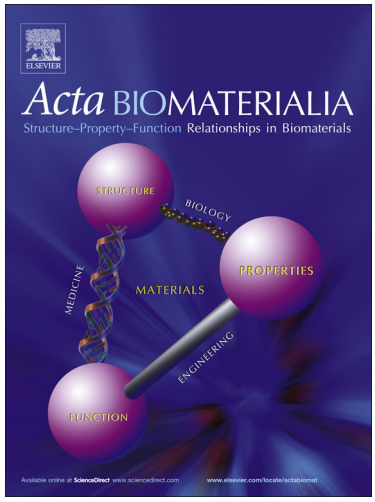

Co-delivery of doxorubicin and interleukin-2 via chitosan based nanoparticles for enhanced antitumor efficacy

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Co-delivery of doxorubicin and interleukin-2 via chitosan based nanoparticles for enhanced antitumor efficacy

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Abstract

In order to reduce toxicity and improve antitumor therapeutic effects of doxorubicin (DOX) and recombinant human interleukin-2 (rhIL-2), we developed a hydrophilic cationic polymer (N,N,N-trimethyl chitosan, TMC) based nanocomplexes (FTCD/rhIL-2) which could efficiently mediate systemic co-delivery of hydrophobic DOX and water-soluble rhIL-2 to achieve the purpose of combination therapy. DOX was covalently conjugated to TMC through *cis*-aconitic anhydride (CA) which endowed nanocomplexes a pH-senstive release of DOX, while rhIL-2 was loaded through electrostatic adsorption without compromise of bioactivity. The resultant nanocomplexes exhibited sub-spherical shape (~200 nm) and positive charge (>20 mV). Folate (FA) modification was utilized with the intention of active targeting, which was however correlated with weakened tumor growth inhibition, emphasizing the importance of balance in overcoming diverse delivery barriers for efficacious antitumor therapy. Compared with free drugs, FTCD/rhIL-2 nanocomplexes significantly delayed tumor growth, increased the serum immunoglobulin G (IgG)