Pegylated magnetic nanocarriers for doxorubicin delivery: A quantitative determination of stealthiness in vitro and in vivo

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The aim of this work was to elucidate the impact of polyethylene glycol (PEG) polymeric coating on the in vitro and in vivo stealthiness of magnetic nanocarriers loaded or not with the anticancer drug doxorubicin. The comparison was made between aqueous suspensions of superparamagnetic iron oxide nanoparticles (SPIONs) stabilized by either citrate ions (C-SPIONs) or PEG\textsubscript{5000} (P-SPIONs), the latter being loaded or not with doxorubicin via the formation of a DOX-Fe\textsuperscript{2+} complex (DLP-SPIONs). After determination of their relevant physico-chemical properties (size and surface charge), nanoparticle (NP) stealthiness was studied in vitro (ability to activate the complement system and uptake by monocytes and macrophage-like cells) and in vivo in mice (blood half-life; \( t_{1/2} \), and biodistribution in main clearance organs). These aspects were quantitatively assessed by atomic absorption spectrometry (AAS). Complement activation dramatically decreased for sterically stabilized P-SPIONs and DLP-SPIONs in comparison with C-SPIONs stabilized by charge repulsion. Monocyte and macrophage uptake was also largely reduced for pegylated formulations loaded or not with doxorubicin. The \( t_{1/2} \) in blood for P-SPIONs was estimated to be 76 ± 6 min, with an elimination mainly directed to liver and spleen. Thanks to their small size (<80 nm) and a neutral hydrophilic polymer-extended surface, P-SPIONs exhibit prolonged blood circulation and thus potentially an increased level in tumor delivery suitable for magnetic drug targeting applications.

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