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The preparation and properties of monodisperse core-shell silica magnetic microspheres

Min-yi Lou · Qiu-ling Jia · De-ping Wang · Bing Liu · Wen-hai Huang

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Abstract The monodisperse core-shell silica magnetic microspheres (MMS) were synthesized by sol–gel method gelling in the emulsion. Optical microscope (OM), field emission scanning electron microscope (FE-SEM), nitrogen adsorption and desorption Brunauer Emmett Teller Procedure (BET) isotherms and Barrett-Joyner-Halenda (BJH) pore size distribution measurements, X-ray diffraction (XRD), energy dispersive spectrometer (EDS) and vibrating sample magnetometer (VSM) were used to characterize the appearance, size distribution, phase, specific surface area, chemical composition and magnetic property of silica MMS. The results showed that silica MMS prepared through sol–gel method with acid-alkali two-step catalyze and gelling in emulsion exhibited the superior core-shell structure and size distribution of the microspheres concentrated in about 20 μm. The main phase of microspheres was amorphous silica and spinel ferroferric oxide. Meanwhile, the microspheres remained the superparamagnetic behavior and could be used as biomaterials.

Introduction

MMS are used widely in many fields. They can be used in catalyze to improve the activity of the catalyzer [1, 2] and also in magnetic imaging field [3, 4]. Because of their minisized effect, easily targeted, good biocompatibility, superparamagnetism and etc., they can be used in targeted drug field [5–7]. Under the magnetic field, they have the magnetic response, so they can be used in bioseparation field [8–10]. When their size exceeds the critical diameter, their superparamagnetism will disappear and the hysteresis loss will appear, so they can be used in tumor hyperthermia therapy [11, 12].

MMS can be divided into polymer, biomolecular and inorganic MMS according to their composing. There are quite a number of magnetic materials of polymer and biomolecular MMS reported in the literature [13, 14]. Recently, silica MMS have been vestigated for separation of nucleic acid, enzyme immobilization and ultra-sonic echography, and so on. There are three main advantage of the silica MMS compared with the polymer and biomolecular MMS [15]. First of all, the silica have the better stability, which can be used in both organic and inorganic solution. The other two MMS will swell in organic solution. Secondly, the surface area of the silica MMS is bigger, which can improve the bonding power and carry more drug. Lastly, the surface of the silica MMS can couple the functional groups more easily.

There are two main methods to prepare the silica MMS, directly chemical precipitation method and sol–gel method. The characterization of the silica MMS that prepared by sol–gel method is more uniform, so it is the method that researchers choose more often.

The sol–gel method to prepare the silica MMS is utilizing the hydrolytic polymerization of TEOS to form

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M.-y. Lou (✉) · Q.-l. Jia · D.-p. Wang · B. Liu · W.-h. Huang
School of Material Science and Engineering,
Tongji University, Shanghai 200092, China
e-mail: louminyi@163.com

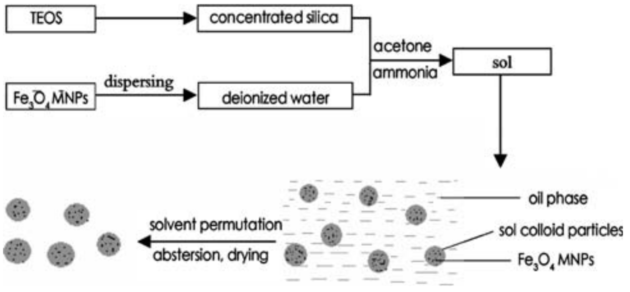
M.-y. Lou · Q.-l. Jia · D.-p. Wang · B. Liu · W.-h. Huang
Shanghai Key Laboratory of Metallic Material,
Shanghai 200092, China

the silica shell modified the Fe_3O_4 magnetic nanoparticles (MNPs). At the present time, most researchers chose the single acid or alkali as the catalyzer in the hydrolytic polymerization of TEOS [10, 16, 17]. In this paper, the acid-alkali two-step catalyze method is used innovatively which can utilize the two catalyzer fully according the different mechanism and the speciality. At the same time, gelling in emulsion is used to prepare the spherical silica microspheres which is novelly used in the preparation of the silica MMS before. The two techniques aren't the new ones, but using them to improve the sphericity of silica MMS is the first attempt and finally do a good job in this research. The obtained silica MMS exhibit the fine superparamagnetism and good magnetic response. The size of the silica MMS concentrate in about 20 μm, and they show the fine core-shell structure. The back-scattered electrons SEM photographs are used to depict the core-shell structure of silica MMS, which is more direct and clear. In the traditional characterization of silica MMS, the secondary electron SEM photographs or the transmission electron microscope (TEM) photographs are often chose to depict the core-shell structure, and the back-scattered electrons SEM photographs are merely to use.

Experimental

The preparation of the silica MMS

The Fe_3O_4 MNPs prepared by partial reduction chemical precipitation were ultra sonic dispersed in concentrated silica to be the precursor materials. Then the precursor was mixed with acetone, deionized water and ammonia as the water phase which was added into the oil phase slowly to form the W/O emulsion. Vigorous stirring was continued for about 2 h to alter form sol to gel. Finally, silica MMS were gained after the solvent permutation, filter, abstersion, drying and heat treatment. In this paper, Span80 was used as emulsifying agent to control the size distribution of silica MMS. The whole experimental progress was depicted in the following figure.



Characterization

Appearance of silica MMS

The appearance of silica MMS was characterized by the OM and QUANT 200FEEG field emission SEM. The light microscope was operated easily and could be used to depicted the glancing appearance and rough diameter of silica MMS. The back-scattered electrons SEM photographs were chose to depict the fine core-shell structure of silica MMS, which was more direct and clear compared with secondary electron SEM photographs which was widely used in characterizing the appearance of silica MMS.

Chemical composition of silica MMS

The D/max 2550 XRD patterns were recorded on the fine-grained powders in order to identify the phases obtained in silica MMS using a Dron 2.0 diffractometer (2θ from 5° to 70°) and Cu K α radiation. Nitrogen adsorption-desorption measurements at 77 K were performed on Micromeritic Tristar 3000 BET surface analyzer system. The chemical composition of silica MMS was characterized by QUANT 200FEEG EDS.

Magnetic property of the silica MMS

The Model 4 HF VSM was used to depicted the change of the magnetic property between Fe_3O_4 MNPs and silica MMS under the room temperature.

Results and discussion

Effect of acid–alkali two-step catalyze on silica MMS

The hydrolization and condensation of TEOS was utilized in the preparation of silica MMS. With the effect of deionized water, the reaction of TEOS was processed as follows:

$$Si(OC_2H_5)_4 + 4H_2O \overset{\text{hydrolization}}{\rightleftharpoons} Si(OH)_4 + 4C_2H_5OH$$

$$nSi(OH)_4 \overset{\text{condensation}}{\rightleftharpoons} nSiO_2 + 2nH_2O$$

Since the complex of the reaction process, the reaction functional groups were used to describe the hydrolization and condensation of TEOS:

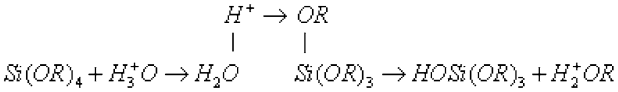
$$Si-OH+HOH\overset{\text{hydrolization}}{\rightleftharpoons}Si-OH+R-OH$$

$$Si-OH+Si-OR\overset{\text{condensation}}{\rightleftharpoons}Si-O-Si+R-OH$$

$$Si-OH+Si-OH\overset{\text{condensation}}{\rightleftharpoons}Si-O-Si+HOH$$

If none catalyzer was used in this reaction, the reaction velocity would be very slow. If proper amount of the acid or alkali was used, the reaction velocity would be improved; even the reaction would be completed in a split second. Through controlling the amount of the acid or alkali, the reaction velocity could be controlled.

The reaction mechanism was proton electrophilic reaction when acid was used as catalyzer [18]:



$$Si(OR)_4+H_3^+O\rightarrow \overset{\overset{\displaystyle H^+}{|}}{H_2O}\quad \overset{\overset{\displaystyle \rightarrow OR}{|}}{Si(OR)_3}\rightarrow HOSi(OR)_3+H_2^+OR$$

Because of the big steric effect, the hydrodrolization velocity of the monomer was quicker than that of chain end and chain middle. The resultant polymer was relative small and the polymerization degree was very low. The polymer was inclined to be the linear chain structure. The stronger of the acidity was, the quicker of the hydrolization would be and the slower of the condensation would be. In this situation, it was reputed that the reaction was first hydrolization then condensation.

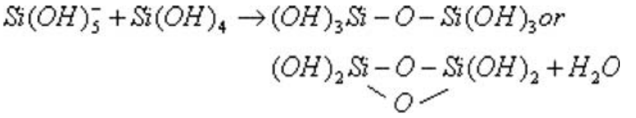
Otherwise, the reaction mechanism was nucleophilic reaction when alkali was used as catalyzer [19]. –OH group directly reacted with silicon of the Si(OR)$_4$ or the reaction intermediate, Si(OR)$_x$(OH)$_{4\text{-}x}$:

$$H_2O+Si(OC_2H_5)_4\xrightarrow{OH^-}Si(OC_2H_5)_3OH+C_2H_5OH$$

$$Si(OC_2H_5)_3OH+(x-1)H_2O\xrightarrow{OH^-}Si(OC_2H_5)_{4-x}(OH)_x+xC_2H_5OH$$

The hydrolization of the first –OC$_2$H$_5$ group was slower, and the hydrolization of the second, third and fourth –OC$_2$H$_5$ group was much more quickly. With the hydrolization reaction, the condensation of the intermediate Si(OC$_2$H$_5$)$_{4\text{-}x}$(OH)$_x$ started:

$$(OR)_3Si^-+(OR)_3Si-OH\rightarrow(OR)_3Si-O-Si(OR)_3(OH)^-$$



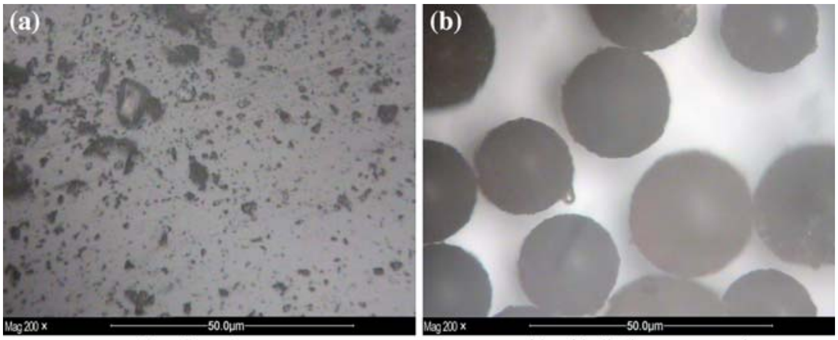
$$Si(OH)_5^-+Si(OH)_4\rightarrow(OH)_3Si-O-Si(OH)_3 or$$
$$(OH)_2\underbrace{Si-O-Si}_{O}(OH)_2+H_2O$$

$$n(OH)_2Si-(OH)_2-Si(OH)_2\rightarrow Si_xO_y(OH)_z+mH_2O$$

In this situation, the hydrolization and condensation happened almost at the same time. The reaction resultant was the gelatin with extensive cross bonding and high polymerization. It was inclined to be the grain structure. The obtained Si$_x$O$_y$(OH)$_z$ was very active, it would directly take a part in the growth of silica colloid particles or forming the new silica colloid particles.

In this research, acid–alkali two-step catalyze was used innovatively. First, the acid was used as catalyzer, the hydrolization was accelerated and the condensation was restrained. TEOS was hydrolyzed partially to form concentrated silica under the substoichiometry, then the dispersed Fe$_3$O$_4$ MNPs were added in to be the precursor materials. The precursor was mixed with acetone, deionized water and ammonia as the water phase that was added into the oil phase slowly to form the W/O emulsion. Using the ammonia as catalyzer this time would be propitious to form the grained silica MMS. The acid-alkali two-step catalyze made the full use of the their respective reaction mechanism, in the different stage of the reaction process the different catalyzer was used. The gelation time was reduced, and the sol–gel process could be controlled. Furthermore gelling in emulsion technique, silica MMS with good sphericity would be obtained.

Figure 1 illustrates the OM photographs of silica MMS prepared with different catalyze methods. Figure 1a depicts silica MMS obtained with only acid as the catalyzer. Using this method, silica MMS was almost chippy and there was



with acid catalyze

with acid-alkali two-step catalyze

Fig. 1 OM photographs of silica MMS prepared with different catalyze methods hardly grain with spherical shape. Under the only acid catalyze, the reaction was first hydrolization then condensation, the resultant was inclined to be the gel with low polymerization degree and finally formed the blocky silica with Fe_3O_4 MNPs in it. Figure 1b depicts silica MMS obtained with acid–alkali two-step catalyze method. This time, silica MMS had the fine grain with good sphericity. When under the alkali catalyze, the reaction resultant was the gel with extensive cross bonding and high polymerization. It was inclined to be the grain structure. But if alkali was used only, the reaction was too quick to make Fe_3O_4 MNPs dispersed in silica shell uniformly, and the percentage yield of silica MMS was low even many microspheres would be the pure silica grains with no Fe_3O_4 MNPs in them.

Effect of Span80 on silica MMS

Gelling in emulsion technique is a special method to prepare spherical carrier. The basic principle is to form the W/O emulsion. The internal phase, the water phase, as the microreactor has the condensation reaction happened in it. Finally, the gel solidifies to be the microspheres with Fe_3O_4 MNPs dispersed uniformly in.

Emulsion is a multiphase disperse system, which is a kind of liquid dispersed in another kind of liquid in the form of teeny dripping. And the two kinds of liquid can't be dissolved in each other. The system isn't thermodynamic stable, but has some dynamic stability in a way. The emulsion has two main types, W/O emulsion and O/W emulsion. In the former one, the internal phase is water phase and the external phase is oil phase. And it is the opposite in O/W emulsion. [20]

When the liquid is dispersed to many small droppings, the area of the interface between the two liquid phases expands. The system is thermodynamic unstable and inclined to make the free energy descend themselves. In other words, the small droppings collide each other to form the big droppings, even to alter to the two layers of the liquid. In order to have the stable emulsion, the interfacial free energy of the system must be reduced to avoid the droppings colliding. So the surfactant will be added as the emulsifying agent to reduce the interfacial free energy. There are so many kinds of the emulsifying agents, such as cationic, anionic, nonionic, natural product, solid power and etc. The nonionic emulsifying agent is often used in W/O emulsion. The emulsifying agent of a specific system is chose by the HLB value of the agent. The higher the HLB value is, the stronger the hydrophilicity is and the more easily W/O emulsion form. As the emulsifying agent of the W/O emulsion, the HLB value is often between 3 and 6 [20]. Besides the HLB value, the affinity of the emulsifying agent and the disperse phase, matching effect, the particularity of the emulsifying agent system should also be considered. According to the rules above, Span80 was chose as the emulsifying agent in this research whose HLB value was 4.3.

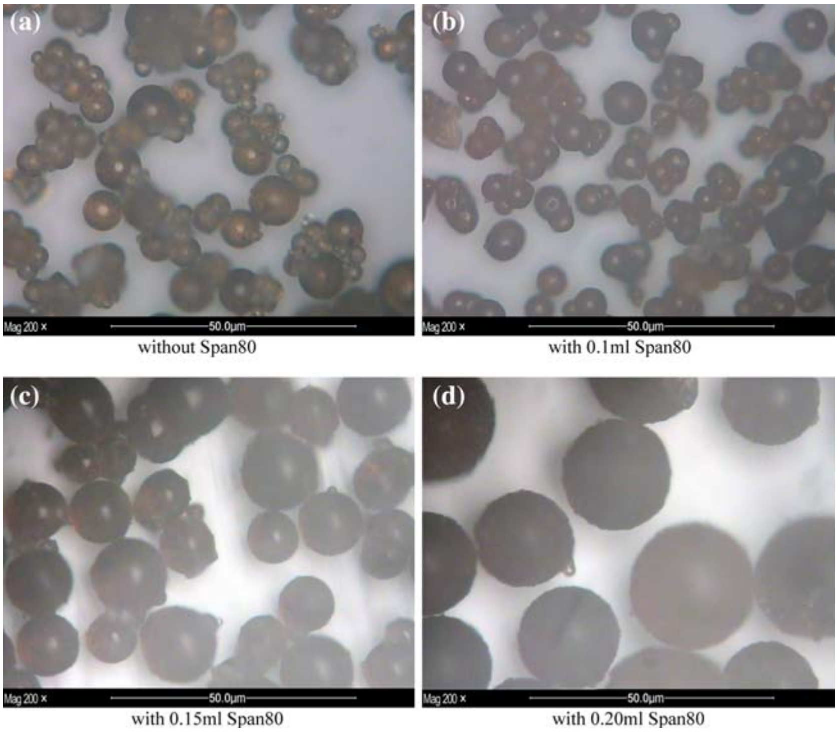


Fig. 2 OM photographs of silica MMS

Figure 2 illustrates the OM photographs of silica MMS with different amount of Span80. Silica MMS in Fig.2a was prepared without any Span80 which exhibit the multiple dispersion state; their diameters are concentrated in 3 and 8μm two ranges. And the MMS are agglomerated badly. Figures 2b–d depict silica MMS prepared with 0.10, 0.15 and 0.20 ml of Span80 in the emulsion. With the raise of the Span80 amount, the size distribution of silica MMS altered from multiple dispersion to mono-dispersion. At the same time, the size distribution range narrowed and the diameters were increased. The thick silica shell would impact the magnetic response of silica MMS. So the amount of Span80 should be the proper amount. In this research, 0.20 ml of Span80 added in the emulsion would prepare silica MMS with 20 μm diameter and remained the good magnetic response. The discussion below was all with this silica MMS.

Appearance of silica MMS

Figure 3 depicts the secondary electron SEM photographs of silica MMS. Figure 3a is shown many silica MMS with good sphericity concentrate in about 20 μm, and the surface of them is rather rough. Figure 3b depicts the section of an intact silica MMS, inside the silica shell, the Fe_3O_4 MNPs or the agglomeration of them are dispersed uniformly which concentrate mainly from 100 to 200 nm.

Figure 4 depicts the backscattered electrons SEM photographs of silica MMS. The atomic contrast effect of the back-scattered electrons photograph is more obvious than that of the secondary electron photograph, so that it's more easily to tell from the different phases through the back-scattered electrons one. In the back-scattered electrons photograph, the image of the bigger atomic number area appears light, and the image of the smaller atomic number area appears dark. The brilliant white particles are Fe_3O_4 MNPs or the agglomeration of them, and the gray area is the silica shell. Figure 4a depicts the back-scattered electrons SEM photograph of an intact silica MMS, it's seen that Fe_3O_4 MNPs or the agglomeration of them are dispersed in the silica shell more easily and more directly than the secondary electrons ones showed above. Figure 4b depicts the back-scattered electrons SEM photograph of an intact silica MMS.

Figure 5 depicts N_2 adsorpition/desorption isotherm of MMS. The isotherm is a Type IV shape. It indicates that silica MMS has mesopores structure. The BET specific surface area and the BJH desorption cumulative volume of pores of silica MMS nanospheres are 408m^2/g and180m^3/g, respectively. Calculated from the desorption branch of the nitrogen isotherm with the BJH method, the average pore

Fig. 3 Secondary electron SEM photographs of silica MMS

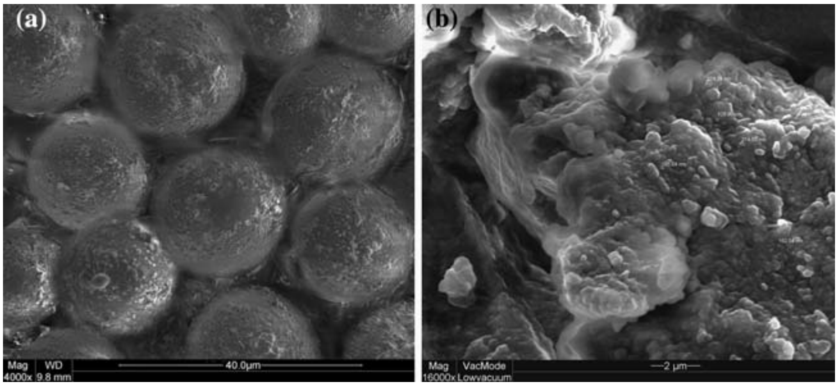
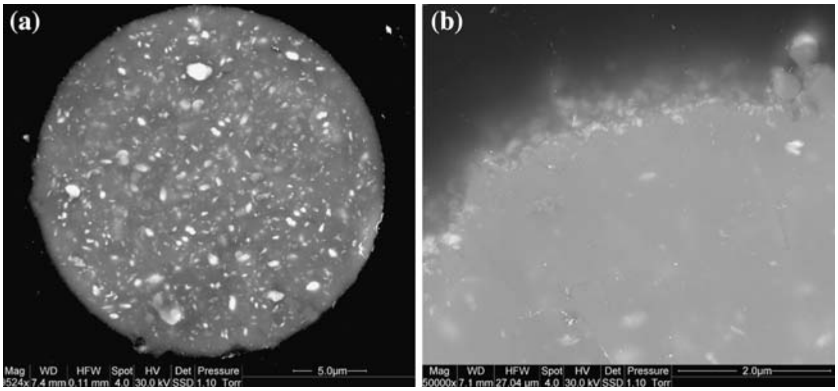


Fig. 4 Back-scattered electrons SEM photographs of silica MMS



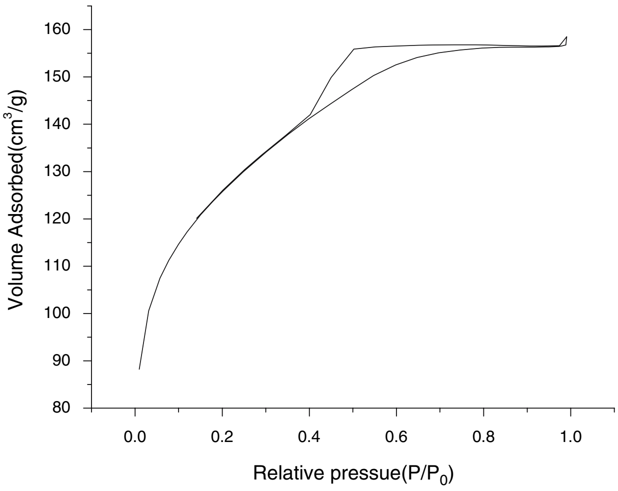


Fig. 5 N_2 adsorpition/desorption isotherm of MMS

diameter is determined to be 2.90 nm. It is considerably large. The surface of the microspheres is rather rough and the specific surface area is so big, so it's propitious to carry more drugs when used as targeted drug carrier.

There are two traditional core-shell structure, one is the core material enwrap by another material which is the shell material. Another one is the core material disperses in the shell material [21]. Silica MMS prepared in this paper is the second core-shell structure according to Figs.3 and 4.

Chemical composition of silica MMS

Figure 6 depicts the EDS spectrum of silica MMS. In this figure, the silicon, carbon, oxygen, iron peaks coming from the silica MMS and aurum peak coming from the coating of the samples are easily to be seen. The silicon peak intensity is very strong which suggests the silica shell with the appropriate thickness. The carbon peak intensity is also strong which came from the oil remains in the preparation of silica MMS. The third strong peak is the oxygen peak that was from both the silica shell and the oil remains. The iron peak indicates Fe_3O_4 MNPs or the agglomeration of them inside the silica shell.

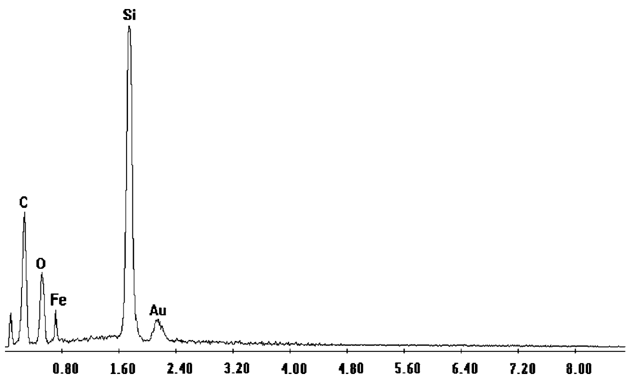


Fig. 6 EDS spectrum of the silica MMS

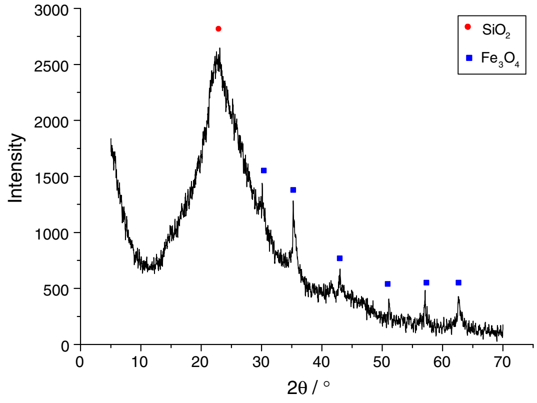


Fig. 7 XRD pattern of silica MMS

Figure 7 depicts the XRD pattern of silica MMS. An amorphous phase silica peak and some spinel ferroferric oxide peaks are seen. The results from the Figs.3–6 are shown that silica MMS prepared in his paper have the good core-shell structure, the Fe_3O_4 MNPs or the agglomeration of them disperse in silica shell uniformly.

The Magnetic property of silica MMS

Figure 8 depicts the hysteresis loops of Fe_3O_4 MNPs and silica MMS. Both Fe_3O_4 MNPs and silica MMS exhibited the good superparamagnetism behavior. They both had the sensitive magnetic response under the magnetic field. Utilizing this ''magnetic switch'' character, they could both be used in bioseparation, targeted drug fields. Comparing with

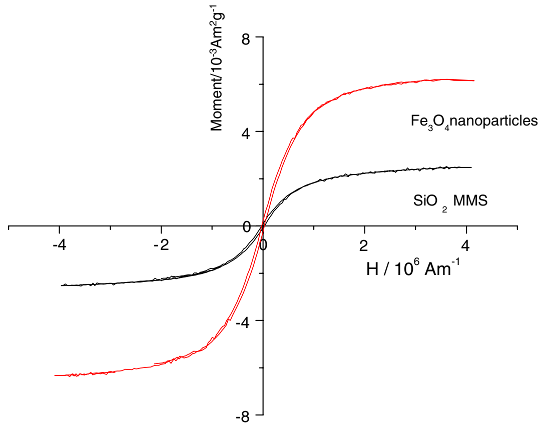


Fig. 8 hysteresis loops of Fe_3O_4 MNPs and silica MMS

these two loops, the saturation and remanent magnetization values of Fe_3O_4 MNPs are 6.24131×10^{-3} and $2.2215 \times 10^{-4} Am^2g^{-1}$, and the values of silica MMS drop to 2.47002×10^{-3} and $7.867 \times 10^{-5} Am^2g^{-1}$, which are the 39.6 and 35.4% of Fe_3O_4 MNPs values. The percent is related with the volume fraction of Fe_3O_4 MNPs in silica MMS. At the same time, the coercive force value of MMS is improved from 2.396×10^4A/m, the Fe_3O_4 MNPs value, to 2.953×10^4A/m. Since the decrease of the magnetic phase proportion in the two materials, the saturation and remanent magnetization decreased. On the other side, the silica shell would impact the effect of the outside magnetic field acting on the core Fe_3O_4 MNPs, so that under the determination of silica MMS, the magnetic change slowed when the magnetic field strengthened or weakened. And it would lead to increasing of the coercive force.

Conclusions

1. Acid–alkali two-step catalyze and gelling in emulsion technique could solve the silica MMS sphericity problem.
2. With proper amount of Span80, silica MMS could be prepared monodisperse and the size distribution was narrow.
3. The obtained silica MMS in this paper had the good core-shell structure and exhibited the good superparamagnetism behavior.

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