Low Molecular Weight Chitosan-Coated Polymeric Nanoparticles for Sustained and pH-Sensitive Delivery of Paclitaxel

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Abstract:

Low molecular weight chitosan (LMWC) is a promising polymer for surface modification of nanoparticles (NPs), which can impart both stealth effect and electrostatic interaction with cells at mildly acidic pH of tumors. We previously produced LMWC-coated NPs via covalent conjugation to poly(lactic-co-glycolic) acid (PLGA-LMWC NPs). However, this method had several weaknesses including inefficiency and complexity of the production as well as increased hydrophilicity of the polymer matrix, which led to poor drug release control. Here, we used the dopamine polymerization method to produce LMWC-coated NPs (PLGA-pD-LMWC NPs), where the core NPs were prepared with PLGA that served best to load and retain drugs and then functionalized with LMWC via polydopamine layer. The PLGA-pD-LMWC NPs overcame the limitations of PLGA-LMWC NPs while maintaining their advantages. First of all, PLGA-pD-LMWC NPs attenuated the release of paclitaxel to a greater extent than PLGA-LMWC NPs. Moreover, PLGA-pD-LMWC NPs had a pH-dependent surface charge profile and cellular interactions similar to PLGA-LMWC NPs, enabling acid-specific NP–cell interaction and enhanced drug delivery to cells in weakly acidic environment. Although the LMWC layer did not completely prevent protein binding in serum solution, PLGA-pD-LMWC NPs showed less phagocytic uptake than bare PLGA NPs.

Keywords:

Dopamine polymerization, drug delivery, low molecular weight chitosan, nanoparticles, pH-sensitive, sustained release

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