THE EFFECT OF DIAZAAMINO DERIVATIVES OF GOSSYPOL ON THE PROCESS OF LIPID PEROXIDATION IN LIVER MITOCHONDRIAL MEMBRANES OF RATS WITH STREPTOZOTOCIN-INDUCED DIABETES.

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Introduction. Under streptozotocin-induced diabetic conditions, the transition of the liver mitochondrial permeability transition pore (mPTP) to its open conformation is associated with the process of membrane lipid peroxidation. In this study, the effect of polyphenols on the Fe^{2+}/citrate-induced lipid peroxidation (LPO) process in rat liver mitochondria under STZ-induced diabetes was investigated. It is well known that mitochondrial lipids are essential for maintaining the integrity and function of the mitochondrial membrane. Iron and iron complexes stimulate LPO [Gogvadze V., 2003]. To determine the Fe^{2+}/citrate-induced lipid peroxidation (LPO) process in liver mitochondria and to ensure the accuracy of the method, the LPO process was examined in liver mitochondria under incubation conditions without the addition of Fe^{2+}/citrate to the medium. Under these conditions, where Fe^{2+}/citrate was absent from the incubation medium, the LPO process did not occur. Thus, in experimental conditions, without the presence of Fe^{2+}/citrate (i.e., without inducers), LPO resulting from mitochondrial swelling did not take place. This confirms that the LPO process is not initiated without Fe^{2+}/citrate. Streptozotocin (STZ) disrupts the secretory function of the pancreas and acts as a stress factor on other cells as well, primarily impairing the body's antioxidant defense system. This leads to increased formation of reactive oxygen species (ROS)-such as superoxide anion radicals, hydroxyl radicals, hydroperoxides, etc.-along with enhanced lipid peroxidation (LPO) and increased permeability of cellular and mitochondrial membranes [Fomenko S.E., et al., 2023].

Materials and Methods. The experiments were conducted on healthy male white rats weighing 180-200 grams. The laboratory animals were maintained under standard conditions in a vivarium and fed a standard diet. Streptozotocin was used to induce diabetes in the experimental animals.

The rats selected for the experiment were divided into groups: group I – Control (n=5), Group II – Experimental (STZ-induced diabetes, n=5), Group III – Experimental (STZ-induced diabetes + YaN-2 at a 6:1 ratio, n=6), Group IV – Experimental (STZ-induced diabetes + YaN-2 at a 4:1 ratio, n=6), Group V – Experimental (STZ-induced diabetes + quercetin).

In Groups II, III, IV, and V, diabetes was induced by a single intraperitoneal injection of streptozotocin at a dose of 50 mg/kg (in 0.2 ml of 5% distilled water solution) after 24 hours of fasting [Aghzamov Kh., 1983]. Blood glucose levels were monitored every three days by taking blood samples from the diabetic rats.

Twelve days after the streptozotocin injection, when blood glucose levels exceeded 11 mmol/L, the treatment began: animals in Group II received 0,2 ml of 0,9% NaCl solution once daily, while Groups III and IV received the test compound orally once daily for 10 days. Experimental procedures were carried out after glucose levels dropped below 11 mmol/L.

Liver mitochondria were isolated from rats by differential centrifugation using the W.C. Schneider method [Schneider et al., 1951].

Results and Analysis: In the control group (Group I) consisting of healthy rats, the optical density (OD) of the Fe^{2+}/citrate-induced lipid peroxidation (LPO) process in liver mitochondria was 0,135 ΔA540/min. In Group II, which included STZ-induced diabetic rats, the OD value of Fe^{2+}/citrate-induced LPO was 0,339 ΔA540/min, indicating a 151,1% increase compared to the control group.

In Group III (STZ-diabetic rats treated with the water-soluble supramolecular complex of the diazaamino derivative of gossypol, YaN 6:1), the OD value for Fe^{2+}/citrate-induced LPO in liver mitochondria was 0,282 ΔA540/min, showing a 16,9% reduction compared to the untreated STZ-diabetic group (Group II).

In Group IV (STZ-diabetic rats treated with the YaN 4:1 water-soluble supramolecular complex), the LPO OD value was 0,325 ΔA540/min, reflecting a 21,8% reduction compared to Group II.

In conclusion, the water-soluble supramolecular complexes YaN 6:1 and YaN 4:1 of the diazaamino derivatives of polyphenols contribute to the recovery of liver mitochondrial integrity under streptozotocin-induced diabetic conditions.

References

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