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Magnetic polymeric nanoparticles with hyperthermia-triggered gemcitabine release

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Magnetic nanoparticles (MNPs) have been widely used to increase the efficacy of chemotherapeutics, largely through passive accumulation provided by the enhanced permeability and retention effect. Their incorporation into biopolymer coatings enables the preparation of magnetic field-responsive, biocompatible nanoparticles that are well dispersed in aqueous media. Here we describe a synthetic route to prepare functionalized, stable magnetite nanoparticles (MNPs) loaded with gemcitabine hydrochloride, the active drug of the resulting nanostructure. The magnetite/polymer composition and the gemcitabine-loaded particles are detected by Fourier Transform Infrared Spectroscopy (FTIR), electrhophoresis and quantified by thermogravimetric analysis. These nanostructures are tested regarding their ability to release the active drug while heating the surroundings by magnetic hyperthermia, doubling in principle their chances as antitumor agents. The *in vitro* cytotoxicity of gemcitabine-loaded nanoparticles is tested using treated pancreatic cancer cell lines. The release, with first-order kinetics, is found to be faster when carried out in a thermostated bath at 43 ºC than at 37 ºC, as expected. But the main result of this investigation is that while the particles retain their hyperthermia response, with reasonably high heating power, they release the drug faster and with zeroth-order kinetics when they are maintained at 43 ºC under the action of the alternating magnetic field used for hyperthermia. The therapeutic possibilities of the designed nanostructures as effective heating agents for magnetic hyperthermia are demonstrated, and specific absorption rates as high as 150 W/g, with 20 mT magnetic field and 205 kHz frequency, are obtained. This magnetic heating response could provide a promising nanoparticle system for combined diagnostics and cancer therapy.

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