

Title of the project: Effect of cardiovascular drugs on the development of non-alcoholic steatohepatitis.

Grant Agency: Charles University

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Principal Investigator: H. Laštůvková

Co-investigators: S. Mičuda

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Summary of 2018 results

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Authors: H. Laštůvková (1), S. Mičuda (1). Fac. Med., Charles Univ., Hr. Králové: Dept. of Pharmacology(1)

Biliary secretion is essential pathway for elimination of lipophilic agents from the organism. This pathway is modified by numerous liver diseases, which may worsen accumulation of toxic compounds and predispose for further liver impairment. Nonalcoholic steatohepatitis (NASH) is a frequent disease associated with numerous metabolic and cardiovascular risks. Recent works demonstrated that bile acid homeostasis and bile formation markedly contributes to pathophysiology of NASH. It is therefore important to describe modulation of these mechanisms by all drugs regularly prescribed for therapy of NASH and accompanying risks. Primary aim of this project is to study in detail effects of drugs commonly used for these risks, carvedilol, metformin, and atorvastatin, and their combinations on the mechanisms of bile production and bile acid homeostasis using relevant mice model of NASH. During the first year of the project solution, we completed an in vivo study based on continuous 24 week administration of high fat diet with glucose and fructose to induce NASH. Designed groups of animals received carvedilol, metformin or their combination. Long term design of study enabled harvesting of the samples in the December 2018, and the samples are currently analysed by analytical, histological, and molecular-biology methods. Preliminary data uncovered positive but also negative effects of administered drug during NASH. This part of the study will be finished during second year of the project.

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Address for correspondence: S. Mičuda, Dept. of Pharmacology, Charles University, Faculty of Medicine in Hradec Králové, Šimkova 870, 500 03 Hradec Králové, Czech Republic