Research in Pharmaceutical Sciences, 2012;7(5)
School of Pharmacy and Pharmaceutical Sciences
Isfahan University of Medical Sciences

Optimization of 7-ethyl-10-hydroxycamptothecin loaded PLGA nanoparticles with regard to their drug loading

N. Sepehri[1,*], H. Rouhani[*,1], R. Dinarvand[2]

[1]Novel Drug Delivery Systems Laboratory, Faculty of Pharmacy, Department of Pharmaceutics, Tehran University of Medical Sciences, Tehran, Iran
[2]Medical Nanotechnology Research Centre, Faculty of Pharmacy, Tehran University of Medical Sciences, Tehran, Iran

Background and Aims: Irinotecan (Camptosar®) is a soluble camptothecin derivative (CPT-11) which is widely used for treatment of colorectal cancer and some other solid tumors. In the patient's liver, Irinotecan is converted to7-ethyl-10-hydroxy camptothecin (SN38) with more than 100 fold increase in cytotoxicity. SN38 is poorly soluble in aqueous solutions and any pharmaceutically acceptable solvent. Furthermore, SN38 is changed to an inactive ring-opened format in physiological pH. Present study mainly focuses on formulation and optimization of SN38 loaded PLGA nanoparticles (NPs) by central composite experimental design to improve drug loading using the modified emulsification/evaporation process.
Methods: A two level half factorial screening design, constructed to investigate the effect of five preparative variables such as amount of polymer, acetone volume, co-solvent (DMSO) volume, PVA volume and power of sonic on particle size and drug loading.Due to the screening study, three independent variables (amount of polymer, DMSO volume and acetone volume) were selected and a central composite design was applied.
Results: For all type of NPs, appropriate size ranged from 150-190nm with narrow unimodal distribution (PdI: 0.138±0.06) were obtained. The optimum level of the independent factors leads to optimized NPs with 3.54±0.12% drug loading. Scanning electron microscopy (SEM) and Atomic Force Microscopy (AFM) revealed that nanoparticles are spherical, non-porous and with smooth surface morphology. Differential scanning calorimetry (DSC) studies proved that starting drug is amorphous in nature and may have been homogenously dispersed in the PLGA matrix.
Conclusions: Our obtained result demonstrated that biodegradable PLGA NPs can be a promising carrier for delivery of SN38 as a hydrophobic anticancer agent. However, further in vitro and in vivo studies are needed to confirm these NPs efficacy.

Keywords: Nanoparticle; Optimization; SN38