Charles University, Faculty of Pharmacy in Hradec Králové

Department of: Pharmaceutical technology

Mentor: PharmDr. Ondřej Holas, PhD.

Consultant: Mgr. Nancy Mrózková

Student: Daniela Hatalová

Title of diploma thesis: Optimization of lyophilization process of polymer nanoparticles

Nanoparticles (NP) are gaining popularity in several fields including medicine, due to possibilities they offer that are linked to their size. In this project, PLGA NP were prepared, as they are non-toxic, biocompatible and biodegradable. Final formulation is always in a form of a water suspension, which is unstable due to hydrolyzation and leakage of potentially encapsulated drug into medium. Lyophilization is used to convert nanoparticles from an aqueous suspension to a water-free form. Lyophilization allows us to obtain solid and dry NPs without exposing them to higher temperatures. The aim of this work was to find suitable concentrations of lyoprotectants for lyophilization of PLGA NPs. The resulting NPs should reach a size of 170–200 nm with a narrow size distribution (PDI $\leq$ 0.2) and stability after freezing.

In this work we prepared NP with the method of nanoprecipitation. Subsequently, we added different lyoprotectants: trehalose, sorbitol, glycine, dextran and xylitol in following concentrations: 1 %, 2 %, 5 % and 10 %. These particular lyoprotectants were selected based on a literature review of publications related to the lyophilization of PLGA NPs and their appropriate physico-chemical properties (Fonte et al., 2016). After lyophilization of the colloidal nanosuspension with lyoprotectants, the reconstitution time was measured followed by measurment of size, polydispersity index (PDI) and ζ-potential. Two different lyophilization protocols, fast and slow freezing, were tested as another variable that may affect the final properties of the NPs after reconstitution.

The best of the initial five lyoprotectants for our purposes were trehalose and sorbitol. The most promising results were obtained with 10 % trehalose solution in both slow and fast freezing methods. The second best would be 5 % trehalose and 5 % sorbitol in the slow-freezing method. In summary, we found the best adepts for lyoprotectants and standardised procedure that would produce stable NP that meet our criteria.

Key words: lyophilization, PLGA, nanoparticles, lyoprotectants