OP-18

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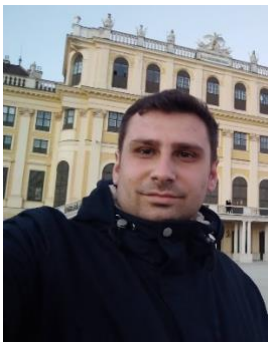

Development of nanoformulations for targeted delivery of obeticholic acid

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Nanosized materials such as nanospheres play an important role in personalized medicine. Their benefits include the possibility of targeting, enhanced bioavailability, reduced side effects, and site-specific controlled drug release. They can effectively encapsulate a wide range of therapeutic and diagnostic agents and deliver them into specific cells, reducing their non-specific action. PLGA is an FDA-approved, biocompatible, biodegradable tunable polymer with an excellent safety profile [1]. PLGA nanospheres are one of the most effective and safe polymeric nanoparticles for targeted delivery. The aim of this work was to develop PLGA nanoparticles with incorporated FXR agonist (obeticholic acid; OCA), for the targeted delivery into macrophages. Macrophages are key homeostasis regulators and their targeting could be exploited for the treatment of metabolic liver disorders. Desired nanoparticles for macrophage-specific delivery should be within a size range of 100 nm to 300 nm. Nanospheres were prepared using nanoprecipitation method and size, polydispersity, and zeta-potential were determined. Spectrophotometrical and HPLC assay for OCA was developed. OCA was extracted from PLGA nanoparticles using an ethanol/acetone extraction system. The dependence of the size and polydispersity index of PLGA nanoparticles from different types of water phases used during nanoprecipitation was studied. As a water phase, buffers with various pH ranges were used. For PLGA 50:50, with the increasing pH from 2.5 to 10, size decreases from 189 ± 3.87 nm to 42 ± 1.51 nm. For PLGA 75:25 with the increasing pH from 2.5 to 10, size decreases from 194 ± 2.27nm to 35 ± 0.74 nm. In vitro release of OCA from PLGA nanoparticles was studied. At physiological pH (7.3), around 86.63 % ± 0.61 % OCA was released from OCA-loaded PLGA nanoparticles in a 4 h study. At lysosomal pH (4.5) around 88.27 % ± 1.67 % OCA was released from OCA-loaded PLGA nanoparticles in a 355 h study.

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References

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