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Controlling the calcium to phosphate ratio in preparation of lipid coated calcium phosphate nanoparticles to enhance gene delivery to breast cancer cells

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Lipid-coated calcium phosphate (LCP) nanoparticles (NPs) remain an attractive option for siRNA systemic delivery for anti-cancer treatment. Previous researchers revealed the influence of the stoichiometry of reactants on the size and morphology of nanostructured calcium phosphate (CaP) particles. There are very few reportson investigating the influence of synthesis parameters such as the Ca/P molar ratio and mixing style on the siRNA loading onto LCP NPs and protection by LCP NPs and subsequent siRNA delivery efficiency. Thus in this research, we examined the effect of Ca/P molar ratio on the size, zeta potential, dispersion and siRNA loading onto LCP NPs and optimized the Ca/P molar ratio in terms of the siRNA loading efficiency and siRNA protection from enzyme degradation. Our data indicated that the particle size and zeta potential of LCP NPs decreased with an increase of the Ca/P molar ratio from 25 to 100 and was maintained at ~40 nm and ~-20 mV when the ratio was over 100. Interestingly, LCP particles synthesized at a lower Ca/P ratio exhibited higher gene encapsulated efficiency (i.e., higher percentage of gene loaded from reaction solution) and provided more effective protection of siRNA from degradation by serum-derived nucleases but had a decreased gene loading capacity per particle. LCP NPs synthesized at the optimized Ca/P ratio (100) had a hollow, spherical structure with an average size of about 40 nm and were able to maintain their stability in serum containing media and PBS for over 24 hours. Moreover, LCP NPs exhibited a growing dissolution in aqueous solutions with a lower pH value indicating that the siRNA release from LCP NPs is pH sensitive. The superior ability of optimized LCP NPs to maintain the integrity of encapsulated siRNA and the colloidal stability in culture medium of the nanoparticles allow this formulation to achieve improved cellular accumulation of siRNA and enhanced growth inhibition (a two-fold high than Oligofectamine™) of human breast cancer cells *in vitro*.

Biography

Jie Tang completed her MPhil from West China School of Pharmacy, Sichuan University. She is now studying as a PhD candidate sponsored by Chinese Scholarship Council and UQI scholarship in Australian Institute for Bioengineering and Nanotechnology, the University of Queensland. She has published more than 5 papers in high impact journals in the field of cancer therapy.

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