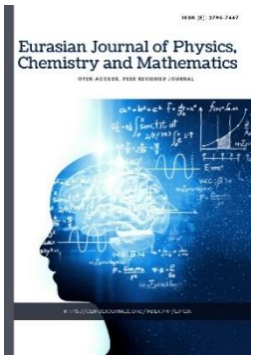

The study of the hypoglycaemic activity of GA, menthol and its GA: Mt (4: 1) supramolecular compounds in alloxan diabetes mellitus

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ABSTRACT

In this article, we investigated the effect of GA and menthol supramolecular complex on blood glucose level and glycogen synthesis in liver of rats under conditions of alloxan-induced diabetes in the *in vivo* experiments we performed. According to the obtained results, menthol, GA and the GA:Mt (4:1) supramolecular compound derived from them can restore the functional impairment of liver mitochondria in alloxan-induced diabetes and inhibit the peroxidation of lipids in the membrane. In this case, the hypoglycemic activity and mitochondrial membrane stabilizing properties of the supramolecular compound GA:Mt (4:1) in the conditions of alloxan diabetes were shown to be stronger than menthol, GA and its compounds GA:Mt (2:1) and GA:Mt (9:1).

Keywords: Menthol, glycyrrhizic acid, homeostasis, alloxan diabetes, glycogen, lipid peroxidation, supramolecular complex.

Introduction

Menthol ($C_{10}H_{20}O$) is a monoterpenoid that exhibits many biological activities in experiments. Currently, their biological activity is being studied in many scientific laboratories. Menthol monoterpenoid has been shown to exhibit gastric ulcer repair using ethyl alcohol [1]. A dose of 50 mg / kg of menthol has a gastroprotective effect and exhibits apoptosis, anti-inflammatory and antioxidant activity in cells of the gastric mucosa [1]. Menthol monoterpenoid also affects the physiological processes associated with Ca^{2+} ions present in the cell. Menthol exhibits relaxant activity by inhibiting Ca^{2+} channels in smooth muscle cells of the rat aorta and coronary blood vessels [2]. Based on the literature, it can be said that the relaxant effect of menthol may lie in the blockade of potential-dependent Ca^{2+} -channels. The effect of menthol on the membrane is due to its hydrophobic properties. The breakdown of menthol and other monoterpenes that are part of the biological composition affects membranes and leads to a number of changes. The effect of hydrophobic compounds on membranes is manifested by altering the physicochemical properties of integral proteins (e.g. ion channels, carriers) and the phospholipid layer and by indirectly affecting channel function [3]. In vitro studies have shown that menthol and other hydrophobic monoterpenes affect membrane ion channels in concentrations in the range of 10 μM to 10 mM .

Currently, antioxidant and mitoprotective properties of megaferon and GA + quercetin supramolecular complexes in rat liver and brain mitochondria have been identified, which are mainly manifested in young animals. Aging of animals has been shown to have a corrective effect of megaferon and glycyrrhizinic acid + quercetin complex, which reduces the activity of respiratory chain enzymes in the liver and brain mitochondria, decreases ATF (adenosine triphosphate) synthesis and decreases protein biosynthesis. This will allow in the future to create drugs with geroprotective activity on the basis of supramolecular complexes megaferon and GA + quercetin. However, the biological activity of menthol and GA-based supramolecular compounds has been little studied at present, and their effects on the functional parameters of rat liver mitochondria have been almost never studied. For this purpose, in our experiments, the effects of menthol, GA and their

supramolecular complexes obtained in different proportions on rat liver mitochondria in in vitro and in vivo studies were studied. These results were carried out in collaboration with scientists from the Institute of Biophysics and Biochemistry of the Ministry of Higher and Secondary Special Education.

The results obtained and their analysis

Glycogenesis processes in the liver play an important role in the maintenance of glucose homeostasis in blood plasma . Glycogen is an important reserve for the body, a polysaccharide, which can be up to 20% in the liver. In diabetes mellitus, a decrease in glycogen synthesis in the liver is observed. In determining the hypoglycemic and antidiabetic activity of many compounds, the amount of glycogen in the liver is checked along with the amount of glucose in the plasma. In our in vivo experiments, it was found that the supramolecular complex of GA and menthol partially restored blood glucose levels and glycogen synthesis in the liver of rats in diabetes conditions caused by alloxan. The effect of GA, menthol and its supramolecular complex on the amount of glucose in the blood of rats and the amount of glycogen in liver tissue in patients with diabetes caused by alloxan is shown in the following table (Table 1).

The results showed that in alloxan diabetes, a sharp increase in blood glucose was observed compared to control, and a sharp decrease in glycogen in the liver. Impairment of glycogen synthesis in the liver in alloxan diabetes is likely to be associated with decreased glycogen synthetase activity and decreased glucose oxidation due to a deficiency in the pyruvate dehydrogenase complex. Oral administration of menthol (50 mg / kg), GA (50 mg / kg) and GA: Mt (4: 1) (50 mg / kg) to animals with diabetes mellitus once daily for 10 days results in increased glucose levels and glycogen in the liver. the amount was found to decrease relative to control (Table 1). When rats treated with the Glox, menthol, and supramolecular complex of the alloxan diabetes model were found to be effective at lowering blood glucose and increasing glycogen in the liver at GA: Mt (4: 1) (Table 1).

Effect of supramolecular complex of GA and menthol on the amount of glucose in the blood of rats and glycogen in liver tissue in rats in alloxan diabetes (M ± m, n = 4)

Animal groups	The amount of glucose mmol / l	Glycogen content in mg / 100 g% relative to body weight
Control	5,3	100
Alloxan diabetes	17,2	41,0
Alloxan diabetes + menthol 50 mg / kg	13,4	58,5
Alloxan diabetes + GA 50 mg / kg	11,7	65,3
Alloxan diabet + GA: Mt (4: 1) 50 mg / kg	9,5	74,5

In this case, one of the mechanisms of restoration of glucose concentration in the blood of animals after taking GA: Mt (4: 1) may occur as a result of restoration of carbohydrate metabolism between blood and liver due to changes in glycogenesis processes.

Conclusion

Based on the results obtained, it can be concluded that the membranefaol properties and antioxidant activities of the studied menthol, GK and supramolecular compounds of different ratios based on them may depend on the number of hydroxyl groups in their structure, their mutual location. Thus, the supramolecular compound menthol, GK, and GK: Mt (4: 1) derived from them, alloxan, can restore functional dysfunction in the liver mitochondria, i.e., in diabetes, and inhibit membrane lipid peroxidation. The hypoglycemic activity and mitochondrial membrane stabilizing properties of the supramolecular compound GK: Mt (4: 1) in alloxan diabetes were more pronounced than those of menthol, GK and its GK: Mt (2: 1) and GK: Mt (9: 1) compounds.

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