Synthesis of Iron Oxide Nanoparticles with Biological Coatings

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For biological and biomedical applications, it is required to produce nanoparticles that are water soluble and biocompatible. Here, we report the synthesis of iron oxide nanoparticles coated with biological molecules (e.g., gluconic acid, lactobionic acid, or polyacrylic acid) via a co-precipitation method. These nanoparticles have narrow size distribution and are highly water soluble. Because of the biological coatings, they will have great potential in numerous biomedical applications such as tissue engineering.

Introduction

Magnetic nanoparticles have shown great potential in many biological and biomedical applications such as targeted drug delivery, magnetic fluid hyperthermia, magnetic resonance imaging, and tissue engineering [1, 3, 5, 6]. All these applications require magnetic nanoparticles to be water soluble and biocompatible.

For biological and biomedical applications, magnetic iron oxide nanoparticles are the primary choice because of their biocompatibility and chemical stability. Many synthesis methods have been explored for magnetic iron oxide nanoparticles. These include organic solvent heating method, polyol method, and co-precipitation method [2, 4, 7]. The co-precipitation method is the most effective technique for preparing aqueous dispersions of iron oxide nanoparticles because the synthesis is conducted in water. For this report, we studied several biological molecules as surface coatings to achieve biocompatibility such as gluconic acid (GA), lactobionic acid (LBA), and polyacrylic acid (PAA). These molecules were used to control the particle size, to prevent the nanoparticles from aggregation, and to achieve biocompatibility.

Experimental

Synthesis

Iron oxide nanoparticles were synthesized by a modified co-precipitation method. Ferric chloride ($FeCl_3$, 0.074 g) and ferrous chloride ($FeCl_2$, 0.190 g) at a ratio of 2 to 1 were dissolved in 20 mL deionized water, which was then stirred and heated to 60 °C. The solution was bubbled with Argon gas to prevent unwanted oxidation. Subsequently, 10 mL of 2.5 M NaOH solution was injected at 60 °C and the reaction continued at that temperature for 20 minutes before the flask was removed from heating and stirring. The nanoparticles were then removed from solution by magnetic separation. During synthesis, the concentration and amount of NaOH was varied to control the particle size. A schematic drawing of the reaction set-up is shown in Figure 1.

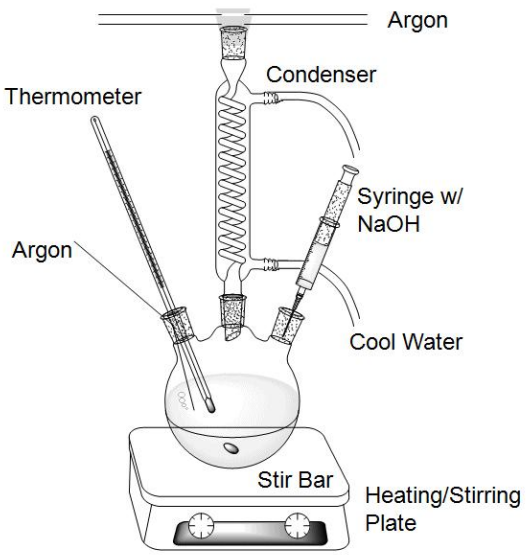

Figure 1. Schematic drawing of the experimental set-up.

Surface coatings

After synthesis, the black precipitates were collected, washed with DI water, and then re-dispersed into 10 mL GA, LBA, or PAA solutions (100 mM) under sonication. The pH was adjusted to 8 in order to simulate a biological environment and facilitate surfactant attachment to the iron oxide nanoparticles. Three hours of sonication were required to obtain well dispersed nanoparticles. The

nanoparticle solutions were then left at room temperature.

Characterization

The size and morphology of nanoparticles were studied by transmission electron microscopy (TEM); the crystal structure was verified using x-ray diffraction (XRD); the hydrodynamic size of the nanoparticles in solution was studied using dynamic light scattering (DLS). The solutions were also checked for precipitation. Solutions with a high level of precipitate indicated aggregation of nanoparticles. These aggregates are not suitable for biological applications.

Results and Discussion

Figure 2 shows the representative TEM images of iron oxide nanoparticles coated with GA and LBA. Although the sizes of both types were roughly 10 nm, the GA coated nanoparticles were more dispersed than the LBA coated nanoparticles, which showed a certain degree of aggregation.

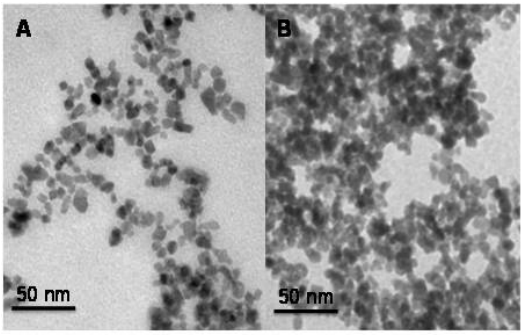

Figure 2. TEM images of iron oxide nanoparticles coated with (A) GA and (B) LBA.

The TEM image was not produced for the PAA coated iron oxide nanoparticles due to the large amount of the polymers present on the TEM grid, which interfered with the electron beam. However, the nanoparticle solution was well dispersed with no evident precipitate. Normally, precipitation is an indication of aggregation of nanoparticles.

The crystal structures of these nanoparticles were studied on GA coated nanoparticles. It was confirmed that these iron oxide nanoparticles are maghemite (Fe_2O_3), as shown in Figure 3, instead of the commonly formed magnetite nanoparticles (Fe_3O_4). This study suggests that the nanoparticles were fully oxidized either during or after the synthesis.

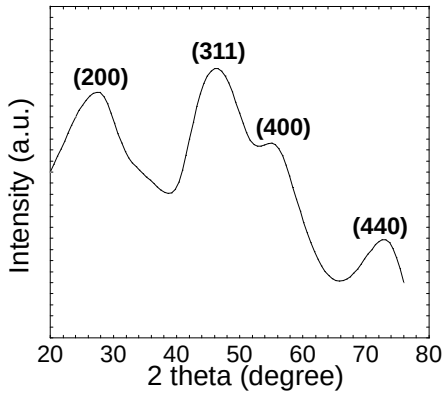

Figure 3. XRD scan of iron oxide nanoparticles.

For biological applications, nanoparticles are normally used in solution form. Therefore, it is important to study their hydrodynamic size in solution. DLS was used to measure the size of the synthesized nanoparticles. GA produced the smallest particles, showing a peak around 90 nm. LBA and PAA both had peaks around 140 nm as shown in Figure 4. The hydrodynamic sizes of the synthesized nanoparticles were significantly larger than those indicated by their TEM images. This is possibly due to the hydrogen bond formation between the carboxyl groups on adjacent surfaces, which can cause cross-linking between particles and result in a large hydrodynamic size. The size from DLS did not reveal a large difference between the MNPs synthesized with 2.5 M NaOH and 5 M NaOH.

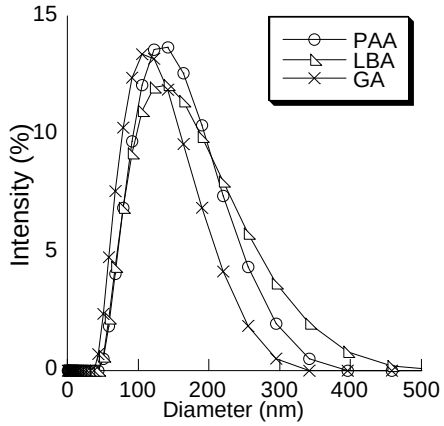

Figure 4. DLS plots of iron oxide nanoparticles coated with GA (cross), LBA (triangle), and PAA (circle).

Conclusion

In conclusion, water soluble iron oxide nanoparticles were synthesized using a co-precipitation method. These nanoparticles were subsequently coated with GA, LBA, or PAA. Both GA and LBA coatings produced well dispersed nanoparticles. They were in fully oxidized oxide form as confirmed by XRD. In solution, these nanoparticles showed a much larger hydrodynamic size, possibly due to hydrogen bond formation.

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David Dozier is a junior from Thomasville, Alabama, majoring in chemical engineering with a minor in biology. He currently works in the laboratory of Dr. Yuping Bao in the Department of Chemical and Biological Engineering. David also has an interest in going to medical school after graduation. He is a Presidential Scholar and a member of the Golden Key Honor Society.