Synthesis and Biological Evaluation of Drug-Carrying Magnetic Nanocomposite Particles for Targeted Drug Delivery

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Abstract. Drug-carrying magnetic nanocomposite spheres were synthesized using $Co_{0.5}Zn_{0.5}Fe_2O_4$ nanoparticles and poly (D, L-lactide-co-glycolide)(PLGA) for the purpose of magnetic targeted drug delivery. Magnetic nanoparticles (MNP) (~10 nm) were prepared by a chemical co-precipitation of Sulphate salts in the presence of sodium hydroxide. Oil-in-oil emulsion/solvent evaporation technique was conducted at 7000 rpm and 1.5-2 hrs agitation for the synthesis of nanocomposite spheres. Specifically, PLGA and the cancer drug 5-Fluorouracil were first dissolved in Acetonitrile (oily phase I) and combined with MNP. The drug, MNPs and polymer solution was added drop-wise into viscous paraffin oil combined with Span 80 (oily phase II). 10%, 15% and 20% of MNP in the nanocomposite spheres were evaluated in terms of particle size, morphology and magnetic properties using X-ray and SQUID, Fluid flow and Biological trials were carried out to determine their effectiveness in targeted drug delivery.

1. Introduction

To help meet the goal of eliminating cancer, the national Cancer institute (NCI) is engaged in efforts to use nanotechnology to change the way we diagnose, image and treat cancer [1] through funding research aimed at integrating the new ideas in nanotechnology with biomedical applications. Nanotechnology has the potential to offer solutions to these obstacles in cancer therapies, because of its unique size (1-100nm) and large surface to volume ratios [2]. There is an increase in the use MNP [3] by embedding in biodegradable polymers which deliver drug to the target site thus increasing drug efficiency, maximizing patient compliance and increase drug options[4, 5]. The drug is guided by an external magnet to the targeted site and released [4].

MNP are prepared by ceramic, sol gel and co-precipitation techniques and exhibit super paramagnetic properties allowing them to gain magnetism easily with an applied magnetic field and lose when the applied field is removed [10].. In this research, mixed ferrites of cobalt and zinc ($CO_{0.5}ZN_{0.5}FE_2O_4$) were prepared while previous experimental studies have been done on the fabrication and characterization of these ferrites in various concentrations at nanoscale and in bulk [7-13], a comprehensive study has not been done on the suitability of cobalt substituted zinc ferrite for targeted drug delivery.

2. Experimental methods, Results, Discussion and Significance

Magnetic nanocomposite preparation. This process involves the preparation of magnetic nanocomposite by emulsion- solvent evaporation method. The polymers PLGA 50:50 m (wt 40,000 -75,000) are dissolved solvent Acetonitrile placed in a conical flask in the first phase. The flask is then placed on a mixer operating at 7000rpm for about 30 minutes. The MNP and the Drug are then added to the solution until the nanoparticles are fully dispersed. The second phase on the other hand is prepared by adding paraffin to a surfactant in a separate beaker. The first phase is then added to this phase drop wise under a mixer operating at 7000rpm.using a centrifuge running at 1700rpm for 20 minute at 10 degrees, magnetic polyspheres are separated, washed, filtered and dried at room temperature

Magnetic characterization and Fluid flow studies. Figure 1 shows the XRD patterns of the MNP prepared and dried at room. The broad peak at 2θ equal to 35^0 consistent with (311) plane observed confirms the formation of spinel oxides with a cubic structure and small particle size. The average particle size is about 10 nm Figure 2 shows typical saturation magnetization curve for three different samples of magnetic nanocomposite.With constant PLGA concentration the MNP concentration was added in three concentrations of 10%, 15% and 20%. As could be seen from the figure 2, the saturation magnetization increased with MNP concentration. The hysteresis loop is consistent with super paramagnetic behavior of MNP existing as single domains. The temperature dependence of the magnetic field in figure 3 shows an increase in the blocking temperature (T_B)

with an increase in the MNP concentration. Above T_B the magnetization decreases in all cases with increasing temperature. .Figure 4 shows the MNP characteristics when made to flow within a magnetic field of 0.47 T. A decrease in the percentage of MNP captured with increasing speed and also increasing tube size is observed. Biological trials were carried out on normal cell cultures using magnetic nanocomposite, the polymer, the medium and the drug. Figure 5 shows a low activation index implying a decrease in the number of normal cell in the samples when the cells were exposed to the nanocomposite and the drug. the effectiveness of the additions were all affected by the concentration in the individual wells.

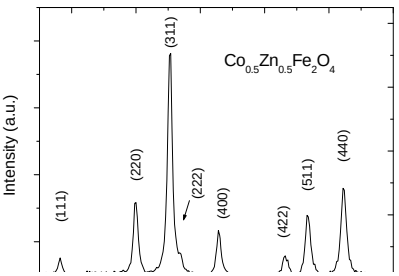

Figure 1. XRD patterns of MNP

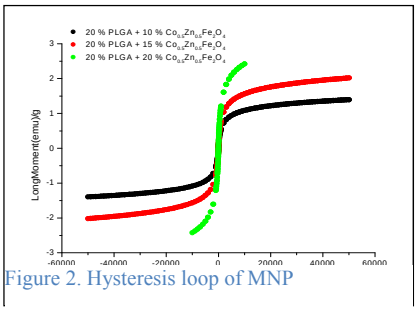

Figure 2. Hysteresis loop of MNP

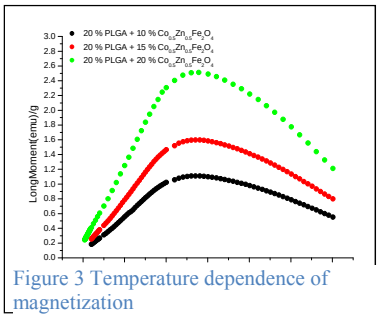

Figure 3 Temperature dependence of magnetization

3. Conclusion

Drug-load magnetic nanocomposite spheres were fabricated, characterized and tested to determine their suitability in magnetic drug delivery. Mixed ferrites of cobalt and zinc ($CO_{0.5}ZN_{0.5}FE_2O_4$) at the concentrations identified(X=0.5) were prepared by co-precipitation and magnetic nanocomposite by emulsion- solvent evaporation method. The samples showed super paramagnetic behavior with MNP approximately 10nm in size. the magnetic saturation and the locking temperature increased with increasing concentration.

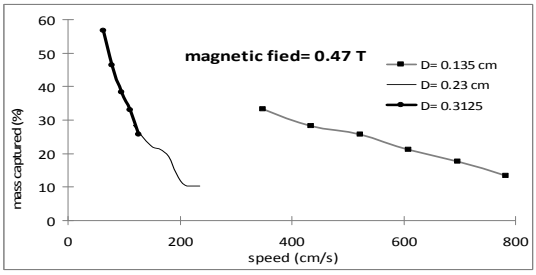

Fig. 4. Relationship between MNP captured at different speed

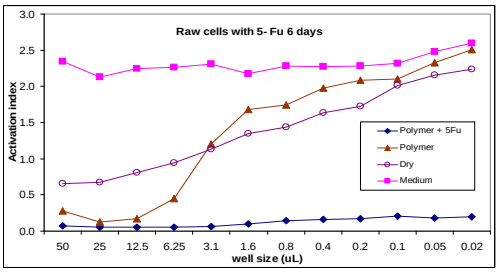

Fig. 5. Effect of different conjugates on cell population index

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