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Targeted Delivery of Sustained Release Polymeric Nanoparticles for Cancer Therapy

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Abstract : Among the potent anti-cancer agents, curcumin has been found to be very efficacious against various cancer cells. Despite multiple medicinal benefits of curcumin, poor water solubility, poor physiochemical properties and low bioavailability continue to pose major challenges in developing a formulation for clinical efficacy. To improve its potential application in the clinical area, we formulated poly lactic-co-glycolic acid (PLGA) nanoparticles. The PLGA nanoparticles were formulated using solid-oil/water emulsion solvent evaporation method and then characterized for percent yield, encapsulation efficiency, surface morphology, particle size, drug distribution within nanoparticles and drug polymer interaction. Our studies showed the successful formation of smooth and spherical curcumin loaded PLGA nanoparticles with a high percent yield of about 92.01±0.13% and an encapsulation efficiency of 90.88±0.14%. The mean particle size of the nanoparticles was found to be 145nm. The in vitro drug release profile showed 55-60% drug release from the nanoparticles over a period of 24 hours with continued sustained release over a period of 8 days. Exposure to curcumin loaded nanoparticles resulted in reduced cell viability of cancer cells compared to normal cells. We used a novel non-covalent insertion of a homo-bifunctional spacer for targeted delivery of curcumin to various cancer cells. Functionalized nanoparticles for antibody/targeting agent conjugation was prepared using a cross-linking ligand, bis(sulfosuccinimidyl) suberate (BS3), which has reactive carboxyl group to conjugate efficiently to the primary amino groups of the targeting agents. In our studies, we demonstrated successful conjugation of antibodies, Annexin A2 or prostate specific membrane antigen (PSMA), to curcumin loaded PLGA nanoparticles for targeting to prostate and breast cancer cells. The percent antibody attachment to PLGA nanoparticles was found to be 92.8%. Efficient intra-cellular uptake of the targeted nanoparticles was observed in the cancer cells. These results have emphasized the potential of our multifunctional curcumin nanoparticles to improve the clinical efficacy of curcumin therapy in patients with cancer.

Keywords : polymeric nanoparticles, cancer therapy, sustained release, curcumin
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