УДК: 61:615.1(043.2)
ББК: 5:52.8
ISBN: 978-985-21-0532-3

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THE INFLUENCE OF COUMESTROL ON STEATOSIS AND INFLAMMATION DEVELOPMENT IN THE LIVER. A POSSIBLE THERAPEUTIC POTENTIAL FOR LIVER INFLAMMATORY CONDITIONS?

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Background. Coumestrol (COM) is a potent, natural occurring phytoestrogen. It is the most studied agent among the coumestans family, which is a subtype of isoflavonoids group and occurs in variety of plants (mostly in alfalfa and clover sprouts, but also in legumes – soy, many beans and peas, likewise brussel sprouts or spinach). COM is known from its high affinity to the ERα and ERβ nuclear estrogen receptors, therefore, this compound is responsible for estrogen-like activity in human cells. COM is being intensively studied for many metabolic conditions because of its possible anti-inflammatory, anti-oxidative, and anti-steatotic properties.

Aim: The aim of this study was to evaluate the impact of COM on accumulation of lipid fractions and expression of pro-inflammatory proteins in rat hepatocytes during lipid-overload state.

Materials and methods. The study was performed on primary rat hepatocytes isolated during rat liver collagenase perfusion. The cells were incubated with COM alone or combined with palmitic acid (PA) for 18h. Total intracellular lipid content and fatty acid composition of free fatty acids (FFA), di- (DAG) and tri- (TAG) acyloglycerols were measured using Gas-Liquid Chromatography (GLC). Also ω-6/ω-3 ratios were calculated in all of the lipids fractions above mentioned. The expresion of pro-inflammatory proteins (NF-κB, TGF-β) and enzymes involved in eicosanoids and prostanoids production (COX-2, 15-LOX) were evaluated using Western Blot.

Results and discussion. The concentration of DAG was significantly decreased in hepatocytes incubated with PA + COM in comparison to PA group. A shift in the balance between ω6/ω-3 PUFA fatty acids in the PA and COM group showed that COM stimulated redistribution of the fatty acids towards synthesis of anti-inflammatory lipid metabolites, but only in the lipid overload state. Moreover, COM significantly decreased total expression of proteins involved in development of liver cells inflammation - NF-κB, TGF-β and 15-LOX, whereas it had no influence on COX-2 expression.

Conclusions. The outcome of these study shows that coumestrol probably has strong anti-inflammatory potential in rat hepatocytes during lipid overload state, moreover, it decreased the acumulation of bioactive lipids. These findings could be useful in context of the future research in the topic of inflammatory liver diseases such as NAFLD and NASH. More research is needed to evaluate the possible positive effects of coumestrol and other phytoestrogens as supportive factors in treatment of inflammatory liver diseases.