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EFFECT OF POLYPHENOL COMPOUNDS ON LIVER MITOCHONDRAL ATGF-dependent POTASSIUM CHANNEL ACTIVITY IN CCL4-INDUCED TOXIC HEPATITIS

Mallayeva Majvudaxon Makhramovna
Samarkand State Medical University1, Samarkand, Uzbekistan

Mustafakulov Muhammadjon Abduvaliyevich
National University of Uzbekistan Jizzakh Branch2, Jizzakh, Uzbekistan

ABSTRACT

Hepatoprotective agents have a pronounced therapeutic effect in acute hepatitis models (poisoning with CCl4, paracetamol, D-galactosamine, and allyl). Hepatoprotective agents prevent the death of animals, inflammatory infiltration of the stroma, the development of necrosis, protein and lipid degeneration of hepatocytes, and help restore the function of their specific organelles, such as the endoplasmic reticulum, mitochondria, and lysosomes. Toxic hepatitis leads to an imbalance between oxidative phosphorylation and antioxidant systems in liver mitochondria. Increased free radical concentration due to impaired electron transport through respiratory chain complexes alters the permeability of mitochondrial ion channels. Under conditions of toxic hepatitis or excessive oxidative stress, activation or inhibition of the ion transport systems of the inner membrane of liver mitochondria can occur. Mitochondrial ion channels are identified as targets for the majority of currently available drugs.

INTRODUCTION

The aim of the study was to investigate the effect of polyphenolic compounds on the activity of hepatic mitochondrial ATP-dependent potassium channels in CCl4-induced toxic hepatitis.

MATERIALS AND METHODS

Tetrachloromethane (CCl4) was induced by intraparenteral administration of 50% solution in olive oil at a dose of 2 ml/kg twice a day [17]. The drugs were Slimarin (pharmacological trade name Karsil) at a dose of 50 mg/kg, rutin 10 mg/kg, gossitan 10 mg/kg, and then orally administered at a dose of 10 mg/kg for 7 days after hepatitis induction. Liver tissue homogenate was isolated by differential centrifugation. We isolated 150-200 grams of rat liver tissue homogenate.

RESULTS AND DISCUSSION

One such molecular target for hepatoprotective agents is the ATP-dependent potassium channel located in the inner mitochondrial membrane. The entry of K+ into the mitochondrial matrix through the mitoKATR is accompanied by an increase in the volume of the matrix in the mitochondria. This activates K+/H+ antiporters and creates a useless K+ cycle through the inner mitochondrial membrane. A large amount of information has been provided on the function of the mitochondrial ATP-dependent potassium channel structure, its role in ischemia-reperfusion, and its pharmacology. However, there is almost no information on changes in

mitochondrial ATP-dependent potassium channel conductance in pathological processes and the effects of bioactive substances on them. In our next experiment, we aimed to study the effect of glabra and sumac polyphenols on rat liver mitoCATF-channel activity under conditions of toxic hepatitis.

In vivo experiments were conducted to study the effect of bioactive substances on rat liver mitoCATF-channel activity under CCl4-induced toxic hepatitis conditions. Rats were divided into 5 groups for the experiment. Group I was the control group (healthy), Group II was the CCl4-induced toxic hepatitis group, Group III was the toxic hepatitis + glabra, Group IV was the toxic hepatitis + sumac polyphenols, and Group V was the toxic hepatitis + quercetin flavonoid group (Fig. 1).

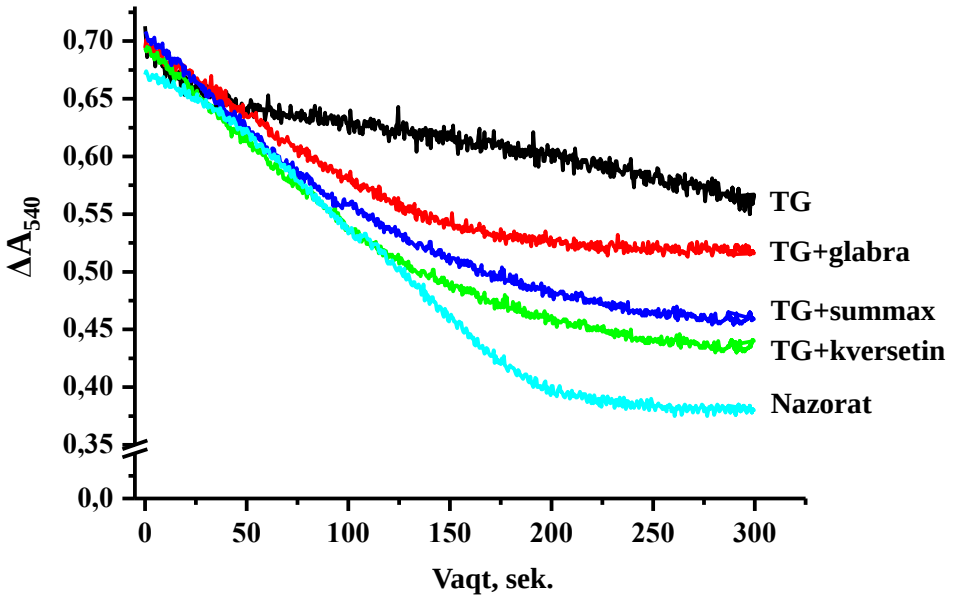

Figure 1. Effects of glabrata, sumac, and quercetin compounds on rat liver mitoCATF-channel activity under CCl4-induced toxic hepatitis conditions (original figure).

In rats of group II, which were induced with toxic hepatitis, the liver mitokaTF-channel permeability was inhibited by 49.8% compared to the control group. In rats of group III, which were induced with toxic hepatitis, the liver mitokaTF-channel permeability was activated by 21.9% compared to the group II (Fig. 2). Mitochondria were isolated from the livers of group IV rats with toxic hepatitis treated with sumac polyphenol. It was found that the mitochondrial ATP-channel conductivity of the isolated mitochondria was activated by sumac polyphenol by 69.2% compared to group II. For comparative purposes, it was found that the flavonoid quercetin increased the hepatic mitoCATF-channel activity of group V rats with toxic hepatitis by 73.9% compared to group II.

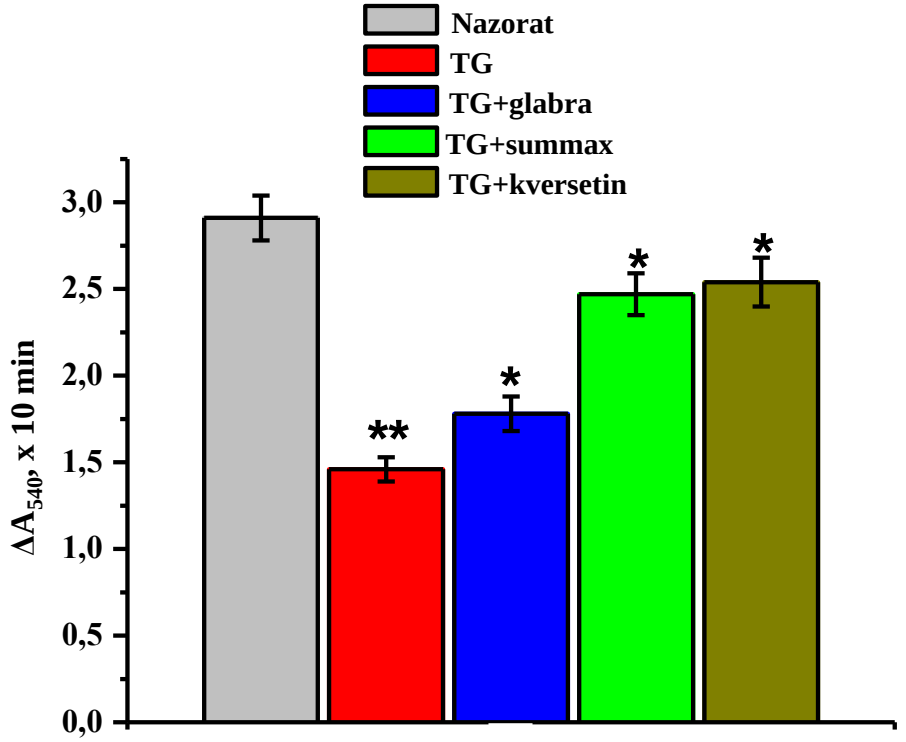

Figure 2. Effects of glabrata, sumac, and quercetin compounds on rat liver mitoCATF-channel activity under CCl4-induced toxic hepatitis conditions (original figure) (p<0.05; n=5).

Thus, in conditions of toxic hepatitis, rat liver mitoCATF-channels were inhibited compared to controls. Inhibition of liver mitoCATF-channels may lead to a decrease in the flux of potassium ions into the matrix. A decrease in the flux of potassium ions may lead to a decrease in the potential value of the inner mitochondrial membrane. This may disrupt the volume control of the mitochondrial matrix and other physiological processes. Selected polyphenolic compounds may increase mitochondrial permeability for K+ ions, provide membrane stability, and allow for evaluation of antitoxic properties under conditions of toxic hepatitis induced by CCl4.

CONCLUSION

Changes in hepatic mitochondrial ATP-channel activity were recorded based on changes in optical density in the appropriate incubation medium and in the presence of ATP.

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