Physical PEGylation Enhances The Cytotoxicity Of 5-Fluorouracil-Loaded PLGA And PCL Nanoparticles

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Abstract

Purpose: The main goal of this study is to evaluate the impact of physical incorporation of polyethylene glycol (PEG) into 5-fluorouracil (5-FU)-loaded polymeric nanoparticles (NPs).

Methods: The 5-FU-loaded NPs were prepared utilizing a simple double emulsion method using polycaprolactone (PCL) and polylactic-co-glycolic acid (PLGA) with or without PEG 6000. The surface charge, particle size, and shape of NPs were evaluated by standard procedures. Both Fourier Transform Infrared Spectroscopy and X-ray diffraction spectra of the 5-FU loaded NPs were compared against the pure 5-FU. The in vitro release profile of 5-FU from the NPs was monitored by the dialysis tubing method. Cell death and apoptosis induction in response to 5-FU NP exposure were measured by MTT and Annexin-V/7-amino-actinomycin D (7-AAD) assays, respectively, in Daoy, HepG2, and HT-29 cancer cell lines.

Results: The 5-FU loaded NPs were found to be spherical in shape with size ranging between 176 +/- 6.7 and 253.9 +/- 8.6 nm. The zeta potential varied between -7.13 +/- 0.13 and -27.06 +/- 3.18 mV, and the entrapment efficiency was between 31.96% and 74.09%. The in vitro release of the drug followed a two-phase mode characterized by rapid release in the first 8 hrs followed by a period of slow release up to 72 hrs with composition-based variable extents. Cells exposed to NPs demonstrated a significant cell death which correlated with the ratio of PEG in the formulations in Daoy and HepG2 cells but not in HT-29 cells. Formulations (F1-F3) significantly induced early apoptosis in HT-29 cell lines.

Conclusion: The physical PEGylation significantly enhanced the entrapment and loading efficiencies of 5-FU into NPs formulated with PLGA and PCL. It also fostered the in vitro cytotoxicity of 5-FU-loaded NPs in both Daoy and HepG2 cells. Induction of early apoptosis was confirmed for some of the formulations.

Keywords

Author Keywords: hepatocellular carcinoma HepG2; emulsification-solvent evaporation technique; colorectal carcinoma HT-29; MTT assay; apoptosis
KeyWords Plus: DRUG-DELIVERY; IN-VITRO; POLYMERIC NANOPARTICLES; CANCER CELLS; APOPTOSIS; RELEASE; NANOTECHNOLOGY; SURFACE; ASSAY; FORMULATION

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