DEVELOPMENT OF NANOFORMULATIONS FOR TARGET DELIVERY OF OBETICHOLIC ACID

Iefremenko, D.[1], Boltnarova, B.[1], Lochman, L.[2], Holas, O.[1],

[1]*Department of Pharmaceutical technology, Faculty of Pharmacy in Hradec Králové, Charles University, Czech Republic*
[2]*Department of Pharmaceutical Chemistry and Pharmaceutical Analysis, Faculty of Pharmacy in Hradec Králové, Charles University, Czech Republic*

Nanoparticles are nanosized materials that can encapsulate different therapeutic and diagnostic agents to deliver them into specific cells, reducing their non-specific action. PLGA is FDA approved, biocompatible and biodegradable tunable polymer with a good safety profile[1]. PLGA nanoparticles are one of the most effective and safe polymeric nanoparticles for targeted delivery. The aim of the work was to develop PLGA nanoparticles with incorporated FXR agonist[2] (obeticholic acid), for the targeted delivery to mononuclear phagocytic cells for the treatment of metabolic liver disorders. Desired nanoparticles were in the size range between 100 nm to 300 nm. Nanoparticles were prepared using nanoprecipitation method and size, polydispersity and zeta-potential was determined. The dependence of the size and polydispersity index of PLGA nanoparticles from different types of water phase, used during nanoprecipitation has been studied. As a water phase, various buffers with a various pH ranges were used. It was discovered that the size of PLGA nanoparticles depend on pH of aqueous phase. With the increasing pH from 3 to 7, size decreases from 180 nm till 90 nm. Moreover, it was shown that ionic strength of aqueous phase also affects the size of nanoparticles: with the increasement of ionic strength of water phase, it was observed increasing the size of nanoparticles. Spectrophotometrical and HPLC assay for OCA was developed. To estimate the encapsulation efficiency of OCA in PLGA nanoparticles, ethanolic extraction method for OCA was developed and optimized. An average encapsulation efficiency of OCA in PLGA nanoparticles was 75%.

The study was supported by GA UK grant No. 1348120.

References

1. Makadia HK, Siegel SJ.:Polymers (Basel), 3(3), 2011,1377-1397.
2. ARMSTRONG LE., GUO GL.: Curr Pharmacol Rep., 3(2), 2017, 92-100.