RNA LOADED PLGA NANOPARTICLES FOR THERAPY OF CHRONIC INFLAMMATORY DISEASES

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This project's aim is the preparation and biological evaluation of a fully biodegradable, biocompatible and macrophage specific nano-drug delivery system for therapeutic RNA as a potential platform for chronic inflammation therapy. The initial focus at this stage is on the preparation of nanoparticles and optimization of granulometric properties and drug loading efficiency. Naked RNA cannot be administered to an organism by itself due to non-specific distribution, fast degradation by endonucleases and poor cell-uptake. The first step in creating a suitable delivery system involves the preparation of a complex composed of oligonucleotides and cationic lipids, namely dimethyldioctadecylammonium bromide or 1,2-dioleoyl-3-trimethylammonium propane using Blight-Dyer technique. The aim was to give the naturally hydrophilic oligonucleotide molecule overall hydrophobic properties. Consequently, nanoparticles based on poly(lactic-co-glycolic) acid (PLGA) were prepared by nanoprecipitation. During nanoprecipitation, various conditions were examined. The solubility of the complex in different organic solvents was investigated along with various surfactants in a water phase for stabilization of created nanoparticles. Further experiments included a different amount and type of PLGA. The most suitable solvent mixture for the complex was chloroform and acetone. Pluronic F-127 in a concentration of 0.5% was chosen as a surfactant due to a good polydispersity index (> 0.2) and size (191.9 ± 10.24 nm) of resulting particles. In the encapsulation efficiency there was no significant difference between different surfactants nor types of complex, therefore the complex of a charge ratio 1:2 (PO_2^- and N^+) was chosen for further use to eliminate the toxicity on the cells in the future experiments. Also, the particle size and polydispersity were found to be satisfactory with the complex 1:2 charge ratio. Under these conditions the resulting encapsulation efficiency for the model oligonucleotide was 82.24 ± 0.27 % and the size of the particles is 193.71 ± 3.51 nm.