Induced Hyperthermia Using Synthesized Iron Oxide Nanoparticles

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Introduction:

Unlike mainstream cancer therapies, such as chemotherapy, radiation, and surgery, induced hyperthermia using magnetic iron oxide nanoparticles (IONPs) has the potential to target cancer cells with reduced cytotoxicity towards healthy tissue. For this reason, research on how to optimize the functionality and delivery of these nanoparticles is currently being conducted.[1] For our project, we have investigated specific synthesis conditions to analyze their effects on nanoparticle size and structure. We hypothesize that manipulating the reactants used to synthesize IONPs will optimize particle size, monodispersity, and heat generation within an alternating magnetic field (AMF). Additionally, we tested different PEG-based coating formulations to enhance biocompatibility and efficacy of the induced hyperthermia therapy.

Materials and Methods:

Synthesis of IONPs: To synthesize iron oxide nanoparticles we reacted surfactants and solvents with an iron oleate precursor, via a high-temperature thermal decomposition process.[2] Using a design of experiments (DOE), we systematically tested combinations of surfactants with solvents; meanwhile ensuring that the heating rate, aging temperature, and reaction time remained constant. The two solvents used interchangeably, at a constant amount of 10ml, were 1-octadecene and N-octyl ether. Oleic acid, stearic acid, and oleylamine were either used individually as surfactants, in amounts of 150µl, 300 µl, or 450 µl, or in pairs at 150 µl of each. Optimal nanoparticles were coated with different ratios of 2-Distearoyl-sn-glycero-3-phosphoethanolamine-Polyethylene glycol (DSPE-PEG) and Polyhalogenated compound (PHC) through a thin film freezing process.
Characterization: Nanoparticle size and monodispersity, both before and after coating, was measured using DLS and TEM. Iron concentration was measured using inductively-coupled plasma optical emission spectroscopy (ICP-OES). IONP efficacy study: IONP efficacy against tumor associated macrophages was assessed using MTT cell proliferation assays. We incubated the coated particles with J774a.1 cells for 4 hours before exposing each sample to AMF for 30 minutes. Temperature changes due to nanoparticle heating were logged over the 30-minute exposure. For each sample run through the AMF, the specific absorption rate (SAR) was calculated.

Results and Discussion:

Hydrodynamic diameters of IONPs: Using data gathered from DLS, it can be seen that surfactants have the largest impact on particle diameter, while solvents had little to no impact at all. When tested in water, DLS data shows that stearic acid produces particles with a generally large diameter, within a range of 250-350 nm. Oleylamine generates much smaller particles with diameters below 200 nm. Oleic acid produces moderate particles within a 200-250 nm range. DSPE-PEG: PHC Formulation: Different ratios of IONP and DSPE-PEG were initially tested. A 3:1 ratio of IONP:DSPE-PEG ultimately proved to be the best formulation for testing PHC concentration. The two ratios that worked really well were 3:1:0.33 and 3:1:0.2 (IONP:DSPE-PEG:PHC). A 3:1 ratio of IONP:DSPE-PEG was initially chosen because the particles resuspended better and were more monodisperse as well as larger. With both optimal ratios, resuspension was clearly seen and there was little to no precipitation in both samples.

Conclusion:

Through the alteration of surfactants and solvents, we have synthesized magnetic iron oxide nanoparticles of different sizes. We have formulated a coating that encapsulates these particles and ensures biocompatibility.

References:

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2) Park, J. *Nat. Materials.* 2004. 3: 891-895.

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