Polymer-Iron Oxide Composite Nanoparticles for EPR Independent Drug Delivery

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Abstract:

Nanoparticle (NP)-based approaches to cancer drug delivery are challenged by the heterogeneity of the enhanced permeability and retention (EPR) effect in tumors and the premature attrition of payload from drug carriers during circulation. Here we show that such challenges can be overcome by a magnetophoretic approach to accelerate NP delivery to tumors. Payload-bearing poly(lactic-co-glycolic acid) NPs were converted into polymer-iron-oxide nanocomposites (PINCs) by attaching colloidal Fe3O4 onto the surface, via a simple surface modification method using dopamine polymerization. PINCs formed stable dispersions in serum-supplemented medium and responded quickly to magnetic field gradients above 1 kG/cm. Under the field gradients, PINCs were rapidly transported across physical barriers and into cells and captured under flow conditions similar to those encountered in postcapillary venules, increasing the local concentration by nearly three orders of magnitude. In vivo magnetophoretic delivery enabled PINCs to accumulate in poorly vascularized subcutaneous SKOV3 xenografts that did not support the EPR effect. In vivo magnetic resonance imaging, ex vivo fluorescence imaging, and tissue histology all confirmed that the uptake of PINCs was higher in tumors exposed to magnetic field gradients, relative to negative controls.

Keywords:

Polymer-iron oxide nanocomposite; magnetic drug delivery; polymeric nanoparticles; polydopamine; in vivo delivery

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