Lamotrigine loaded poly-ὐ-(d, l-lactide-co-caprolactone) nanoparticles as brain delivery system

HUSSEIN OSMAN HASSAN AMAR,Azza Ahmed ,Mahmoud M. Ghorab, Iman M. Higazy

Abstract

Management of epilepsy requires brain delivery therapy, therefore, this study was aimed to prepare lamotrigine loaded poly-ὐ-(d,l-lactide-co-caprolactone) (PLCL) nanoparticles using spontaneous emulsification solvent diffusion method. Nanoparticles for brain delivery required to have a particle size <200 nm, polydispesity index <0.2 and a sustained drug release properties. For such aim different factors were considered in preparing the nanoparticles as PLCL monomers' ratio, type of organic solvent used to prepare the nanoparticles, amount of PLCL and PluronicÈF127 in the nanoparticles. Prepared nanoparticles were characterized for their shape, particle size, polydispersity index, zeta potential, encapsulation efficiency, drug loading capacity, process yield and in-vitro drug release pattern. The in-vivo investigation for brain delivery of selected nanoparticles delivered by intravenous route was investigated in rats and compared to that for oral tablet. The obtained nanoparticles were spherical in shape. The amount of surfactant and PLCL affected the properties of the obtained nanoparticles. Using a mixture of organic solvent in preparing the nanoparticles improved its properties. The nanoparticles prepared using PLCL with monomers' ratio of 25:75, had particle size value of 125 nm, polydispersity index value of 0.184, zeta potential value of ī39 mV and encapsulation efficiency value of 99%, was selected to study their efficacy to deliver the drug to the brain. The tested nanoparticles showed higher values of Tmax, Cmax, AUC, and MRT in homogenized rat brain, compared to oral lamotrigine tablet, while the bioavailability of the oral tablet was higher in rat plasma compared to that for the nanoparticles. This reflects that brain was the main distribution site for tested nanoparticles, and plasma was the main distribution site for oral tablets. This confirms the goal of the selected formulation as brain delivery nanoparticles.

European Journal of Pharmaceutical Sciences 2018, March