## 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

liver was perfused by cold saline and 10% homogenate was prepared in ice cold Tris-HCl buffer (50 mM, pH 7.4) using a homogenizer. Thiobarbituric acid reactive substances (TBARS), conjugated dienes (CD) and reduced glutathione (GSH) were measured. Silibor was used as a reference preparation. The data obtained were processed statistically.

**Results and discussion.** Ethanol oral administrations significantly increased TBARS, CD levels in 1.8 and 1.7 times, respectively. GSH was decreased in 1/63 times in the liver alcohol-injured liver. The data obtained lipid peroxidation activation and reducing of the antioxidant defense in these conditions. Both plum extracts normalize the studied indicators in the liver. Analysis of the experimental data showed that DEF was more effective in dose 200 mg/kg. DEF decreased TBARS and CD in 1.38 and 1.45 times, respectively, and increased GSH level in 1. 27 times. The effectiveness of DEF is not inferior to the comparison preparation silibor.

**Conclusions.** Dry plum fruit extracts exhibit antioxidant activity. Dry plum fruit extract with fibers was more active in dose 200 mg/kg body weight. The experimental data obtained prove the advisability of further pharmacological studies of this extract.

## STUDY OF NEWLY SYNTHESIZED COMPOUNDS ANTI-INFLAMMATORY PROPERTIES

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**Introduction**. Despite the fact that nonsteroidal anti-inflammatory drugs (NSAIDs) are the most frequently prescribed drugs, during the last years were found serious treatment side effects. So, the search of new synthetic compounds with anti-inflammatory activity is steel topical.

**Aim.** The aim of this study was to examine anti-inflammatory activity of the drugs, which are newly synthesized at the NPhU organic chemistry department, on the modelled inflammation in rats.

**Materials and methods.** Experiment was conducted using adult white outbred rats of both sexes; weighting 180-220 g. Anti-inflammatory activity was studied on the model of on model of carrageenan edema paws: 0.1 ml of 1% flogogen injected subcutaneously. For the purpose of the experiment, animals were divided into 5 groups, including group of control pathology and group of rats administered reference preparation – indomethacin. As an object of research were used three compounds chosen in previous experiments (C1, C2, C3). One hour before injection these compounds and indomethacin were single administered per os in dose 7 mg/kg and 5,25 mg/kg respectively. The size of the edema was measured in 1; 2, 3, 4, 5 and 24 hours after carrageenan administration using an oncotometer.

**Results and discussion.** The results of the studies showed the edema gradual increase up to 3 hours (prostaglandin phase) and further decrease until 24 hours of the experiment. During almost the all experiment, the compounds 1C and 2C did not show sufficient anti-inflammatory activity and did not significantly affect the reduction of edema size compared with the control group. The greatest impact was observed under 3C administration during all phases of the inflammatory process. Beginning from the first hour of experiment, 3C administration significantly reduced inflammation compared with the control pathology. The maximum anti-exudative activity of 58.72% of the 3C compound was fixed after 3 hours during the period of such inflammatory mediators as prostaglandins action, which may indicate the ability of this compound to inhibit COX activity. However, anti-exudative activity was recorded, as for 1 hour - 27,01% (phase of biogenic amines), and 2 hours of experiment - 29,63% (kinin phase). As well as, at 4, 5 and 24 hours, the anti-inflammatory effect of the compound 31C remained rather high (45.66%, 55.69%, and 49.96% respectively).

**Conclusions.** A compound with a conditional code C3 in a dose of 7 mg/kg revealed anti-inflammatory activity that is comparable with activity of reference preparation.