One-Step Co-Precipitation Synthesis of Water-Stable Poly(Ethylene Glycol)-Coated Magnetite Nanoparticles

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Abstract. Magnetite is one of the important materials used in drug delivery systems, magnetic resonance imaging, and cancer therapy due to its low toxicity, durability, high biocompatibility, and low cost. Among the different methods of synthesizing magnetite, co-precipitation presents a facile route for synthesizing nanoparticles. Since rapid crystallization occurs in this method, a coating agent is essential to prevent the aggregation of the nanoparticles and increase its water-stability. In this study, PEG-coated and uncoated magnetite nanoparticles were synthesized by one-step co-precipitation. FeSO4·7H2O, FeCl3·6H2O, and PEG were used as the precursors for the magnetite nanoparticles. Addition of NH4OH while maintaining the reaction in an N2 environment at 80°C completed the synthesis of the nanoparticles. XRD analysis confirmed the structure of the synthesized nanoparticles is magnetite. The addition of PEG coating results in generally weaker diffraction peaks as well as the absence of some peaks, indicating a decrease in the crystallinity of the sample. AFM and SEM measurements reveal a spherical morphology for both PEG-coated and uncoated magnetite nanoparticles. DLS measurements showed that the PEG-coated magnetite nanoparticles had a lower average particle diameter (73.95 ± 0.786 nm) compared to that of the uncoated magnetite nanoparticles (143.72 ± 1.60) nm. The observed values are lower compared to the results of a previous study. DLS also showed that both the uncoated and PEG-coated magnetite nanoparticles are monodisperse. Zeta potential analysis reveals that the PEG-coated magnetite nanoparticles are more stable in water than the uncoated magnetite nanoparticles. Addition of the polymer coating reduces the particle size and enhances the water-stability of the magnetite nanoparticles, making it useful for biomedical applications.

1. Introduction
The unique properties of magnetite (Fe3O4) made it useful in biomedical applications such as drug delivery, cancer therapy, and magnetic resonance imaging (MRI), as well as in other fields such as
microbial fuel cells and sensors [1-4]. Its low toxicity, durability, high biocompatibility, and low cost have made it one of the most promising materials of today [5].

Magnetite nanostructures have been a recent material of interest due to the strong dependency of its properties to its morphology [6, 7]. The method of synthesizing magnetite nanostructures has been known to have good correlation to its size and shape. Nanospheres, nanocubes, and nanoneedles have been synthesized by hydrothermal methods, solvothermal methods, and co-precipitation methods [8-13]. Co-precipitation is one of the easiest methods to use since it only involves the simultaneous precipitation of a normally soluble component with a macro-component from the same solution [13]. However, the synthesized nanoparticles tend to aggregate because of the rapid crystallization during co-precipitation [14]. Several organic reagents, such as polyvinylpyrrolidone and oleic acid, which served as coating or capping agents, have been used to prevent the aggregation [15, 16]. Furthermore, the addition of these coating agents improved the dispersion in of the synthesized nanoparticles in aqueous media.

In this study, water-stable poly(ethylene glycol)-coated (PEG-coated) magnetite nanoparticles were synthesized using a one-step co-precipitation method. The structure, size, morphology, and water stability of the synthesized nanoparticles were also investigated.

2. Experimental Methods

2.1 Co-precipitation synthesis of uncoated and PEG-coated magnetite nanoparticles

Gas-free aqueous solutions of FeCl₃•6H₂O (Sigma-Aldrich) and FeSO₄•7H₂O (Sigma-Aldrich) (2:1 mole ratio) were mixed and diluted to 50 ml with deionized water in a three-neck flask. Subsequently, the reaction vessel was purged with nitrogen gas. Afterwards, poly(ethylene glycol) 400 Da (Alfa Aesar) was added to the mixture. The mixture was placed under vigorous stirring and 25% NH₄OH (Sigma-Aldrich) solution was added. The black solution was then heated to 80°C for 30 minutes. Finally, the magnetic products were collected via magnetic separation and were re-dispersed in deionized water. Some of the samples were dried at 110°C for further analysis. The synthesis of the uncoated samples follows the same route but without the addition of PEG.

2.2 X-ray diffractometry

Dried samples were characterized using a Rigaku X-ray Diffractometer (Cu Kα = 1.542Å) at the Department of Mining, Metallurgical, and Materials Engineering (DMMME), University of the Philippines, Diliman. The X-ray tube was set at a voltage of 40.0 kV and a current of 30.0 mA with 2θ scan range 10° to 90°.

2.3 Scanning electron microscopy (SEM) and atomic force microscopy (AFM)

Uncoated magnetite and PEG-coated magnetite nanoparticles were mounted in carbon tape and were aspirated using compressed air. Morphology of the samples was studied using a Hitachi SU8230 field emission-scanning electron microscope (FE-SEM) housed at the Department of Mining, Metallurgical, and Materials Engineering (DMMME), University of the Philippines, Diliman. The accelerating voltage was set to 10.0 kV with probe current at 21 pA.

Drop casted samples (mica plates as substrates) were characterized using a non-contact high resolution mode atomic force microscope (Park AFM NX10) housed at the Institute of Chemistry, University of the Philippines, Diliman.

2.4 Dynamic light scattering and zeta potential analysis

The average particle diameter, size distribution, and stability of the water-dispersed uncoated and PEG-coated magnetite nanoparticles were analysed using dynamic light scattering (DLS) and zeta potential measurements via Malvern Zeta-sizer Nano ZS90 at the Institute of Chemistry, University of the Philippines, Diliman.
3. Results and Discussion

3.1. Co-precipitation synthesis of uncoated and PEG-coated magnetite nanoparticles

The simple and efficient classical co-precipitation method using FeCl₃ and FeSO₄ as the chemical precursors was used in this study. The synthesis also does not require extreme temperature or pressure conditions. Furthermore, the synthesis route is irreversible, non-hazardous, and reproducible. The summary of the reaction involved is shown in equation 1:

\[
2\text{Fe}^{3+} + \text{Fe}^{2+} + 8\text{OH}^- \rightarrow \text{Fe}_3\text{O}_4 + 4\text{H}_2\text{O} \quad (1)
\]

\[
4\text{Fe}_2\text{O}_3 + \text{O}_2 \rightarrow 6\gamma-\text{Fe}_2\text{O}_3 \quad (2)
\]

\[
\text{Fe}_3\text{O}_4 \rightarrow \gamma-\text{Fe}_2\text{O}_3 \rightarrow \alpha-\text{Fe}_2\text{O}_3 \quad (3)
\]

Equation 2 shows the synthesis reaction of magnetite and oxygen, forming \( \gamma-\text{Fe}_2\text{O}_3 \) (Maghemite). The yield of \( \text{Fe}_3\text{O}_4 \) (magnetite) nanoparticles can be maximized by depleting the reaction vessel from oxygen. Purging the vessel with an inert gas, like nitrogen, favors the reverse reaction. The oxidation of the \( \text{Fe}^{2+} \) ions into \( \text{Fe}^{3+} \) also leads to formation of \( \gamma-\text{Fe}_2\text{O}_3 \) and this was prevented by the vigorous stirring used in the synthesis. Equation 3 shows the transformation of magnetite into other forms of iron oxide at certain temperatures. Magnetite transforms to \( \gamma-\text{Fe}_2\text{O}_3 \) at temperatures 110-230°C. \( \gamma-\text{Fe}_2\text{O}_3 \) transforms into \( \alpha-\text{Fe}_2\text{O}_3 \) (Hematite) at temperatures greater than 250°C. The drying temperature ensures that magnetite will not be transformed to maghemite [13].

Uncoated magnetite nanoparticles exhibit incipient stability in water (at neutral pH) or in physiological conditions. As such, uncoated magnetite tends to agglomerate and precipitate quickly [17]. Stable dispersion of magnetite nanoparticles in aqueous media can be achieved by either sterically or electrostatically. Addition of polymer-stabilizers, or coating, can also be used to stabilize the magnetite nanoparticles. Formation of the polymer-stabilized nanoparticles is characterized by a morphological change of the polymer chain from its chain form to a globular or spherical form. Increase in the ionic strength of the solution or exposure of the polymer to cations greatly contribute to this morphological change [18]. Electrostatic interaction of PEG with the \( \text{Fe}^{3+} \) and \( \text{Fe}^{2+} \) ions forms spherical shells by the exposure of the hydrophilic -OH groups to water [6]. The synthesis then proceeds inside the spherical shells which results in controlled particle sizes.

3.2. X-ray diffractometry

X-ray diffractometry was used to confirm the structure of the synthesized nanoparticles. Figure 1 shows the obtained XRD pattern of both the PEG-coated and uncoated nanoparticles. The uncoated magnetite sample shows peaks at \( 2\theta = 30.29^\circ, 35.62^\circ, 43.11^\circ, 53.75^\circ, 57.28^\circ, 62.96^\circ, \) and \( 71.39^\circ \), corresponding to (220), (311), (400), (422), (511), (440), and (533) planes. These peaks match well with those from the JCPDS card No. 19-0629 for a cubic magnetite with inverse spinel structure [19]. On the other hand, the PEG-coated nanoparticles showed similar peaks however, there was an absence of the peak corresponding to the (533) plane. With the presence of the PEG coating, it is observed that the diffraction peaks became noticeably weaker, which may have also caused the disappearance of certain reflections, indicating the decrease in crystallinity [20].

3.3. Scanning electron microscopy (SEM) and atomic force microscopy (AFM)

Morphological and particle size studies of the uncoated and PEG-coated magnetite nanoparticles are essential because the magnetic behaviour of such particles are highly influenced by particle size [6,7]. As an example, superparamagnetism is inversely proportional to particle size. The control of magnetite particle sizes within the nanometer scale (diameters range from 2.5 to 14 nm) must be ensured to maintain superparamagnetic behavior [21].

Figure 2 shows the SEM images of the synthesized uncoated (left) and PEG-coated (right) magnetite nanoparticles. The average diameter of the uncoated magnetite nanoparticles is around 28.63 ± 2.75 nm. It is observed that the nanoparticles tend to agglomerate. Voids can be seen at the SEM micrograph for the PEG-coated magnetite nanoparticles. The voids indicate that PEG has been
melted (melting point of PEG is 75 °C) due to the high-energy electron beams that hit the surface of the PEG-coated magnetite nanoparticles. A closer look at the micrograph reveals degradation and damage to the outer portions to the sample, which is primarily due to the destructive nature of SEM. The damage to the samples made it difficult to assess the average particle size of the PEG-coated magnetite. Therefore, a non-destructive method must be used to further analyze the morphology and particle size of the magnetite nanoparticles.

Atomic force microscopy (AFM) is a non-destructive imaging technique used to further analyze the morphology of the magnetite nanoparticles. The AFM images for the uncoated magnetite (figure 3) and PEG-coated magnetite nanoparticles (Figure 4) are shown below. The spherical morphology observed in SEM was confirmed by AFM. The images also show that the dried nanoparticles aggregate and pile up to a height of about 50 nm.

**Figure 1.** X-ray diffractometry patterns of (top) PEG-coated magnetite nanoparticles and (bottom) bare (uncoated) magnetite nanoparticles.

**Figure 2.** Scanning electron microscopy micrographs of (a) uncoated and (b) PEG-coated magnetite nanoparticles.
Figure 3. (a) 2D and (b) 3D AFM images of the uncoated magnetite nanoparticles.

Figure 4. (a) 2D and (b) 3D AFM images of the PEG-coated magnetite nanoparticles.

3.4. Dynamic light scattering and zeta potential analysis
SEM and AFM images in figure 2-4 reveal that both the uncoated and PEG-coated magnetite nanoparticles are particles less than 100 nm in diameter. However, we must take note that the nanoparticles in both SEM and AFM are dried. Materials for drug delivery applications are often dispersed in aqueous media in order to be transported throughout the body, thus determination of particle sizes and stability (using DLS and zeta potential analysis) when dispersed in an aqueous medium was also necessary to study its potential for such applications.

Table 1. Zeta potential, hydrodynamic diameter and polydispersity index of the uncoated and PEG-coated magnetite nanoparticles.

| Sample            | Zeta Potential (mV) | Z-average hydrodynamic diameter (nm) | Polydispersity Index (PDI) |
|-------------------|---------------------|--------------------------------------|---------------------------|
| Uncoated magnetite| -29.3               | 143.72 ± 1.60                        | 0.171                     |
| PEG-coated magnetite | -33.0              | 73.95 ± 0.786                        | 0.216                     |
Based on the results shown in table 1, samples were successfully synthesized in the nanoscale. The dispersed solutes in aqueous solution resulted to particles with an average hydrodynamic diameter of 143.72 ± 1.60 nm and zeta potential value of -29.3 mV. The zeta potential value indicate that the particles exhibit incipient stability in water. Thus, the uncoated magnetite nanoparticles have a slight tendency of agglomeration [22]. Polydispersity index values of around 0.200 indicate that the sample is monodisperse [23]. Thus, the polydispersity index value of 0.171 is a measure of high uniformity of the particle size distribution.

On the other hand, PEG-coating of the magnetite nanoparticles resulted to smaller hydrodynamic diameter (with an average of 73.95 nm), slightly higher polydispersity index value (0.216) and a more stable zeta potential (-33.0 mV) compared to the uncoated magnetite. The stabilizers do not attract each other because of the electrostatic repulsion. In the case of PEG, the negatively-charged oxygen atoms of PEG repel thus hinder the stacking of polymer layers, which leads to a lower zeta potential value resulting to a more stable colloidal solution. Furthermore, the 0.216 polydispersity index value also indicates monodispersity of the particle size distribution of the PEG-coated magnetite nanoparticles.

Amici et al. (2011) also studied the synthesis and characterization of PEG-coated magnetite nanoparticles [24]. The synthesis procedure was the same as reported in this paper but with an additional step of UV-curing in water. DLS measurements of the samples reported an average particle size of 400 nm, which is significantly larger than this paper’s average particle size of 73.95 nm. Furthermore, there were no reported zeta potential values which might explain the high average particle size.

4. Conclusions
Water-stable uncoated and PEG-coated magnetite nanoparticles were successfully synthesized using a one-step co-precipitation method. XRD confirmed the structure of the nanoparticles to be magnetite, with cubic crystal structure. SEM and AFM images show that the nanoparticles are spherical in shape. DLS and zeta potential measurements revealed that the uncoated magnetite nanoparticles have an average zeta potential of -29.3 mV, indicating incipient stability in water and adding the PEG coating increased the average zeta potential to -33.0 mV, indicating an increase in its stability. Addition of PEG also controlled the synthesis of magnetite nanoparticles with the average particle diameter decreasing from 143.72 nm (uncoated) to 73.95 nm (PEG-coated). Furthermore, both the uncoated and PEG-coated magnetite nanoparticles exhibit monodispersity, which is a measure of high uniformity of the particle size distribution. The observed PDI values for the uncoated and PEG-coated magnetite nanoparticles were 0.178 and 0.219, respectively.

5. References
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