**Abstract**

Charles University

Faculty of Pharmacy in Hradec Králové

Department of Pharmacology & Toxicology

Student: Jakub Draský

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

Title of diploma thesis: Pharmacological influence of nuclear receptors in diabetes mellitus therapy

Nuclear receptors belong to the superfamily of transcription factors, their main functions include regulating the expression of target genes. In my work I focused mainly on the group of orphan receptors, namely the pregnane X receptor (PXR) and the constitutive androstane receptor (CAR). A common feature of these receptors is their activation by a specific ligand. Both CAR and PXR have an essential function as biological sensors of hydrophobic xenobiotics when they induce enzymes I and II. phase of metabolism. They are also essential in the regulation of gluconeogenesis, insulin response, adipogenesis, cholesterol homeostasis, fatty acids, triglycerides and glycogen.

The aim of this experimental work was to introduce a luciferase reporter assay method for two DNA constructs containing the promoter region of the PEPCK and CYP7A1 genes. We used the known agonist rifampicin and the antagonist SPA70 to activate/deactivate PXR. We used CITCO as a CAR receptor agonist.

We first verified the functionality of the luciferase reporter gene assay method with a luciferase vector for the CYP3A4 gene. The results showed that rifampicin and CITCO significantly activated the CYP3A4 luciferase vector. In further experiments, we observed significant inactivation of the CYP7A1 luciferase vector by rifampicin, corresponding to the function of PXR in suppressing the expression of this gene in vivo. In the case of experiments with the vector for PEPCK, we observed a non-specific reaction of rifampicin, CITCA and SPA70 to the activation of this vector.

In conclusion, we verified the functionality of the luciferase reporter assay method with a vector with the promoter region of the CYP7A1 gene. The method for the second vector was not sufficiently optimized.