EFFECT OF SOPHOROFLAVONOSIDE AND NARCISSIN ON THE MITOCHONDRIAL ATP-DEPENDENT POTASSIUM CHANNEL

Sharipova M.K[1].,
Pozilov M.K[1].,
Mirzaolimov E.I[2].,
Nishanbaev S.Z[3].
[1]National University of Uzbekistan named after M.Ulugbek
[2]Namangan State University
[3]Institute of Chemistry of Plant Substances named after Academic S. Yu. Yunusov

Introduction

One of the most studied mitochondrial factors that regulate the metabolic and functional activity of the cell is the ATP-dependent potassium channel of the inner mitochondrial membrane (mitoK$_{ATP}$-channel). Currently, the biophysical properties of the mitochondrial potassium channel and its physiological significance are well studied [1; 3]. Its participation in the formation of the body's resistance to oxygen deficiency (hypoxia) is shown. A number of scientific studies have shown the important regulatory role of the mitoKATP channel in triggering the body's adaptive reactions to hypoxia [5; 1]. Therefore, the molecular structure of this mitochondrion and the ion transport systems located in its membrane can be a specific target for the action of biologically active compounds. To this end, in our next experiment, the effect of SPL and narcissin polyphenols on the K$_{ATP}$-channel of cardiac mitochondria was studied in vitro under experimental conditions.

Research Methods

Sophoraflavonoside (SFL) (kaempferol-3-O-β-D-sophoroside) is isolated from Crocus sativus L., a plant belonging to the Iridaceae family. Narcissin isolated from plants Alhagi canscens (Regel) B. Keller &Sharp belonging to the Fabaceae family was also used.

The experiments were carried out *in vitro* on outbred white male rats weighing 200-220 g. Mitochondria were isolated from rat heart tissue by differential centrifugation. The permeability of the mitoK$_{ATP}$-channel was determined by changing the kinetics of swelling of mitochondria (0.3–0.4 mg/ml of protein) in an open cell (volume 3 ml) at 540 nm of the optical density of the mitochondrial suspension with constant stirring at 26°C.

Results

According to the results obtained, the conductivity of the mitoK$_{ATP}$-channel (control) in the absence of ATP in the incubation medium was estimated as 100%. While the activity of the cardiac mitoK$_{ATP}$-channel was inhibited by 62.6±4.4% in the presence of ATP in the incubation medium, it was found that the activity of SPL did not undergo significant changes when exposed to 10 μm. An increase in the concentration of the flavonoid SFL to 20-30 μM

led to the activation of the mitoK$_{ATP}$-channel of the heart by 17.4±1.2% and 21.3±2.2%, respectively, compared with the state in which ATP was present. It was found that SPL at a concentration of 40-50 μM acts as an effective activator of the mitoK$_{ATP}$-channel, while at higher concentrations the activity is preserved.

In our next in vitro experiment, we studied the effect of the flavonoid narcissin on the activity of cardiac mitokatef channels. It was found that the activity of the cardiac mitoK$_{ATP}$-channel in the presence of ATP is inhibited by 59.2±4.1% compared with the control group. High concentrations of the flavonoid narcissin in the incubation medium have been found to upregulate cardiac mitocatef channel activity compared to existing ATP conditions. At a narcissin concentration of 10 μm, the effect was not noticeable. Narcissin concentration at 20 μM was noted to slightly activate cardiac mitokatef channel activity compared to existing ATP conditions. High concentrations of 40 and 50 μM narcissin have been found to increase the activity of cardiac mitokatef channels. Therefore, selective concentrations of SPL and narcissin at 30, 40, and 50 μm had an activating effect on the cardiac mitoK$_{ATP}$-channel.

Therefore, a narcissus flavonoid concentration of 10-50 μM activated the cardiac mitokatef channel *in vitro*. Activation of the mitoK$_{ATP}$-channel plays a very important role in the mechanisms of adaptation of cardiomyocytes to conditions of hypoxia and ischemia. Functional and structural changes in the cells of body tissues under conditions of hypoxia and ischemia, as well as the fate of the cells themselves, directly depend on the functional activity of mitochondria and the factors that regulate their proteins. An analysis of the literature showed that in a complex system of cellular regulation, the processes of adaptation of cardiomyocytes to a lack of oxygen and during ischemia, the mitoK$_{ATP}$-channel receives the most active part [4; 2]. The activating effect of SPL and narcissin on the mitoK$_{ATP}$-channel can be explained by activation of the protein subunit of the channel.

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