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COMPARATIVE EFFECT OF "AS LUPINUS" AND GLYCORASMULIN ON ATP-DEPENDENT POTASSIUM CHANNEL ACTIVITY IN SQUID LIVER MITOCHONDRIA IN ALLOXAN DIABETES

Ibragim Rakhmanovich Askarov
Professor, Department of Chemistry, Andijan State University, Doctor of Science
ORCID number- https://orcid.org/0000-0003-1625-0330

Charosxon Sanjarbek qizi Abdujabborova
Fergana Medical Institute of Public Health. Teacher of the Department of Traditional Medicine and Pharmacology
ORCID raqami- https://orcid.org/00090000-3150-3039

Abstract
In this article, when examining the antioxidant activity of a mixture of Japanese safflower (lat. Styphnolobium japo'nicum) and Lupin (lat. Lupus) plants found in Uzbekistan, high antioxidant activity was detected in a 1:1 ratio, so we created a biological food supplement for the treatment of diabetes from this 1:1 ratio and named it "As Lupinus". In order to analyze the biological activity of the "As Lupinus" food supplement, the effect of the "As Lupinus" food supplement on the amount of glucose and insulin in rat blood plasma in alloxan diabetes was studied at the Tashkent Institute of Bioorganic Chemistry using the in vivo method. The aim of the study was to conduct preclinical testing of the biological activity of this "As Lupinus" food supplement and to create and apply it in practice.

Keywords: Japanese safflower (lat. Styphnolobium japo'nicum), Lupine (lat. Lupus), glucose, insulin, MDA, mPTP, mitoKATF, LPO, Alloxan ("Lachema" "Chemapol" Czech Republic), EGTA, EDTA, KH2PO4, K2HPO4, Hepes, KCl, MgSO4, succinate, oligomycin, rotenone, ATF ("Serva", Germany); sucrose, tris-HCl, CaCl2.

Introduction

Mitochondrial potassium channels have been described as important factors in cell survival and death. Activation of mitochondrial potassium channels, such as ATP-gated or calcium-activated large-conductance potassium channels, can have cytoprotective effects in cardiac or neuronal tissues. Activation of mitochondrial potassium channels or inhibition by certain drugs can be used to regulate cytoprotection or cell death [Wrzosek A., et al., 2020]. Studies have shown that the plasma membrane of cells (β-cells, cardiomyocytes, hepatocytes, brain cells, kidneys and other cells) contains K+ channels with selective conductance, and these ion channels are regulated based on changes in ATP concentration present in the cell cytoplasm and are called ATP-dependent K+ channels [Das M., 2003]. A characteristic feature of these ion channels is that the sufficient amount

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of ATP in the cytoplasm ensures that the channels switch to the closed state and their permeability has the lowest value. When the amount of ATP decreases, these channels are activated and switch to the open state, that is, an increase in the permeability value is observed. It is noted that in cases of ischemia in heart cells, the regulation of the KATF channel may play an important role in the development of effective protective agents. However, in diabetes, there is almost no information on the dysfunction of the KATF channel located in the plasma and mitochondrial membranes and the mechanisms of action of chemical, biologically active compounds on them. For this purpose, the effect of biologically active substances isolated from plants on the mitoKATF channel of the liver of rats in the alloxan diabetes model was studied.

PROCEDURE OF CONDUCTING THE RESEARCH

The study of the dysfunction of the hepatic mitoKATF-channel in alloxan diabetes and the effect of "As Lupinus" and glucosamulin on them was carried out in 4 groups of animals. This was done using a method based on the light transmission properties of the mitochondrial suspension isolated from the livers of animals treated with pharmacotherapy with healthy (group I), alloxan-diabetes (group II), alloxan diabetes + "As Lupinus" 20 mg/kg (group III) and alloxan diabetes + glucosamulin 50 mg/kg (group IV). The optical density of the mitochondrial suspension changes under the influence of plant compounds and mitoKATF-channel diabetes, which occurs directly on the basis of matrix depletion.

In this experiment, to determine whether the regulation of mitoKATF-channel in the ATP-dependent state under the influence of "As Lupinus" and glucosamulin in diabetes was changed, the incubation medium was continued with the presence of ATP. In the experiments, it was observed that the mitoKATF-channel activity of the liver mitochondria of group II rats induced by alloxan diabetes decreased by 40.2% compared to the control group (Figure 8). As a result of the administration of "As Lupinus" and glucosamulin to rats induced by alloxan diabetes, their mitoKATF-channel activity increased by 30.2% (group III) and 27.4% (group IV), respectively, compared to the alloxan diabetes group.

Thus, in alloxan diabetes, the activity of the hepatic mitoKATF channel was increased under the influence of "As Lupinus" and glucorasmulin, as a result of which an increase in the permeability of the membrane for K+ ions was observed.

Thus, in the in vivo diabetes model, the activity of the hepatic mitoKATF channel is activated under the influence of "As Lupinus" and glucorasmulin pharmacotherapy, which can ensure homeostasis of potassium ions in the matrix and cytosol. It was found that in intact cells, potassium transport through the mitoKATF channel does not affect other functions of mitochondria, such as oxidative phosphorylation and potassium transport [Skarga Yu.Yu., 1987]. Activation of the mitoKATF channel briefly changes the gradient cycle between the K+ uniporter and the K+/N+ antiporter. This process can continue until the rate of potassium exit from the matrix equals the rate of entry. Free radicals that occur under pathological conditions have an activating effect on the mitoKATF channel [Raha S., 2001]. Changes in the functional activity of the mitoKATF channel under alloxan diabetes were observed mainly in the presence of ATP in the incubation medium.

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Thus, functional changes in the KATF channel under alloxan diabetes may lead to a decrease in the influx of K+ ions into the matrix, a decrease in Δψm, and a disconnection of oxidative phosphorylation processes. In pathological processes, as well as in experimental diabetes, inhibition of the mitoKATF channel may be associated with a decrease in the concentration of adenine nucleotides.

RESULTS AND DISCUSSION

The creation of new drugs for the treatment of diabetes mellitus, the identification and pure isolation of local plant substances with hypoglycemic properties, the study of their corrective mechanisms of action at the molecular, cellular and tissue levels are one of the urgent tasks of modern medicine, physiology and pharmacology. Compounds with hypoglycemic properties isolated from plants differ from hormonal and chemically synthetic drugs in their physiological activity and pharmacological effects. These compounds, unlike synthetic drugs (sulfone urea preparations, biguanides), do not have a toxic effect on cells, membranes and mitochondria. In order to identify membrane disorders of mitochondria in experimental diabetes and correct them with natural substances, the hypoglycemic properties of biologically active compounds were evaluated in this master's thesis. Also, disorders of rat liver mitochondria in diabetes were identified, and the mechanisms of their corrective action with hypoglycemic substances were studied. The doses of “As Lupinus” and glucorazmulin that reduced blood glucose levels in animals under alloxan diabetes conditions were as follows: “As Lupinus” 20 mg/kg; glucorazmulin 50 mg/kg;

In the future, the identified properties of these compounds and the developed approaches can be used to create antidiabetic drugs for the treatment of diabetes.

CONCLUSION

The composition of the biological food supplement "As Lupinus" contains the fruit and leaves of Japanese safflower, and the seeds of Lupin flowers in a 1:1 ratio. In order to analyze the biological activity of this food supplement, the effect of this food supplement on the level of glucose and insulin in the blood plasma of rats with alloxan diabetes was studied in vivo. According to the results, oral administration of "As Lupinus" to rats with experimental diabetes at a dose of 20 mg/kg for 10 days reduced the level of glucose and total cholesterol in their blood plasma. It was found that insulin secretion increased. Combining scientific medicine and folk medicine, it is recommended to produce and put into practice "As Lupinus" antioxidant food supplements that help prevent and treat diabetes, anti-inflammatory, nervous diseases, joint diseases, gastrointestinal inflammation, liver, spleen, cardiovascular diseases, and many diseases caused by immunodeficiency.

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