JNK INHIBITOR SP600125 DECREASED LIPID PEROXIDATION IN ISOLATED HEPATOCYTES

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Introduction. JNK is a protein kinase, which belongs to the MAP-kinase family, is activated in response to numerous intra- and extracellular stimuli and takes part in cell division and differentiation, apoptosis, cancerogenesis. The JNK1 kinases play a central role in obesity-driven insulin resistance by direct phosphorylation of IRS leading to reduced of the PI3K signaling pathway in response to insulin. The use of JNK inhibitors is a promising direction in the treatment of insulin resistance. Therefore, the study of the biological activity of JNK inhibitors is an important and urgent problem.

Aim. The purpose of this study was to study the antioxidant activity of the JNK inhibitor SP600125in vitro in isolated hepatocytes.

Materials and methods. The studies were conducted on female rats weighing 190±15 g, kept under standard conditions in the vivarium NUPh. Hepatocytes were isolated from intact rats by Seglen method and incubated in Eagle medium during 3 hours at 37^{o}C in the presence of 10 μmol JNK activator acetaminophen (APAP). In some cases, 10 minutes prior to the adding of APAP hepatocytes were incubated with the JNK SP600125 inhibitor (10 μmol). Lipid peroxidation intencity was evaluated by TBARS and conjugated diens (CD) levels. The data obtained were processed statistically.

Results and discussion. It was shown that adding JNK inhibitor SP600125 to the hepatocytes incubation medium did not change TBARS and CD content. The results obtained indicate that this compound does not possess antioxidant activity. Incubation of hepatocytes with APAP increased the CD level in 1.7 times and TBARS level in 2.1 times. Cells preincubation with SP600125 decreased TBARS and CD accumulation. APAP are partly metabolized by cytochrome P450 into highly reactive intermediate metabolite N-acetyl-p-benzoquinone imine, which stimulates H_2O_2 production and JNK phosphorylation (pJNK) and activation. pJNK translocates to mitochondria and causes its dysfunction and ROS release. These ROS continue to phosphorylate and activate JNK. This leads to the pathological loop formation. Cells preincubation with SP600125 decreased TBARS and CD accumulation.

Conclusions. The use of SP600125 decreased lipid peroxidation by affecting JNK. The data obtained indicate also that the APAP toxicity is mediated by JNK activation.

HYPOGLYCEMIC ACTION OF APPLE POLYPHENOL EXTRACT

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Introduction. Diabetes mellitus type 2 (DM2) is the most abundant endocrine disease in the world and one of the biggest challenge for the health care system. There is a plenty information that medicinal plants normalize glucose level and improve secondary disorders of metabolism caused by DM2, in particular, provide prevention of liver and kidney diseases and cardiovascular disorders.

Aim. The aim of the recent experiment was to study hypoglycemic activity of apple polyphenol extract (PE) under dexamethasone induced DM2.

Materials and methods. The white male inbred rats 18 month earth old were randomized into 4 groups: 1 – intact animals (IA); 2 – control pathology (DM); 3 – animals with DM that *per os* were administered PE (obtained at NPhU Pharmacognosy department) 1 hour before glucose loading in dose 50 mg/kg bw (DM+PE); 4 – diabetic animals that were administered herbal tea “Arfazetin” in dose 24 mg/kg bw 1 hour before glucose loading (DM+Ar). The DM2 was developed under subcutaneous dexamethasone injections in dose 0.125 mg/kg bw during 13 days. The glucose homeostasis was