Abstract

Background: targeted drug delivery to cancer tissue has become one of the promising tools for cancer therapy. It increases the effectiveness of the drug on cancer tissue and also reduces the side effects of the drug on normal tissues. Nanoparticles also reduced the drug resistance by co-delivery of different types of drugs with different functions to the target tissue. Therefore, the aim of this study was to design and synthesize the PLA-Chitosan-Spermine , PLA-PEG-Glucose and Fe3O4 (PCSPGFe) nanoparticles targeted for co-delivery of PTX and siRNA-FAM to MCF-7 cells. For this purpose, PLA-PEG-Glucose and PLA-Chitosan-Spermine were first synthesized separately, then these copolymers were used to encapsulate PTX, siRNA-FAM, and Fe3O4 nanoparticles. In this research, magnetic nanoparticles were synthesized using Carduus marianus L. extract based on the green synthesis method. Fe3O4 nanoparticles, PTX and siRNA-FAM were encapsulated into PCSPGFe/PTX/siRNA-FAM nanoparticles by solvent diffusion technique.

Methods: The characterization of the nanoparticles was investigated using scanning electron microscopy (SEM) and dynamic light scattering (DLS). The release pattern of PTX and siRNA-FAM from the nanoparticles was investigated in both acidic (pH=6) and neutral (pH=7) PBS buffers. MTT assay was used to evaluate the biocompatibility of the blank nanoparticles (PCSPGFe) and anticancer efficiency of the PTX/siRNA-FAM encapsulated nanoparticles (PCSPGFe/PTX/siRNA-FAM). The ability of PCSPGFe nanoparticles to deliver siRNA-FAM to MCF-7 cells was also evaluated using fluorescence microscopy and flow cytometry.

Results: The results of the present study showed that PCSPGFe/PTX/siRNA-FAM nanoparticles had a spherical morphology with a size of about 200 to 250 nm. The siRNA-FAM encapsulation efficiency was higher compared to PTX. The results of the release assay showed that the release of both PTX and siRNA-FAM in an acidic medium was significantly increased compared to their release in a neutral medium. Also showed that siRNA-FAM release was higher than PTX in both acidic and neutral media. The biocompatibility of these nanoparticles as well as their ability to deliver PTX and siRNA-FAM to MCF-7 cells were confirmed by MTT assay and fluorescence microscopy. The results showed that PCSPGFe nanoparticles have good biocompatibility. Also, the surface coating of nanoparticles using glucose increased the efficiency of the drug and siRNA-FAM delivery to MCF-7 cells.

Key words: Targeted drug delivery, MCF-7 cells, Codelivery, siRNA-FAM, PTX.