THE EFFECT OF GOSSYPOL DIAZOIMINO DERIVATIVES ON THE HIGH CONDUCTIVITY PORES OF HEART MITOCHONDRIA IN EXPERIMENTAL MYOCARDIA

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Abstract

In recent studies it is proved that mitochondria plays a major role in cardiomyocyte function, regulation of apoptosis and cell necrosis [1]. The functional activity of mitochondria depends on the activity of many ion channels, and the physiological importance of the megapore (mPTP -mitochondrial permeability transition pore) is very important. MPTP is a channel that physiologically regulates the release of Ca2+ ions from the mitochondrial matrix and is involved in the homeostasis and signaling of Ca2+ ions between the cell cytosol and the matrix during the normal life of cells [6]. Mitochondrial megapore (mPTP) is a channel that passes through the outer and inner membranes of mitochondria and it is consists of potential-dependent anion channel (VDAC), adenine nucleotide translocase (ANT) and cyclophilin D protein [3] . Mitochondrial megapores have an active conduction and they are highly permeable to Ca2+ and in the cell show an active conformation when the charge of ions increases, regulate the homeostasis of ions in the matrix and thus the control of metabolic processes [2]. Experimental studies have shown that an increase in the amount of Ca2+ in the mitochondria , which in turn stimulates the opening of mRTR, and the release of Ca2+ ions from the mitochondria, correspondingly, leads to the entry of H+ ions into the mitochondrial matrix [4]. A sharp increase of permeability of mitochondrial megapore is observed in certain pathological conditions such as ischemia, neurodegenerative diseases, toxic hepatitis, diabetes mellitus and various hypoxic conditions[5]. It is known that the cardioprotective value of bioactive substances that inhibit the state of cardiac mPTP is high in myocarditis and is currently being widely studied in research.

Keywords: heart, mitochondria, myocarditis, mPTP channel.

Objective:

The research consists of comparative study of the effect of derivatives of polyphenols gossypol diazoimino YaN-1 and YaN-2 with quercetin flavonol on the heart mitochondria of in the experimental model of myocarditis induced by adrenaline.

Research methods

Experiments were carried out in vivo in purebred white male rats weighing 180-200g. Heart mitochondrias of experimented rat were isolated by using differential centrifugation. The composition of the separation medium is as follows: 250 mM sucrose, 10 mM tris-chloride, 1 mM EDTA, pH 7.4.

Results

The turgescence of heart mitochondria was realized with the usage of CaCl2 in concentration of 20 μM. In the presence of CaCl2 20 μM as an incubation medium the turgescence of rat heart mitochondria was scored as 100% as a control. According to the obtained results, the II group of animals with experimental myocarditis model of heart mitochondria caused a sharp increase of turgescence compared to the control (I group). Using of 0.1 ml of 0.1% adrenaline solution to rats for 7 days resulted the growth of PTP permeability in cardiac mitochondria. The cardiac mitochondria was isolated by carrying out pharmacotherapy for 10 days in: III group of rats with experimental myocarditis by using induced gossypol diazoimino derivative YaN-1 20 mg/kg, IV group of rats by using gossypol diazoimino derivative YaN -2 to polyphenol 10 mg/kg, V group of rats by using of quercetin flavonol 20 mg/kg. Thus, when experimental myocarditis induced III, IV and V group of rats were treated with pharmacotherapy with gossypol diazoimino derivative YaN-1, YaN-2 and quercetin flavonol, respectively , PTP opening in heart mitochondria was 9.5% compared to control group II; 24% and 18.5% reliable reduction was found .

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