

Preparation of Polymer-Coated Functionalized Ferrimagnetic Iron Oxide Nanoparticles*

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Abstract—A simple chemical method to synthesize PMAA coated maghemite nanoparticles is described. Monomer methacrylic acid molecules were absorbed onto the synthesized ferrimagnetic nanoparticles followed by polymerization. The carboxylic group of PMAA coating allowed surface immobilization of foreign molecules. An anti-cancer drug was successfully adsorbed onto the PMAA coated maghemite nanoparticles for potential targeted drug delivery.

Index terms—PMAA; Maghemite; Nanoparticles; Adsorption; Polymerization; Drug

I. INTRODUCTION

Ferrimagnetic iron oxide nanoparticles, due to high saturation magnetization, high magnetic susceptibility and low toxicity, are promising candidates for applications such as magnetic resonance imaging [1], DNA extraction [2] and gene and drug delivery [3-4]. General approach to tailor the surface properties of the particles for applications can be achieved by coating or encapsulation [5].

Carboxylic acid group (-COOH) can be used for immobilization of oligonucleotides and protein on polymeric surface via the covalent bonding [6]. In this work, a chemical method was developed to synthesize functionalized polymer-coated magnetic nanoparticles. The free carboxylic acid group of polymer coating of iron oxide nanoparticles provided for surface adsorption of desirable molecules for potential applications. Carboplatin, highly stable in water, is an anti-cancer drug in the therapy of a variety of neoplasm. The adverse side effects of the cancer drug include nausea, vomiting and hair loss. Targeted drug delivery may enhance the drug efficiency and reduce undesirable side effects. In this work Carboplatin was adsorbed on the ferrimagnetic nanoparticles with surface functionalized carboxylic acid group. The coupling was

achieved between the carboxylic acid group of the particle coating and the ammonium group of the drug.

II. EXPERIMENTAL METHODS

Ferrimagnetic iron oxide particles were fabricated following a reported method for synthesizing magnetite nanoparticles [7]. Aqueous solution of Fe(II)/Fe(III) was prepared from FeCl₃ and FeCl₂·4H₂O in acidic condition. Precipitation of particles occurred at room temperature upon reaction with NaOH. The colloidal suspension was mixed with sodium dodecyl sulfate and MAA in water. K₂S₂O₈ was added to the solution and polymerization was carried out at 70°C in argon.

The structure of the synthesized iron oxide particles was investigated using x-ray diffraction. The lattice parameter and the average crystallite size of particles (with and without PMAA coating) were calculated from diffraction data. Transmission electron microscopy was used to characterize the morphology and the microstructure of the particles. The electrokinetic properties (zeta potential) as a function of pH were determined. Vibration sample magnetometry was also used to measure the magnetic properties of the particles.

The measurement of carboplatin adsorption on the synthesized PMAA coated maghemite particles was carried out using high performance liquid chromatography (HPLC).

III. RESULTS AND DISCUSSION

Figure 1 (a) and (b) show X-ray diffraction spectra of the synthesized iron oxide particles without and with PMAA coating, respectively. All detected Bragg peaks were assigned to the characteristic peaks of spinel iron oxide, indicating both samples did not contain crystalline α -Fe₂O₃ and iron hydroxides. The calculated lattice parameter a was 8.346 Å and 8.344 Å for particles with and without PMAA coating, respectively. The known lattice parameters of γ -Fe₂O₃ is 8.346 Å, thus both samples could be identified as γ -Fe₂O₃. The average crystallite size from x-ray line broadening for both samples was about 9 nm.

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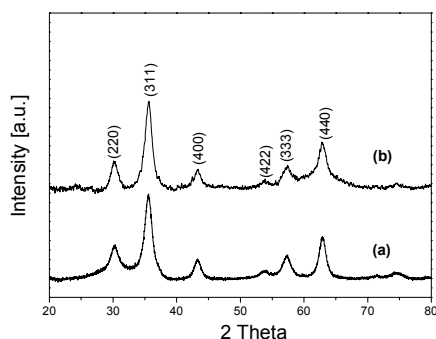


Figure 1. X-ray diffraction spectra of synthesized $\gamma\text{-Fe}_2\text{O}_3$ nanoparticles without (a) and with PMAA coating (b).

The TEM images of PMAA coated and uncoated $\gamma\text{-Fe}_2\text{O}_3$ nanoparticles are shown in Fig. 2. The average particle size for both samples was approximately 9 nm, consistent with the XRD data. These results confirmed that the synthesized nanoparticles were single crystals.

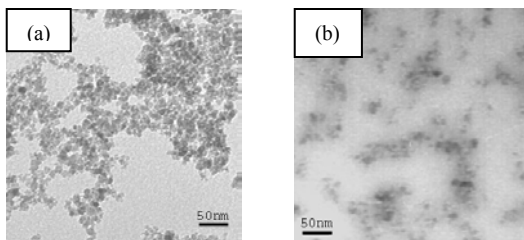


Figure 2. TEM images of the PMAA uncoated (a) and coated $\gamma\text{-Fe}_2\text{O}_3$ nanoparticle (b).

The zeta potential of the synthesized maghemite nanoparticles with and without PMAA coating as a function of pH values was analyzed (data not shown). After coated with PMAA, the origin of surface charge changed to carboxylic acid groups, which can be neutral COOH or dissociated to COO^- . The pK_a (intrinsic acidity constant) of PMAA is at $\text{pH}=3\text{-}5$ [8]. The observed shift of isoelectric point from $\sim\text{pH } 8$ for uncoated maghemite nanoparticles to $\sim\text{pH } 3.4$ for PMAA coated maghemite nanoparticles could be explained by the formation of PMAA layer on the surface of the maghemite nanoparticle.

Room temperature hysteresis loops of the PMAA coated and uncoated maghemite nanoparticles indicated that both samples could be not saturated at applied magnetic field of 9 T. The magnetization at 9 T for was about 57 emu/g and 50 emu/g for uncoated and coated samples, respectively, lower than the reported bulk counterpart (74 emu/g). The reduced magnetization could be attributed to the small particle surface effect [9].

The absorption of anti-cancer drug on the PMAA coated maghemite nanoparticles was carried out as a function of pH. The absorption of drug on the PMAA coated maghemite can be attributed to the coupling between COO^- of PMAA and NH_4^+ of carboplatin. The highest drug loading capacity was obtained at a pH value of ~ 7 .

Increasing or decreasing the pH value reduced the amount of adsorbed drug. It can be understood that the dissociated COO^- groups of the coated PMAA layer decreased with decreasing pH value, whereas the protonated NH_4^+ groups of carboplatin decreased with increasing pH value.

III. SUMMARY

In this work, a chemical method was developed to fabricate PMAA coated maghemite nanoparticles. The approach can be extended to synthesize other polymer-coated functionalized metallic or ceramic nanoparticles. The coated magnetic nanoparticles retained their magnetic properties. The anti-cancer drug carboplatin was adsorbed on the coated polymeric surface via the coupling between COO^- of PMAA and NH_4^+ of carboplatin. Using the carboxylic moiety as binding site, various functional molecules can be immobilized for other potential applications.

REFERENCES

- [1] K. A. Hinds, J. M. Hill, E. M. Shapiro, M. O. Laukkanen, A. C. Silva, C. A. Combs, T. R. Varney, R. S. Balaban, A. P. Korotky, and C. E. Dunbar, "Highly efficient endosomal labeling of progenitor and stem cells with large magnetic particles allows magnetic resonance imaging of single cells," *Blood*, vol. 102, pp. 867-872, 2003.
- [2] B. Yoza, M. Matsumoto, and T. Matsunaga, "DNA extraction using modified bacterial magnetic particles in the presence of amino silane compound," *J. biotech.*, vol. 94, pp. 217-224, 2002.
- [3] F. Scherer, M. Anton, U. Schillinger, J. Henke, C. Bergemann, A. Krüger, B. Gänsbacher, and C. Plank, "Magnetofection: enhancing and targeting gene delivery by magnetic force in vitro and in vivo," *Gene therapy*, vol. 9, pp. 102-109, 2002.
- [4] C. Bergemann, D. Müller-Schulte, J. Oster, L. À Brassard, and A. S. Lübke, "Magnetic ion-exchange nano- and microparticles for medical, biochemical and molecular biological applications," *J. Magn. Mater.*, vol. 194, pp. 45-52, 1999.
- [5] F. Caruso, "Nanoengineering of particle surfaces," *Adv. Mater.*, vol. 13, pp. 11-22, 2001.
- [6] E. P. Ivanova, M. Papiernik, A. Oliveira, I. Sbarski, T. Smekal, P. Grodzinski, and D. V. Nicolau, "Feasibility of using carboxylic-rich polymeric surfaces for the covalent binding of oligonucleotides for microPCR applications," *Smart Mater. Struct.*, vol. 11, pp. 783-79, 2002.
- [7] Y. S. Kang, S. Risbud, J. F. Rabolt, and P. Stroeve, Synthesis and characterization of nanometer-size Fe_3O_4 and $\gamma\text{-Fe}_2\text{O}_3$ particles, *Chem. Mater.*, vol. 8, pp. 2209-2211, 1996.
- [8] F. Shojai, A. B. A. Pettersson, T. Mäntylä, and J. B. Rosenholm, "Electrostatic and electrosteric stabilization of aqueous slips of 3Y-ZrO₂ powder," *J. Eur. Ceram. Soc.*, vol. 20, pp. 277-283, 2000.
- [9] B. Martinez, X. Obradors, Ll. Balcells, A. Rouanet, and C. Monty, "Low temperature surface spin-glass transition in $\gamma\text{-Fe}_2\text{O}_3$ nanoparticles," *Phys. Rev. Lett.*, vol. 80, pp. 181-184, 1998.