact rate 24 h after injection of EL. a) hyperplasia of mitochondria, secondary lysosome with lipid inclusions (17,000×); b) condensation of mitochondrial junctions, accumulation of glycogen (26,000×).

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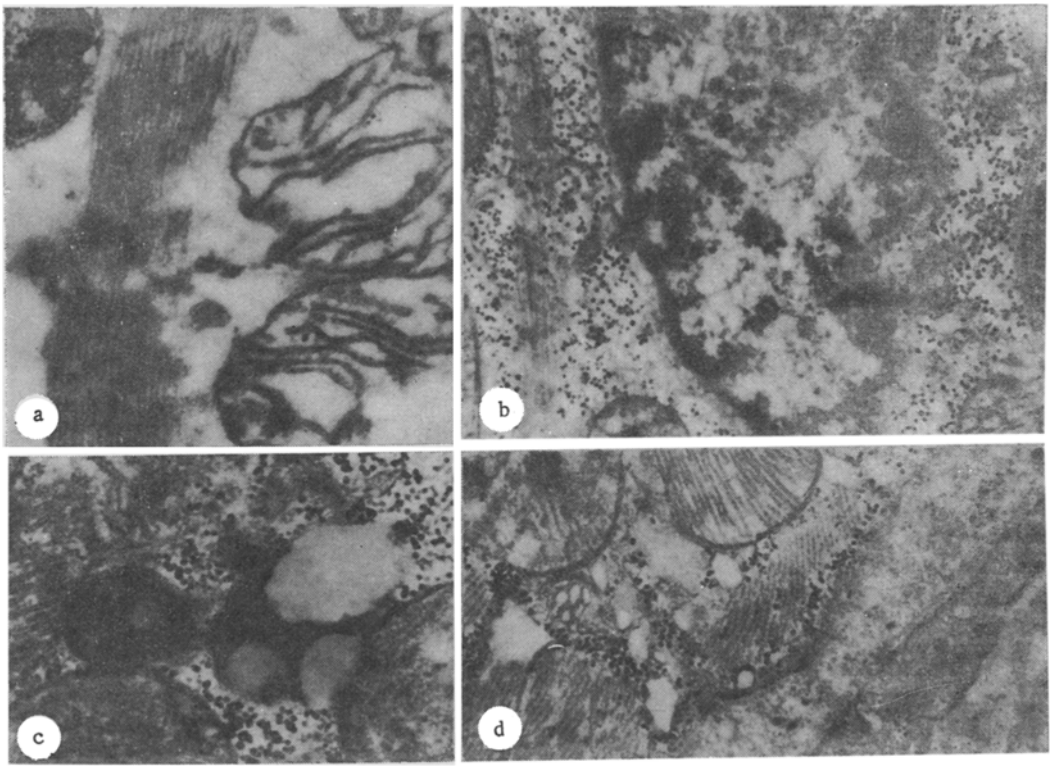

Fig. 2. Effect of EL on cardiomyocyte ultrastructure in zone of acute focal ischemia (36,000 ×). a) Marked intracellular edema and swelling of mitochondria of rat cardiomyocyte in zone of acute focal ischemia 2 h after occlusion of the left coronary artery; b) Increase in number of cytogranules and formation of new myofilaments in perinuclear zone of cardiomyocyte in acute focal ischemia 2 h after occlusion of left coronary artery and injection of EL; c) Increase in content of glycogen and its association with lysosomes, lipid inclusions, and mitochondria in rat cardiomyocyte against the background of acute focal ischemia, 24 h after occlusion of left coronary artery and injection of EL; d) Intensification of pinocytosis in plasmalemma and increase in number of cytogranules in sarcoplasm of cardiomyocytes and endotheliocytes.

was produced in 32 animals by ligation of the left coronary artery in its middle third, and these rats were treated by injection of isotonic sodium chloride solution (group 3), and 38 animals with MI received EL (group 4). The animals of group 2 received EL in the form of the liquid extract in a dose of 1 ml/kg subcutaneously, daily for 15 days, whereas the rats of group 4 received EL by the same scheme after occlusion of the left coronary artery. Tissue from the left ventricular myocardium was taken for investigation at various stages of MI, and of MI treated with EL: in the zone of acute focal ischemia 2 and 24 h, in the perinecrotic zone 3, 7, 10, and 15 days, and in the zone around the scar 30 days after occlusion of the left coronary artery. Material was taken at the same times from animals without MI, and treated with EL. The material for investigation was fixed in 2.5% glutaraldehyde solution in phosphate buffer, postfixed with OsO_4 by the usual method, and embedded in Epon-812. Ultrathin sections were cut on a Reichert Ultracut ultramicrotome, stained with lead citrate, and studied under the ÉVM-100 electron microscope.

EXPERIMENTAL RESULTS

During the first few days after injection of EL into the intact animals the number of mitochondria and the packing density of their cristae, and the content of ribosomal and glycogen granules in the sarcoplasm increased considerably in the cardiomyocytes, and lipid inclusions appeared, most frequently near the mitochondria and inside the secondary lysosomes. Pinocytosis was intensified in the plasmalemma of the cardiomyocytes and endotheliocytes (Fig. 1). These changes persisted throughout the period of injection of EL.

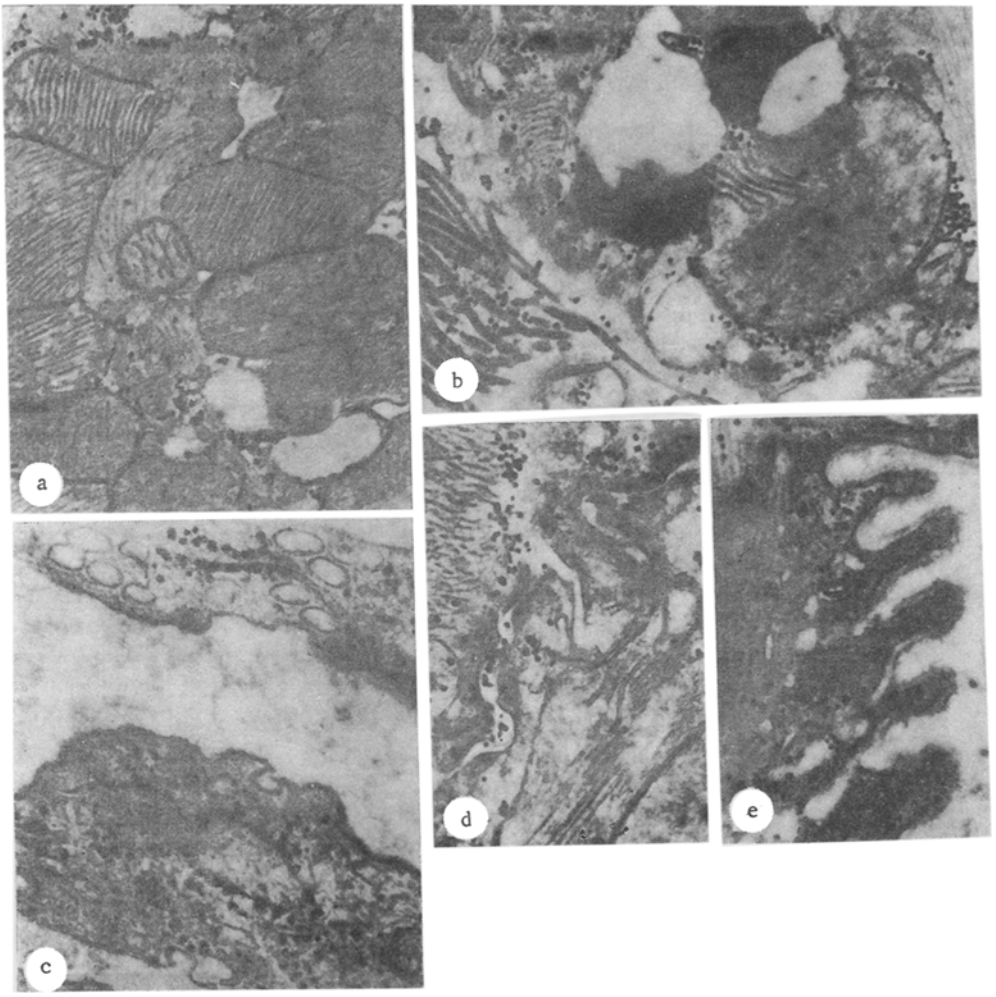

Fig. 3. Effect of EL on cardiomyocytes in zones surrounding infarct and scar. a) Hyperplasia of mitochondria, clearly defined mitochondrial junctions, accumulation of glycogen granules around lipid inclusions on 15th day after occlusion of left coronary artery (26,000×); b) Marked pinocytosis and increase in number of ribosomal and glycogen granules in an endotheliocyte on 15th day after occlusion of left coronary artery (26.000×); c) Association of lysosomes containing lipid inclusions with mitochondria and glycogen. Collagen fibers and glycogen granules in interstices on 30th day after occlusion of left coronary artery (36,000×); d) Glycogen granules in intercollated disk on 30th day after occlusion of left coronary artery (36,000×); e) Dense concentrations of glycogen granules beneath sarcolemma of a cardiomyocyte on 7th day after occlusion of left coronary artery (26,000×).

Under the influence of EL the degree of intracellular edema and of injury to the subcellular structures of the cardiomyocytes was reduced in the zone of acute focal ischemia. Signs of intracellular regeneration were observed in the cardiomyocytes more frequently than in MI not treated with EL, in the form of hyperplasia of the mitochondria, accumulation of ribosomes and polysomes, and the formation of new myofibrils. More glycogen granules and lysosomes containing lipid inclusions were observed, and the number of pinocytotic vesicles in the plasmalemma of the muscular and endothelial cells also was recorded.

In the peri-infarct zone in the early stages of MI hyperplasia of the mitochondria and the presence of clearly defined mitochondrial junctions were observed in animals treated with EL compared with the identical zone in animals with MI but not receiving EL, and also in the zone of acute focal ischemia against the background of EL, secondary lysosomes with lipid inclusions were found more frequently, and there was more glycogen in the sarcoplasm. More cardiomyocytes and capillaries with increased transport activity of the plasmalemma were found. Normalization of the structure of the myofibrils and the appearance of collagen fibers in the intercellular space were observed earlier than in animals with MI (Fig. 2).

In the zone surrounding the scar, in the late stages after MI untreated with EL, a marked decrease in the number of mitochondria and the density of the cristae in them, and weakening of mitochondrial junctions were observed in the cardiomyocytes. Most cardiomyocytes were without nuclei. In many of them zones of overstretching of myofibrils and disturbance of their orientation were observed. The glycogen content in the sarcolemma was lower than in intact animals. Only single collagen fibers were found in the intercellular space. The endotheliocytes contained few pinocytotic vesicles. Meanwhile, in the zone surrounding the scar in animals receiving EL nuclei were frequently found in the cardiomyocytes and endotheliocytes, and hyperplasia of the mitochondria and clarity of the mitochondrial junctions also were frequently seen. Glycogen was distributed universally in the sarcoplasm: between myofibrils and myofilaments, around mitochondria and lysosomes, beneath the sarcolemma, and in the endothelium of the capillaries and in the intercellular spaces. Collagen fibers were more numerous in the interstices and the intensity of pinocytosis was greater in the cardiomyocytes and endotheliocytes (Fig. 3).

The facts described above are evidence that EL reduces the severity of injury to the ultrastructures in the zone of acute focal ischemia, strengthens their intracellular compensatory hyperplasia, intensifies the structural and energy metabolism of the myocardium at all stages of development of infarction, helps to restore the structure of the myofibrils in the perinecrotic zone earlier, and protects the myocardium in the later stages after infarction against the development of destructive changes and prevents the onset of heart failure. The data indicating an increase in the number of cytogranules in the cardiomyocytes in the zone of acute focal ischemia were confirmed by the results of the writers' previous investigations, which showed an increase in the RNA content in this zone by 73% compared with that in intact animals, and by 97% compared with that in animals with MI but not receiving EL [2].

Comparison of the ultrastructural disturbances in the zone of acute focal ischemia and in the zones surrounding the infarct and scar in animals treated with EL and the dynamics of the electrocardiographic disturbances in the early stages of MI under the same experimental conditions [4] shows that the milder degree of injury to the subcellular structures in the zone of acute focal ischemia preceded diminution of the disturbances of myocardial electrical activity in the period of necrosis and correlated with the degree of the electrocardiographic disturbances in the later stages of MI.

Since administration of EL to intact animals and to animals with MI was regularly followed by the appearance of lipid inclusions and secondary lysosomes with lipid inclusions in the cardiomyocytes and by an increase in the glycogen content in the sarcoplasm, and also on the basis of previous data indicating that glycogen can be formed from lipids [9, 10], it can be tentatively suggested that EL promotes the utilization of lipids in the cardiomyocytes, activates glycogen formation from them, and thus leads to increased resistance of the myocardium to hypoxia.

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