A Novel Process to Prepare Magnetic Polymer Microspheres

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A new process for preparation of magnetic microspheres was investigated. In this process, the formation and the encapsulation of magnetic nanoparticles were accomplished in one step. The magnetic polymer microspheres exhibited superparamagnetic property and had a spherical shape with a smooth surface. This method can be used to prepare inorganic and organic composite particle when the inorganic particles can be prepared by chemical coprecipitation reaction.

In the past decades, there has been extensive interest in the preparation and applications of magnetic polymer particles range from nanometer to micron.[1] Magnetic separation, as one of the important applications of magnetic polymer particles, has many advantages compared with the traditional centrifugal separation, such as high speed, low cost, less loss of bioactivity attached on particles, and high efficiency. Because of their high magnetic properties and comparatively high specific surface areas, magnetic polymer microspheres have received much attention and have many applications, especially in cell separation and protein separation.[2]

Up to now, many different techniques have been developed for preparation of magnetic microspheres.[3] Ugelstad made historic contribution to the preparation of magnetic products known as Dynabeads®.[3e] These synthetic methods all involved at least two steps. The first step was to prepare the iron oxide nanoparticles, and the next step was to encapsulate the iron oxide nanoparticles with polymer or adsorb the iron oxide nanoparticles into polymer. However, owing the poor affinity between magnetic nanoparticles and polymer, it was relatively hard to encapsulate inorganic magnetic nanoparticles with polymer, which result in low encapsulation and low magnetic properties.[4]

In this communication, we developed a novel process, multiple emulsion ($W_1/O/W_2$)—in situ deposition for the preparation of magnetic polymer microspheres. In this process, the formation and the encapsulation of magnetic nanoparticles were accomplished in one step. That is to say, the place of formation is also the place of encapsulation of the iron oxide nanoparticles. The in situ deposition process can effectively overcome the difficulty of encapsulation resulting from poor affinity between iron oxide nanoparticles and polymer.

The magnetic polymer microspheres were prepared by multiple emulsion as shown in Figure 1. First, ferrous and ferric ions dissolved in water (W_1) were added into dichloromethane (O) which dissolved emulsifier and poly(styrene-co-2-hydroxyethyl methacrylate), (95:5) (PS-HEMA), and these two solutions were emulsified by an ultrasonic homogenizer to form a W_1/O primary emulsion. Then, the primary emulsion was added to the solution (W_2) which dissolved PVA and Tween20, and were emulsified by a homogenizer to form a multiple emulsion ($W_1/O/W_2$). Next, the multiple emulsion was transferred into a four-neck glass flask under an agitation rate by a half-moon-shaped impellor, and ammonia was slowly added to the multiple emulsion. Ammonia diffused from outer water phase (W_2) to oil phase (O), finally to internal phase (W_1), then magnetic nanoparticles were obtained by a coprecipitation reaction of ferrous ferric solution and ammonia in the internal water phase (W_1). Since O and W_1 phase were liquid, ammonia diffused from W_2 into W_1 easily. The reaction mixture was kept at normal temperature for some time protected by N_2, and the multiple emulsion ($W_1/O/W_2$) was changed to a multiple emulsion ($S/O/W_2$). Then, dichloromethane was evaporated under vacuum to obtain the solid microspheres encapsulating magnetic nanoparticles. Finally, the magnetite polymer microspheres were separated with external magnetic field and washed three times with deionized water and ethanol.

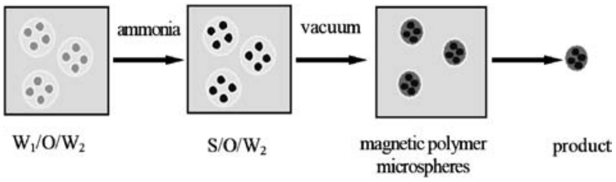

Figure 1. Schematic illustration of the preparation of magnetic polymer microspheres.

The size and morphology of the magnetic polymer microspheres were observed by scanning electron microscopy (SEM) and transmission electron microscopy (TEM), as shown in Figure 2 and Figure 3. It indicated that these particles were spherical in shape with a smooth surface and of 11 μm in average diameter, and the magnetic nanoparticles were relatively well dispersed in the microspheres. There were a lot of cavities in the microspheres which were formed by the coalescence between the drops of internal water phase (W_1). During the process of multiple emulsion preparation and organic solvent evaporation, requirement of minimizing the surface free energy drived the droplet (W_1/O and S/O) to form regular spherical shapes. The size distribution of the magnetic polymer microspheres was measured by a laser particle analyzer and the number of span is 0.992. The loading efficiency of magnetic nanoparticles reached 0.26 mg Fe_3O_4/mg microspheres and the yield of magnetic microspheres exceeded 85%. The particles size can be controlled by the rate of homogenization in the preparation of $W_1/O/W_2$.

The magnetic properties of the magnetic polymer microspheres and the Fe_3O_4 particles were analyzed with VSM as shown in Figure 4. The saturation magnetizations of Fe_3O_4 particles and the microspheres were 8.40 and 35.28 emu/g, respectively, and the deterioration degree of Fe_3O_4 particles

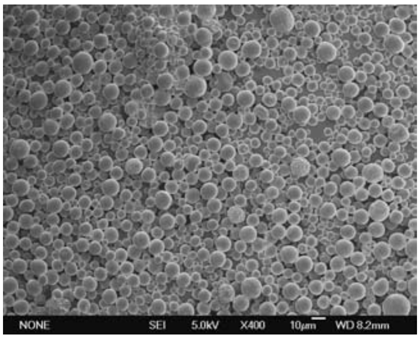

Figure 2. SEM image of magnetic polymer microspheres.

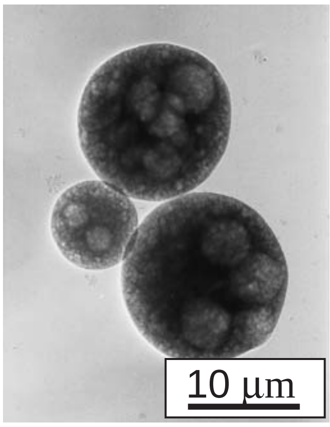

Figure 3. TEM image of magnetic polymer microspheres.

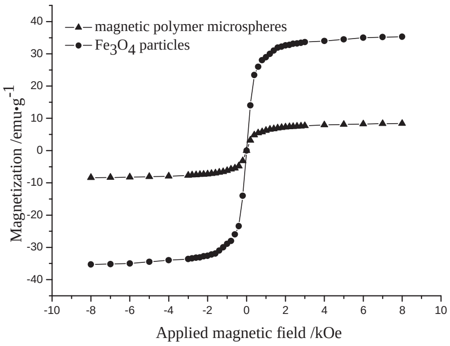

Figure 4. Magnetization curves of magnetic polymer microspheres.

was 8.4% during the encapsulated process. There was no hysteresis in the magnetization curve with both remanence and coercity being zero, which meant that these particles were superparamagnetic. The superparamagnetic property prevents magnetic polymer microspheres from aggregation and enables them to redisperse easily when the external magnetic field is removed.[5] Particles can be separated within 1 min by a conventional permanent magnet (2000 Oe).

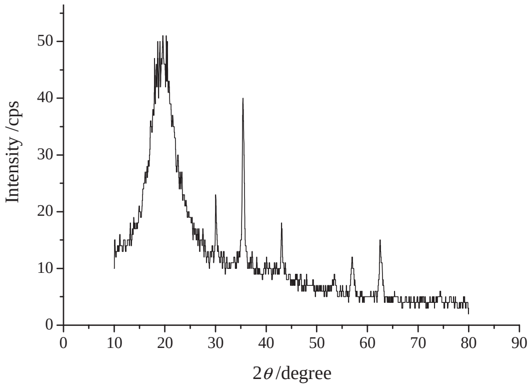

Figure 5. XRD of magnetic polymer microspheres.

Figure 5 shows the X-ray diffraction pattern of magnetic polymer microspheres. It was known from the X-ray diffraction data cards that standard Fe_3O_4 crystal with spinel structure had six diffraction peaks. The XRD pattern of particles shown in Figure 5 fitted the pattern for standard magnetite. So, it can be concluded that magnetic nanoparticles encapsulated in magnetic polymer microspheres are Fe_3O_4.

In summary, we have presented a new and convenient approach to prepare magnetic polymer microspheres which exhibited superparamagnetic property and had a spherical shape with a smooth surface. This method can be used to prepare inorganic and organic composite particle when the inorganic particles can be prepared by chemical coprecipitation reaction. If the application of membrane emulsification[6] is available to prepare multiple emulsion, it may be possible to prepare uniform-sized emulsion and uniform magnetic polymer microspheres.

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