JNK INHIBITOR SP600125 PREVENT TRIACYLGLYCEROL ACCUMULATION IN RAT ISOLATED HEPATOCYTES

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Introduction. c-Jun N-terminal kinases (JNKs) are members of an evolutionarily conserved sub-family of mitogen-activated protein (MAP) kinases that play a central role in stress signaling pathways implicated in gene expression, neuronal plasticity, regeneration, cell death, and regulation of cellular senescence. The JNK1 kinases play a central role in obesity-driven insulin resistance (IR) by direct phosphorylation of IRS1 and IRS2 leading to reduced of the PI3K-AKT signaling pathway in response to insulin. IR is major factor of triacylglycerol (TAG) accumulation in liver cells and pathogenesis of nonalcoholic fatty liver disease.

Aim. The aim of our investigation was the investigation of the participation of JNK in TAG accumulation in rat 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 by Seglen method. Cells were incubated in Eagle medium during 3 hours at 37°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). Lipids were extracted by the Bligh and Dyer methods and separated by thin layer chromatography in solvents heptane: diethyl ether:acetic acid, 40:10:1, v/v. The total lipid content was determined by March and Weinstein's method. VLDL level was determined by using the turbidimetric method. The data obtained were processed statistically.

Results and discussion. JNK activation is a key step in APAP-induced liver injury. We found that APAP adding in isolated hepatocytes primary culture incubation media is accompanied by TAG accumulation in cells and VLDL level decrease in cultural medium. The data obtain may indicate that the main reason of TAG accumulation is imbalance between lipid storage and lipid removal though lipoprotein formation. Cells preincubation with SP600125, an anthrapyrazolone inhibitor JNK prevents APAP-induced TAG accumulation and increase VLDL release in cultural medium.

Conclusions. The results indicate that JNK activation is accompanied by TAG accumulation in liver cells and JNK inhibitor prevents this accumulation by increasing of VLDL releasing. Thus, JNK inhibitor application may prevent nonalcoholic fatty liver disease development.

INVESTIGATION OF THE PLUM FRUIT DRY EXTRACTS ANTIOXIDANT EFFECT

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Introduction. Plum home (lat. Prunus domestica), the family Rosaceae is widespread in Ukraine, has many regional and local varieties of plants and the number second only to apple, pear and cherry. According to published data, plum fruits contain 6-17% sugar, up to 8% of pectin, organic acids of up to 1.6%, flavonoids, tannins and vitamins. In the previous studies, we showed that dry extracts with fibers and polysaccharide complex had laxative effect.

Aim. The aim of our study was to investigate the antioxidant effect of dry plum fruit extract with fibers (DEF) and dry plum fruit extract with the polysaccharide complex (DPC).

Materials and methods. The studies were conducted on female rats weighing 190±15 g, kept under standard conditions in the vivarium NUPh. Liver injury was modeling by alcohol intragastrical administration in dose 7ml/kg body weight during 7 days. Plum fruit extract was administered in doses 100 and 200 mg/kg body weight intragastrically. At the end of the experiment, the rats were decapitated, the