Abstract

Charles University

Faculty of Pharmacy in Hradec Králové

Department of Pharmacology and Toxicology

Student: Petra Ondrašáková, MSc.

Supervisor: Assoc. Prof. Přemysl Mladěnka, Pharm.D., Ph.D.

Co-supervisor: Dr. Haider Sami, University of Vienna, Division of Clinical Pharmacy and Diagnostics

Title of rigorous thesis: Optimization of PEI base LbL capsules with pDNA

In this thesis, we focused on the development of polyethylenimine (PEI) based non-viral capsules, which will enter nucleus of the cancer cell and lead to the expression of the lacking protein, which causes disease.

At first, PEI based layer-by-layer (LbL) polymer capsules were formed. PEI has many advantages - it has protonable amines, good stability and transfection efficiency. When forming the capsule, I followed up on my diploma thesis and continued to optimize the most suitable combination of polymers, that were layered on the $CaCO_3$ core. The aim was to obtain a biodegradable capsule and then to incorporate plasmid DNA (pDNA) therein.

Fluorescently labelled PEI was used as the last layer to visualize particles in fluorescent microscope. Then a scanning electron microscope (SEM) was used to observe capsules in more details. UV-VIS and Dapi staining were used to see whether there is pDNA bound in capsules.

Next steps were *in vitro* cell experiments on mouse mammary cancer cells - cytotoxicity and cellular intake. Visualisation was provided with fluorescent microscopy. 2 types of capsules - one with cross-linked linear polyethylenimine (CL-LPEI), poly(allylamine) (PAH) and other one with CL-LPEI, polyarginine

(pARG) were formed. They were subjected to cell experiments, and microscopic observation suggests, that capsules have passed into cells and are biocompatible.