Selective Inhibition of Osteosarcoma Cell Functions Induced By Curcumin-Loaded Self-assembled Arginine-Rich-RGD Nanospheres

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Osteosarcoma is the most frequent primary bone cancer today. Chemotherapy mostly used for the treatment against osteosarcoma can induce high toxicity [1]. Therefore, the objective of this in *vitro* study was to develop a nanomedicine approach against osteosarcoma with higher selectivity towards osteosarcoma cells and lower cytotoxicity towards normal osteoblasts.

Curcumin (or diferuloylmethane) has been found to have anti-oxidant and anti-cancer effects by multiple cellular and molecular pathways. However, with its polyphenol groups, it has low water solubility and a high degradation rate in alkaline conditions [2].

Self-assembled amphiphilic peptides have various applications as novel nanoscale biomaterials including hydrophobic drug delivery [3]. In this study, the ampiphilic peptide C18GR7RGDS was designed and used as a curcumin carrier in aqueous solution. This peptide contains a hydrophobic aliphatic tail group leading to their self-assembly by hydrophobic interactions, as well as a hydrophilic head group composed of arginine-rich and an arginine-glycine-aspartic acid (RGD) structure, which may lead to efficient cell internalization by macopinocytosis and targeting for

the overexpressed αvβ3 integrins on cancer cells [4]. Through the characterization of transmission electron microscopy (TEM), the self-assembled structures of the presently designed spherical amphiphilic nanoparticles (APNPs) with diameters of 10-20 nm in water and phosphate buffer saline (PBS) were observed, but this structure opened up when the pH value was reduced to 4. Using a method of co-dissolution with acetic acid and dialysis tubing, the solubility of curcumin was enhanced and formed a homogeneous solution with the help of APNPs. The successful encapsulation of curcumin in APNPs was then confirmed by Fourier transform infrared (FT-IR) and X-ray diffraction (XRD) analysis. Also, the cytotoxicity and cellular uptake of the APNP/curcumin complexes on both osteosarcoma and normal osteoblast cell lines were evaluated by MTT assays and confocal fluorescence microscopy. Most importantly, the curcumin-loaded APNPs exhibited a significant selective cytotoxicity against MG-63 osteosarcoma cells (15% of viability) compared to normal osteoblasts (more than 50% of viability). In this manner, it was demonstrated for the first time here that APNPs can encapsulate hydrophobic curcumin in their hydrophobic cores, and the curcumin-loaded APNPs could be an innovative drug for the selective inhibition of osteosarcoma cells over healthy osteoblasts.

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References:

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