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Doxorubicin and Cyclosporine Loaded PLGA Nanoparticles to Combat Multidrug Resistance

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Abstract : Doxorubicin is the most widely used anticancer drugs in chemotherapy treatment. However, problems related to the development of multidrug resistance (MDR) and acute cardiotoxicity have led researchers to investigate alternative forms of administering doxorubicin for cancer therapy. Several methods have been attempted to overcome MDR, including the co-administration of a chemosensitizer inhibiting the efflux caused by ATP binding cassette transporters with anticancer drugs, and the bypass of the efflux mechanism. Co encapsulation of doxorubicin (Dox) and cyclosporine A (CSA) into poly (DL-lactide-co-glycolide) nanoparticles was emulsification-solvent evaporation method using polyvinyl alcohol as emulsion stabilizers. The Dox-CSA loaded nanoparticles were evaluated for particle size, zeta potential and PDI by light scattering analysis and thermal characterizations by differential scanning calorimetry (DSC). Loading efficiency (LE %) and in-vitro dissolution samples were evaluated by developed and validated HPLC method. The optimum particle size obtained is 298.6.8±39.4 nm and polydispersity index (PDI) is 0.098±0.092. Zeta potential is found to be -29.9±4.23. Optimum pH to increase Dox LE% was found 7.1 which gave 42.5% and 58.9% increase of LE% for pH 6.6 and pH 8.6 compared respectively. LE% achieved for Dox is 0.07±0.01 % and CSA is 0.09±0.03%. Increased volume of PVA and weight of PLGA shows increase in size of nanoparticles. DSC thermograms showed shift in the melting peak for the nanoparticles compared to Dox and CSA indicating encapsulation of drugs. In conclusion, these preliminary studies showed the feasibility of PLGA nanoparticles to entrap Dox and CSA and require future in-vivo studies to be performed to establish its potential.

Keywords : doxorubicin, cyclosporine, PLGA, nanoparticles
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