**ABSTRACT**

Charles University in Prague

Faculty of Pharmacy in Hradec Králové

Department of Pharmacology and Toxicology

Candidate: Mgr. Vojtěch Zadák

Supervisor: Doc. PharmDr. Petr Pávek, Ph.D.

Title of rigorous thesis:

Examination of potential ligands of the constitutive androstane receptor CAR

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The constitutive androstane receptor – CAR is a representative of nuclear receptors that form a super-family of ligand-activated transcription factors regulating expression of target genes.

In the last decade, CAR was mainly investigated in connection with an induction of biotransformation enzymes by remedies or other xenobiotics but in the past few years the research has also concentrated on a role of this receptor in hormone, lipid and energy homeostasis. Recently, there have been revealed some new important metabolic functions of CAR that may establish this „xenobiotic receptor“ as a new therapeutic target for treatment of type 2 diabetes, obesity and dyslipidemia.

The aim of this experimental rigorous thesis has been the examination of potential ligands of the human CAR (hCAR) from a given group of 16 chemicals with a defined structure.

Using methods gene reporter assay, two-hybrid assay and one-hybrid assay we have tested this group from the perspective of an interaction with hCAR. The results of our experiments have proved that four of these compounds are ligands – agonists of hCAR. The strongest interaction of hCAR has been identified with 2-(acetylsulfanyl)-4-(2´,4´-difluorbiphenyl-4-yl)-4-oxobutanoic acid. The results of this rigorous thesis imply that this compound might be further examined as a potential reliable specific agonist helping to clarify the functions of the human constitutive androstane receptor or perhaps also as a potential remedy that might, via an activation of this interesting receptor, regulate human metabolism.