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Iron Oxide Nanoparticles for Sustained Delivery of Anticancer Agents

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Iron Oxide Nanoparticles for Sustained Delivery of Anticancer Agents

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Abstract:

We have developed a novel water-dispersible oleic acid (OA)-Pluronic-coated iron oxide magnetic nanoparticle formulation that can be loaded easily with high doses of water-insoluble anticancer agents. Drug partitions into the OA shell surrounding iron oxide nanoparticles, and the Pluronic that anchors at the OA-water interface confers aqueous dispersity to the formulation. Neither the formulation components nor the drug loading affected the magnetic properties of the core iron oxide nanoparticles. Sustained release of the incorporated drug is observed over 2 weeks under in vitro conditions. The nanoparticles further demonstrated sustained intracellular drug retention relative to drug in solution and a dose-dependent antiproliferative effect in breast and prostate cancer cell lines. This nanoparticle formulation can be used as a universal drug carrier system for systemic administration of water-insoluble drugs while simultaneously allowing magnetic targeting and/or imaging.

Keywords: Sustained release; water-insoluble drugs; cellular uptake; breast cancer; targeting; tumor therapy; magnetic nanoparticles

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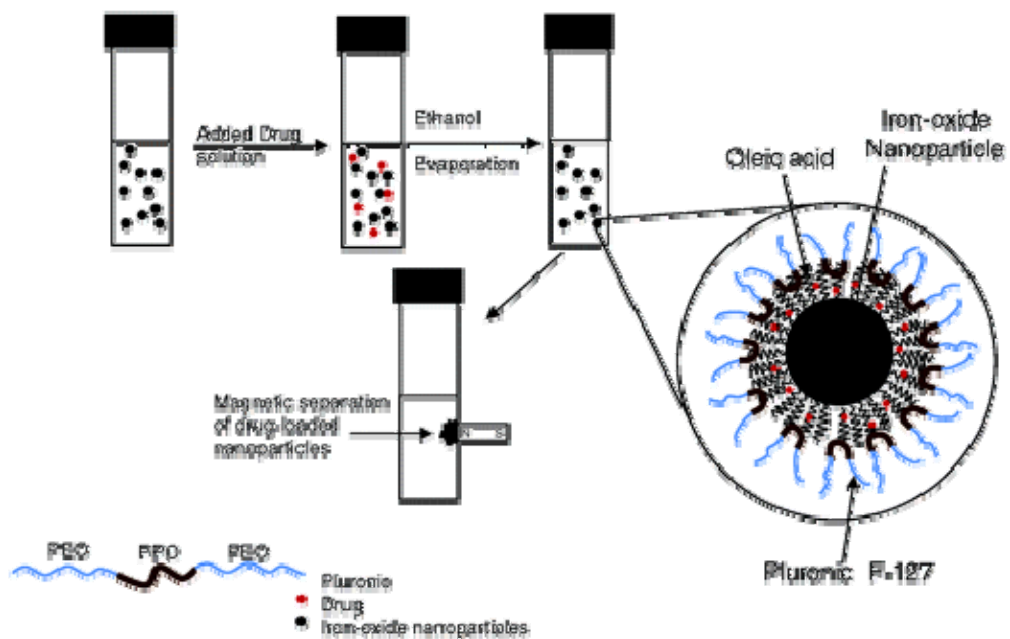


Figure 1 Schematic representing formulation of iron oxide nanoparticles and the process for drug loading.

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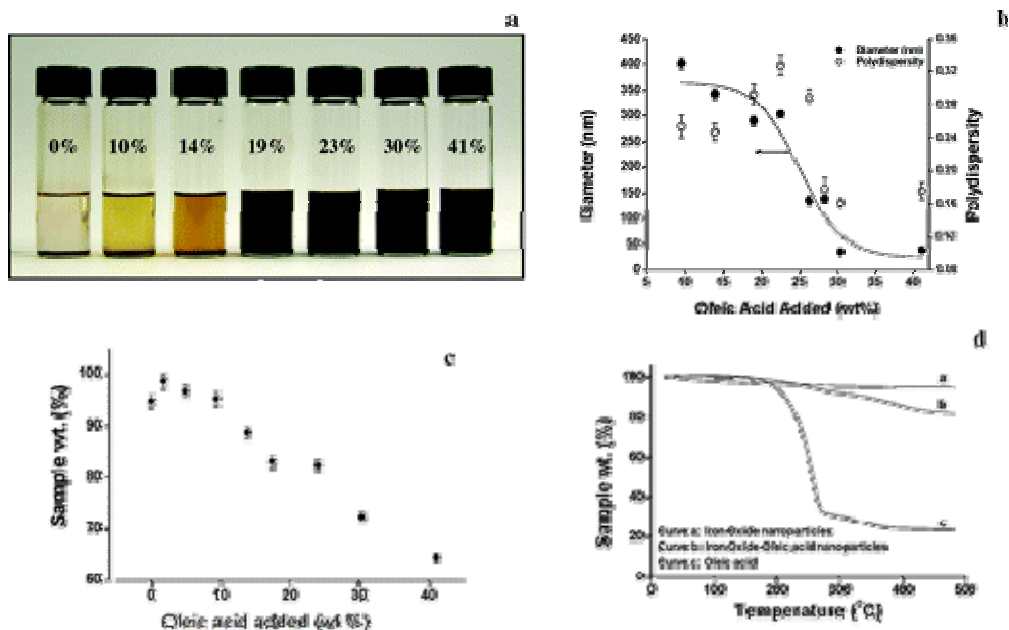


Figure 2 Effect of OA concentration on (a) sedimentation of iron oxide nanoparticles in hexane after 2 days; (b) mean particle size and polydispersity index of OA-coated iron oxide nanoparticles in hexane (data as mean \pm SEM, $n = 10$, a nonlinear square fitting was used to connect data points); (c) mass loss by thermogravimetric analysis of different formulations of OA-coated iron oxide nanoparticles (data as mean \pm SEM, $n = 3$; and (d) typical thermograms of iron oxide nanoparticles, OA, and OA-coated iron oxide nanoparticles (a representative from three different runs).

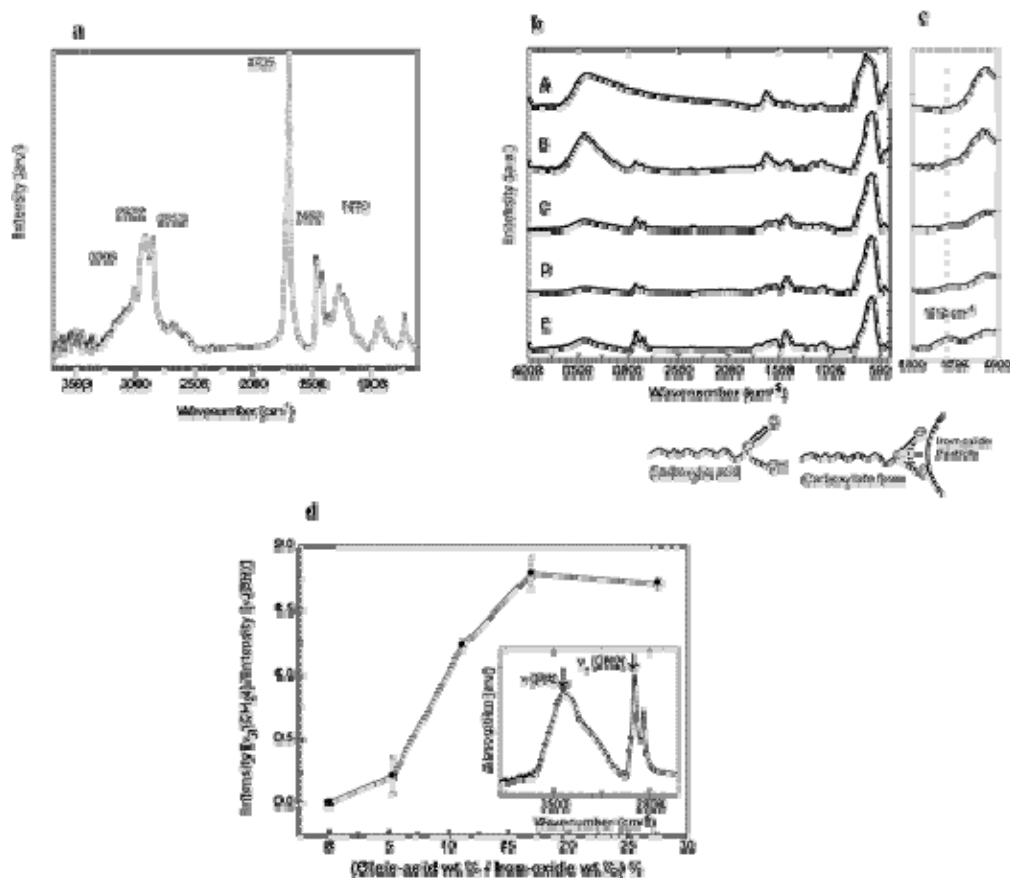


Figure 3 (a) FT-IR spectrum of pure OA. (b) FT-IR spectra of OA-coated iron oxide nanoparticles: (A) pure iron oxide; (B) 5 wt % OA relative to iron oxide; (C) 11 wt % OA relative to iron oxide; (D) 17 wt % OA relative to iron oxide; and (E) 23 wt % OA relative to iron oxide. (c) Zoom of the FT-IR spectra in the range of 1800-1600 cm⁻¹. (d) Relative intensities of the CH₂ symmetric stretch mode to the OH stretch mode versus the relative concentration of OA to the iron oxide (data as mean ± SEM from 32 spectral scans).

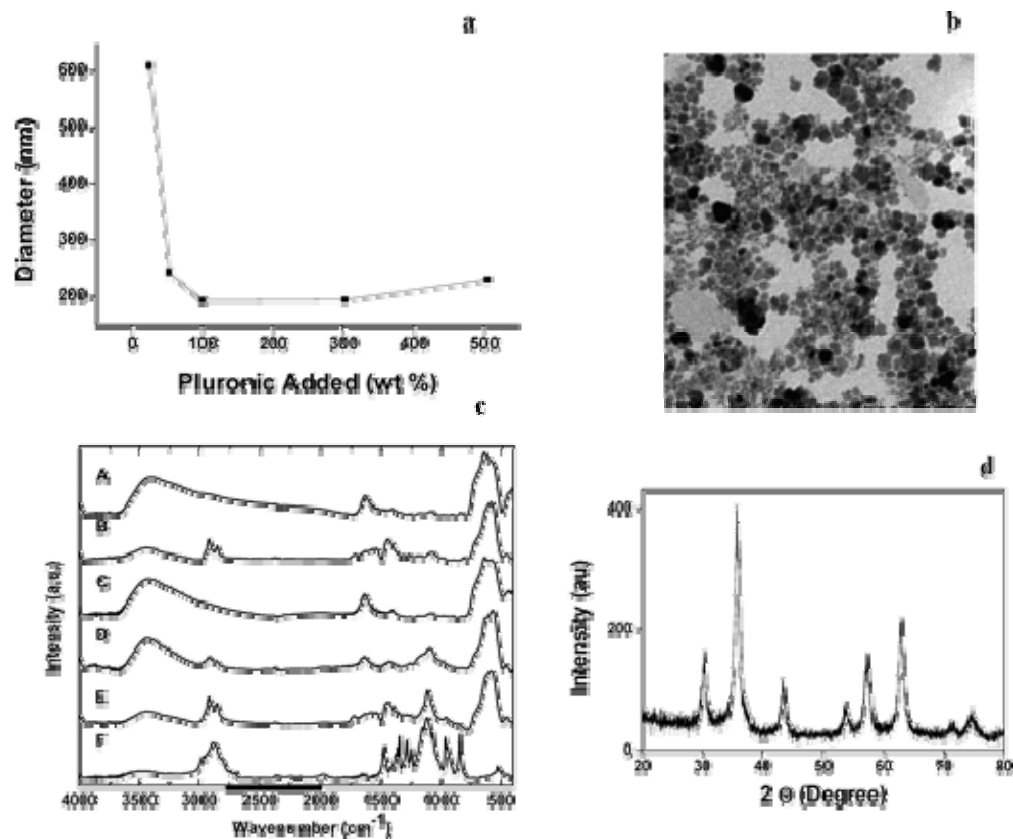


Figure 4 (a) Effect of different concentration of Pluronic on particle size of OA-coated iron oxide nanoparticles in water as measured by laser light scattering method (data as mean \pm SEM, $n = 10$). (b) TEM of OA-Pluronic stabilized iron oxide nanoparticles. (c) FT-IR spectra: (A) pure iron oxide; (B) 78.4 wt % iron oxide, 21.6 wt % OA; (C) 40.4 wt % iron oxide, 0.0 wt % OA, 59.6 wt % Pluronic F127; (D) 54.8 wt % iron oxide, 2.7 wt % OA, 42.5 wt % Pluronic F127; (E) 70.1 wt % iron oxide, 15.4 wt % OA, 14.5 wt % Pluronic F127; and (F) pure Pluronic F127. (d) XRD powder pattern of OA-Pluronic stabilized iron oxide nanoparticles.

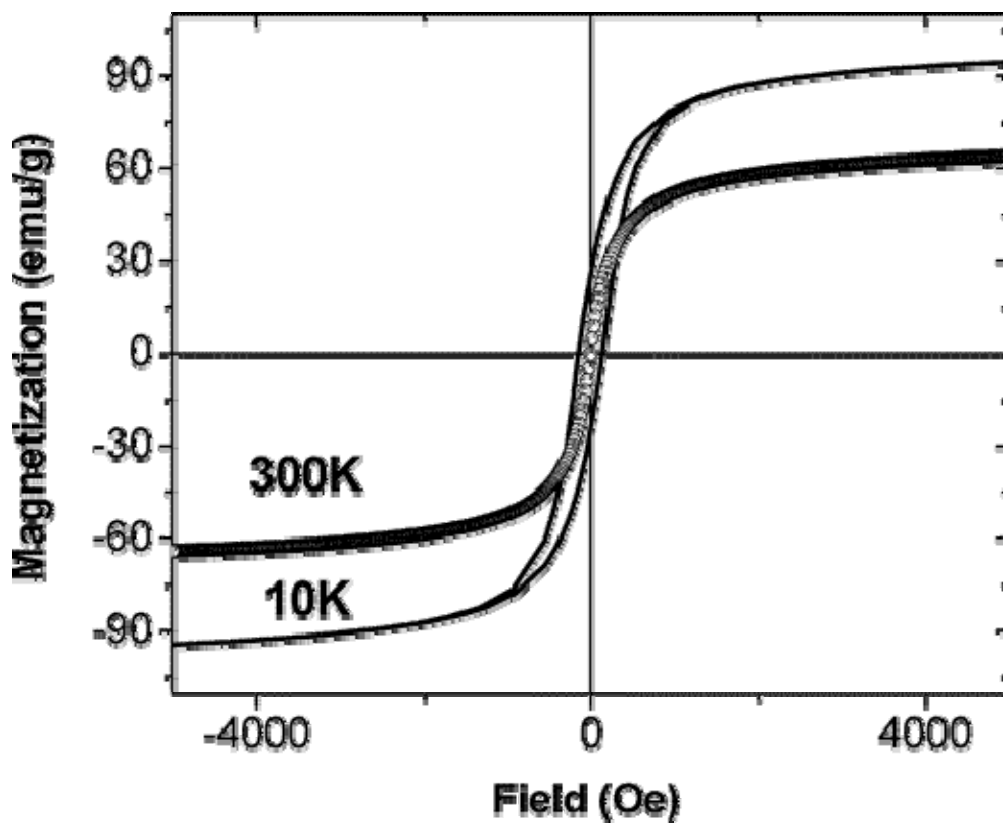


Figure 5 Magnetization as a function of field OA-Pluronic-stabilized iron oxide nanoparticles, measured at 10 K (solid line) and 300 K (circles).

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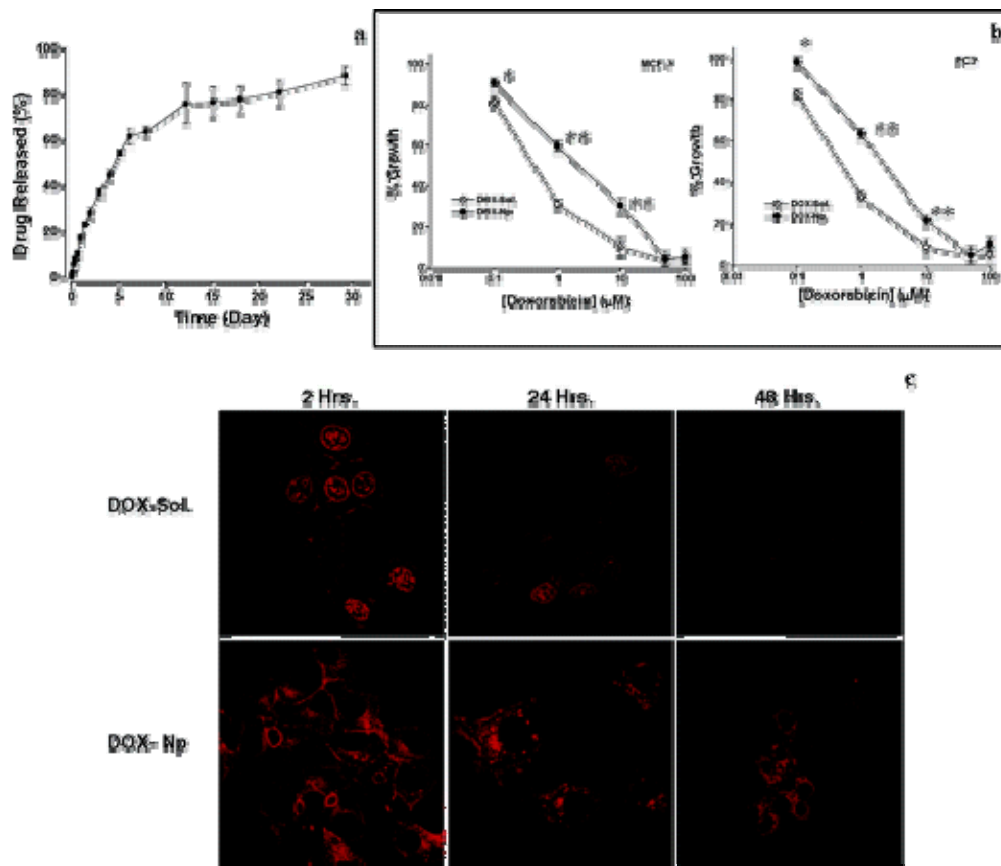


Figure 6 (a) Release of doxorubicin in vitro from drug-loaded OA-Pluronic-stabilized iron oxide nanoparticles. (b) Antiproliferative activity of drug-loaded nanoparticles and drug in solution in MCF-7 and PC3 cells. Data as mean \pm SEM ($n = 6$). * = $p < 0.05$, ** = $p < 0.005$, *** = $p < 0.001$. p values calculated for DOX-Np vs DOX-Sol. (c) Confocal laser scanning microscopic images of MCF-7 cells incubated for 2, 24, and 48 h with drug-loaded nanoparticles or drug in solution. Original magnification, 100 \times .

samples	saturation magnetization M_S (emu/g)	T_{\max} (K)	coercive field H_C (Oe)
iron oxide nanoparticles	66.1 ± 0.1	215 ± 7	201 ± 11
OA-Pluronic-stabilized iron oxide nanoparticles	86.1 ± 0.5	170 ± 5	158 ± 05
drug-loaded OA-Pluronic- stabilized iron oxide nanoparticles	88.8 ± 0.5	160 ± 5	151 ± 06

^a Saturation magnetization is normalized to the weight of magnetite.