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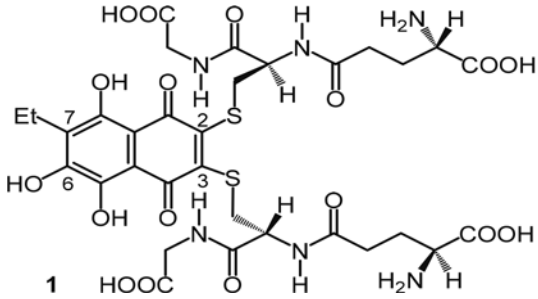
Electrocardiography study of diglutathionyl analog of echinochrome on adrenaline-induced myocardial ischemia in mice

Cardioprotective activity of 7-ethyl-2,3-diglutathionyl-6-hydroxynaphthazarin (DGE) on the model of experimental ischemia in CD1 mice was studied. The model of experimental ischemia was realized by introducing histotoxic doses of adrenaline hydrochloride. Verification of experimental ischemia was carried out by electrocardiography. Histochrome as a reference control was used. The evident cardioprotective properties of DGE were observed at a doses of 10 and 5 mg / kg

Key words: experimental ischemia, adrenaline hydrochloride, electrocardiography, cardioprotective effect; 1,4-naphthoquinone, naphthazarin derivatives, echinochrome, histochrome

Cardiovascular diseases are the most common diseases and occupy a leading position in the world mortality statistics. This fact is due primarily to the widespread coronary heart disease. For this reason, creation of drugs having cardioprotective action remains a topical task. Synthesis and studying of the compounds possessing potential cardioprotective properties are carried out in G.B. Elyakov Pacific Institute of Bioorganic Chemistry of Russian Academy of Sciences. Hydroxynaphthazarins belong to this group of compounds. Previously, the high cardioprotective activity of these compounds in *in vivo* experiments, comparable with echinochrome, was demonstrated [1].

Present research aim was studying of influence 7-ethyl-2,3-diglutathionyl-6-hydroxynaphthazarin (DGE, **1**) on adrenaline-induced myocardial ischemia (MI) in CD-1 mice.



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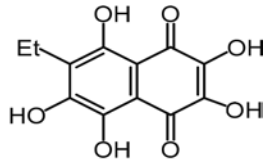

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Experiments with animals were carried out on mature CD-1 mice of both sexes, 8-10 weeks of age, weighing 20-22 g. MI was induced by a single subcutaneous injection of 0.1% adrenaline hydrochloride solution at a dose of 5 mg/kg. Histochrome (echinochrome **2** is active substance) at a dose of 1 mg/kg was used as a reference drug. Changes in the electrical conductivity of the

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heart were recorded by ECG. Before recording the ECG, the mouse was anesthetized using a solution of xylazine at a dose of 27 mg/kg animal weight. Electrocardiogram data were registered from limb lead II with the ECG recorder (Small Animal Instruments, USA). Electrocardiogram data was fixing for 1 hour. It was revealed that a steady electrocardiogram changes were recorded in 15 min after adrenaline injection. Ppeak and ST magnitude, RR and QT intervals, heart rate significantly changed relative to control data. Other ECG parameters such as Pwave width, interval PR, R peak magnitude and QRS complex width remained invariable. DGM subcutaneous injection in doses of 10, 5 and 1 mg/kg was carried out 15 min after adrenaline injection. The effectiveness of DGE was assessed by its ability to return parameters altered by adrenaline to intact parameters, especially ST and QT data, because they indicate ventricle repolarization changes. It was shown that in 15 minutes after adrenaline, DGM injection in a dose of 1 mg/kg significantly reduced QT interval duration, but did not reduce increased ST segment. As for DGM in doses of 10 and 5 mg/kg, the values of both parameters were reduced, which indicates the ventricular repolarization time normalization.

Thus, it is shown that 7-ethyl-2,3-diglutathionyl-6-hydroxynaphthazarin exerts a positive impact on dynamics of processes cardiac muscle recovering at mice with an induced myocardial infarction.

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