Fabrication and Characterization of Quercetin loaded nanoparticulate drug delivery system for Cardiovascular Diseases

Abstract

Cardiovascular Diseases (CVDs) consists of a variety of heterogeneous disorders, whilst is the leading cause of death in the world, with the highest mortality and disease rates according to World Health Organization (2016 revision). Treatment of cardiovascular diseases such as atherosclerosis is achieved through a series of pharmaceutical strategies used to prevent or alleviate disease symptoms, or through surgical procedures. Percutaneous coronary intervention (***PCI***) with a balloon catheter and use of coronary stents is the most frequently used method to treat a blocked ("stenosed") coronary artery. However, post-surgery complications may occur, with the most frequent being restenosis, a new atherosclerosis and vascular thrombosis, which set a need for new therapeutic strategies. Nowadays, it is widely accepted that high levels of oxidative stress are present in almost all cases of PCI, while high levels of free radicals seem to be strongly associated with some of the most crucial risk factors of cardiac disease. Among different procedures used for the prevention and treatment of angioplasty complications, Nanotechnology and Nanomedicine applications, through a series of innovative 3rd generation drug delivery systems coated with polymeric nanoparticles, show considerable advantages compared to bare metal and drug eluting stents. Polymeric nanoparticles are great delivery systems of pharmaceutical substances, able to provide a controlled drug release, while due to their convenient size, they seem to be less harmful to the vessel compared to 2nd generation drug eluting stents (DES). In this study, we fabricated biocompatible polymeric nanoparticles PLGA using Eletrospray technique as basis for the initiation of a delivery system of the antioxidative flavonoid Quercetin. With this method, we developed a nanoparticle coating in the surface of metallic stents, in order to mitigate the impact of high levels of oxidative stress caused after stent-based PCI procedure. Specifically, in the beginning of the study, we formulated blank Quercetin PLGA nanoparticles via Electrospray. After the optimization of these systems in terms of nanoparticle morphology, we continue with the exploration of their morphological properties. Furthermore, we studied the in vitro drug release kinetic behavior of Quercetin from polymeric nanocarriers. The nanoparticles were further studied with respect to stability and crystalline state of constituents.In the next part of this study, we applied the system in a cobalt-chromium

stent surface through Eletrospray Deposition Technique and confirmed its utter coating. Finally, we conducted some cell toxicity experiments and examined the impact of system in the development and cell proliferation. We found that Electrospray technique seems to perform quite well as a single-step method to develop an improved biocompatible drug delivery system of quercetin for the coating of cardiovascular stents, which consequently shows promising results towards post-surgery complications of PCI.