PREPARATION AND CHARACTERIZATION OF MULTIFUNCTIONAL NANO AND MICRO PARTICLES FOR DRUG DELIVERY

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Abstract

We hypothesize that a multifunctional nano/micro-particle drug delivery approach utilizing combinational radiofrequency (RF) heating and chemotherapeutic agents will provide a safe and effective treatment options for cancer therapy. **Methods**: Ethylcellulose microspheres containing iron and the pluronic/glycerylmonostearate (GMS) iron nanoparticles were prepared by an emulsion solvent evaporation method. Iron content was determined using UV vis spectrometry. Particle size of the microspheres was determined by scanning electron microscopy (SEM) and optical microscopy. Surface charge (zeta potential) and particle size of the nano particles were measured by a zeta sizer. Particles contact with X-ray University RF (radiofrequency). The temperature was monitored as a function of RF exposure time and power by use of a PDT Fluoroptic Lab Kit (Luxtron Corp, Santa Clara, CA). **Results**: SEM and optical microscopy revealed that microspheres ranged from a size of 10 to 15 micrometers, were spherical with a smooth surface topography. The nanoparticles, on the other hand, were found to be agglomerated during lyophilization. The average size of iron nanoparticles in the ethylcellulose microspheres was below 4% yet this amount was found to be enough to enhance the temperature of 10 to 15 micrometers, were spherical with a smooth surface topography. 

**Objectives**

1. The the iron nanoparticles as shown in figure 2 are spherical in shape with positive zeta potential and with an average size of 450 nm.
2. The SEM pictures shown in Figure 4 (a) revealed that blank nanoparticles were spherical in shape but with a rough surface morphology, while the iron loaded-nanoparticles were smooth and spherical. Using optical microscopy (Figure 4(a)), the particle size distribution of the nanoparticles were determined and ranged from 10 to 15 micrometers.
3. The iron nanoparticles were subjected to external RF for different time periods and the temperature was determined by a digital probe. The results of this study are depicted in Figure 5. Both nanoparticles as well as nanoparticles showed a linear increase in temperature with an increase in RF exposure time and concentration of RF in the iron. In contrast, nanoparticles, the temperature increased from room temperature to 52.3 °C within 700 seconds at a high iron load to nanoparticles. The data to the iron loaded-nanoparticles, the temperature increase was from room temperature to 42 °C within 1000 seconds possibly due to a very low encapsulation of iron nanoparticles in the microspheres.

**Discussion**

The iron nanoparticles in the ethylcellulose microspheres was within 4% this amount was found to be enough to enhance increase in temperature when exposed to RF energy.

**Implications for Practice**

1. This proof of concept studies show that one can prepare a multifunctional iron micro/nanoparticulate drug delivery system which can produce heat when exposed to an external RF.
2. The chemotherapy present in the multifunctional nanoparticles will cause a rapid reduction in tumor size (up to 3 mm) due to their cooperative uptake in the leukemic vasculature and acidic environmental pH.
3. Once internalized, the nanoparticles containing iron will serve as a target molecule for imaging followed by generation of intracellular heat which can be accomplished when these particles are exposed to an external RF by application of a capacitively coupled external radiofrequency system.

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**Figure 1**: A photograph of the radio-frequency induction machine. (b) - Schematic representation induction machine, copper coils, and a temperature measurement system.

**Figure 2**: (a) SEM pictures of iron nanoparticles at 400x and (b) at 5000x magnifications.

**Figure 3**: Optical microscopy view of the microspheres without iron nanoparticles.

**Figure 4**: (a) SEM picture of microspheres without iron nanoparticles (b) SEM picture of microspheres containing iron nanoparticles.

**Figure 5**: External RF application of iron nanoparticles as well as encapsulated nanoparticles. The temperature was monitored as a function of RF exposure time and power by use of a PDT Fluoroptic Lab Kit (Lutron Corp, Santa Clara, CA).

**Table 1**: Preparation of Iron Oxide Nanoparticles.

**Table 2**: Methods of Preparation of Ethylcellulose Microspheres.

**Table 3**: Optical microscopy (Figure 3) and SEM (Figure 4 and 5) of microspheres.