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Preparation of magnetite–dextran microspheres by ultrasonication

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Abstract

An improved method of preparing magnetite–dextran microspheres by ultrasonication is proposed. Several parameters were evaluated and the characteristics of the microspheres investigated by scanning electron microscope (SEM), atomic force microscope (AFM), particle size analyzer and magnetometer. The results show that the initial Fe/dextran ratio is the most effective parameter for both the size and the magnetic properties.

Keywords: Magnetite–dextran microsphere; Ultrasonication; Atomic force microscopy; Particle size; Dextran; Scanning electron microscopy

1. Introduction

Magnetic ferrofluids are colloidal suspensions that consist of Fe_3O_4 nanoparticles dispersed in liquid. They are widely used in technical fields such as material separation, magnetic domain detection, and pressure-tight rotary-shaft sealing or as damping and cooling agents for loudspeakers [1]. Because ferrofluids have some unique properties, i.e., they are magnetic and fluid, they can also be applied in biomedical applications for magnetic cell separation [2], as contrast agents in magnetic resonance imaging [3], to magnetically embolize blood vessels [4], for magnetic fluid hyperthermia [5], and so on. Furthermore, magnetic nanoparticles carrying chemical drug [6] or nucleic acid [7] with external gradient magnetic fields are being tested for the treatment of cancer.

Magnetic carriers can be manufactured using inorganic materials or polymers. In fact, high mechanical resistance, thermal stability, resistance to solvent and microbial attack, ease of manufacture and excellent shelf life make inorganic materials ideal supports. But they have limited functional groups for selective binding [8].

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Polymers, which can have a variety of surface functional groups that can be tailored to specific applications, are used to manufacture magnetic carriers. Poly ortho-ester (POE), poly lactide co-glycolide (PLGA), polyethylene glycol (PEG), polyvinyl alcohol (PVA), and others, have been used in the preparation of magnetic carriers [9–11].

Dextran is a polysaccharide and has many significant biological advantages such as being biodegradable, biocompatible and bioactive. Its chemical properties include being poly-cationic, hydrophilic and containing poly-hydroxy (-OH) groups (Fig. 1), and it can be used as a base material for magnetic carriers. In 1984, Molday [12] first described the production of colloidal size ferromagnetic iron oxide (Fe_3O_4) coated with a water-soluble polysaccharide (such as dextran) in the chemical coprecipitation method. From then on, some research groups have improved making magnetic microspheres [13,14]. In this study, magnetite–dextran microspheres were prepared in a simple way by ultrasonication and the morphology, size, and magnetic properties were investigated. Some parameters were evaluated to study which were most effective on the formation of the microspheres.

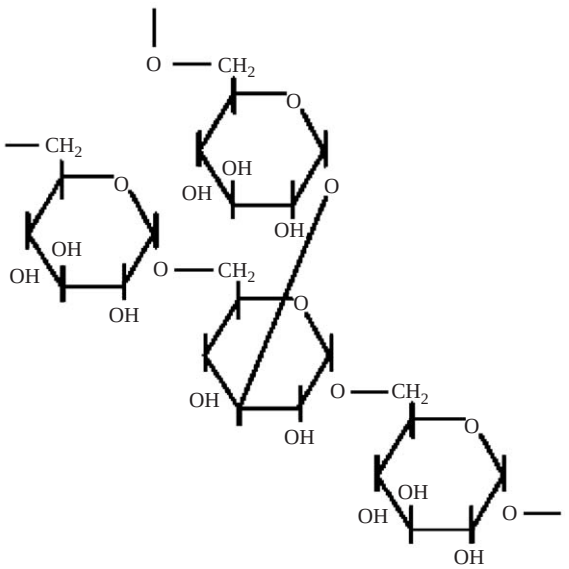

Fig. 1. Structure of dextran.

2. Materials and methods

2.1. Preparation of magnetite–dextran microspheres

Magnetite–dextran microspheres were synthesized using chemical coprecipitation according to Yudelson's method [12], while some processes were different such as ultrasonic was applied instead of stirring and nitrogen gas was ventilated to avoid oxidation. It was described by the following equation:

$$2Fe^{3+} + Fe^{2+} + 8OH^- \rightarrow Fe_3O_4 + 4H_2O.$$

In the study, some parameters were fixed such as the power of the ultrasonicator at 325 W, the reaction solution volume at 20 ml, the operating time as given below and the ratio of $Fe^{3+}/Fe^{2+}/OH^-$ was fixed to 2:1:8. Other parameters, such as quantity of iron, concentration of dextran, calculated ratio of Fe/dextran, and temperature of water bath, were investigated (Table 1). The levels of total iron quantity were 0.03, 0.06 and 0.12 mmol/ml while the mole ratio of Fe^{2+}/Fe^{3+} was fixed to 1:2. The dextran concentrations were 5, 10, and 20 wt%, respectively. The water bath temperatures were 20, 50, and 80 °C, respectively. The procedure to produce sample DX3 serves as an example:

(i) 0.27 ml of 1.5 mmol/ml $FeCl_3$, 0.40 ml 0.5 mmol/ml$FeCl_2$ and 4.0 g of dextran T-10 (Pharmacia Ltd., Sweden) were dissolved in 20 ml deionized water at 4 °C and then filtered through a 0.22 μm filter membrane.
(ii) Nitrogen gas was ventilated through this the solution for 5 min to eliminate air from the reacting tube.
(iii) 0.224 ml of 25–30% $NH_3 \cdot H_2O$ was added dropwise over 5 min while applying a power of 325 W by JY-92II ultrasonic cell crusher (Ningbo Rongshun Instrument Factory, China). As the base was added slowly, the solution changed in color from brown to black. The pH value was approximately 9.
(iv) After further ultrasonication continuously for 60 min in water bath at 80 °C, the suspension was cooled rapidly to below 10 °C. The final pH value was approximately 7–8.

Table 1
The size and the magnetic properties of different samples (DX1–DX9) prepared in different conditions

Sample	Total Fe (mmol/ml)	Dextran (wt%)	Initial ratio of Fe/Dextran (mmol/g)	Water bath temperature (°C)	Effective diameter (nm)	Poly-dispersity	Magnetic susceptibility (emu/g)
DX1	0.03	5	0.6	20	256.3	0.101	25.4
DX2	0.03	10	0.3	50	161.1	0.171	25.3
DX3	0.03	20	0.15	80	105.4	0.196	24.3
DX4	0.06	5	1.2	50	768.1	0.253	26.8
DX5	0.06	10	0.6	80	280.1	0.116	26.4
DX6	0.06	20	0.3	20	132.2	0.133	25.3
DX7	0.12	5	2.4	80	538.1	0.214	28.8
DX8	0.12	10	1.2	20	205.0	0.155	28.1
DX9	0.12	20	0.6	50	124.8	0.205	27.4

Three hundred and twenty five watts was the power of the ultrasonicator, 20 ml was the total reaction solution volume, the operating time was unchanged as described in Section 2.1 and the ratio of $Fe^{3+}/Fe^{2+}/OH^-$ was fixed to 2:1:8.

(v) The suspension was then poured into a 100 ml beaker with a Nd–Fe–B magnet attached below it (magnet remanence 5×10^3 G). After 2 h, the supernatant liquid was carefully poured off and 20 ml deionized water added to the beaker to wash the black aggregated compound on the bottom. The magnet plate was placed under the beaker again for 2 h and the operation was repeated for three times to remove the excessive dextran or ions. The final sample fluid DX3 had a neutral pH.

2.2. Characteristics of magnetite–dextran microspheres

The morphological characterization of the magnetite–dextran microspheres was carried out with a scanning electron microscope (SEM, JSM-5610LV, JEOL Ltd., Japan) and an atomic force microscope (AFM, NanoScope® IV controller, Digital Instruments Corp., Veeco Metrology Group, USA). Before SEM, the sample was dried in the vacuum desiccator and then sprayed plating. And for AFM, the sample was air-dry and the tapping mode was chosen.

The size and size distribution of the magnetite–dextran microspheres were determined by particle size analyzer (ZetaPALS, Brookhaven Instruments Corp., USA). The samples were diluted before testing. The effective diameter (ED), half-width and polydispersity were evaluated for three runs, and the mean value was obtained.

The magnetic properties of the magnetite–dextran microspheres were measured with a magnetometer (3257-35 DC Magnetometer, Japan). A known amount of the sample was placed in the magnetometer. The measurement was carried out at a temperature of 18 °C with an applied magnetic field of 10^4 Oe.

3. Results and discussion

Magnetic carrier technology is a very promising way in various kinds of biochemical or biotechnological applications, especially in drug delivery systems [13]. Meantime, nanotechnology, nanobiotech included, is developing at full speed and the 21st century is regarded as the nano-era. So, nano-magnetic biotech may be a new and promising technology.

In the study, the magnetic microspheres were produced by ultrasonication using inexpensive materials such as $FeCl_2$, $FeCl_3$, $NH_3 \cdot H_2O$ and dextran. The obtained magnetite–dextran microspheres were evaluated based on morphology, size and magnetic properties.

The morphology of the magnetite–dextran microspheres was investigated by SEM and AFM. As can be seen in the SEM micrograph of DX3 (Fig. 2), some of the microspheres are oval or

spherical, some have the shape of a dumbbell, and a few arose with a smooth brim. The size of them is mostly over 100 nm. Besides, most of the microspheres have a dark core and a bright shell. The AFM micrograph (Fig. 3) shows that most of the microspheres are smaller than 50 nm, and are spherical or oval. Several of them adhere to each other to form conglomerates as seen in SEM. The dextran's viscosity might be the reason.

Particle size results are shown in Table 1. Magnetite–dextran microspheres prepared by the above technique have a small size. For instance, the mean effective diameter of DX3 is 105.4 nm, the half-width is 46.5 nm and the polydispersity is 0.196. The results show that the dextran concentration and the initial ratio of Fe/dextran are the most effective parameters determining the size of the microspheres. While the other two parameters, iron quantity and water bath temperature, are not significantly effective. The ED decreases as the dextran concentration increased (Fig. 4). It may be explained that dextran can disperse the particles during the formation of the molecules of the magnetite (Fe_3O_4) particles. The correlation of the initial ratio of Fe/dextran to the size is also demonstrated (Fig. 5). When the ratio of Fe/dextran increases from 0.15 to 2.4, the ED increases rapidly from 105.4 to 538.1 nm. It means that less iron and more dextran can make the resulted particles smaller.

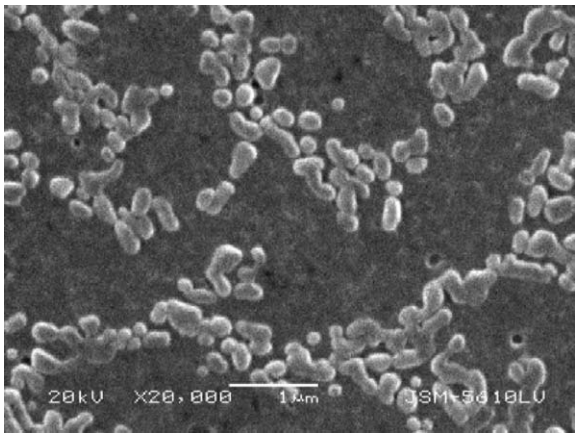

Fig. 2. Representative SEM micrograph of magnetite–dextran microspheres (DX3).

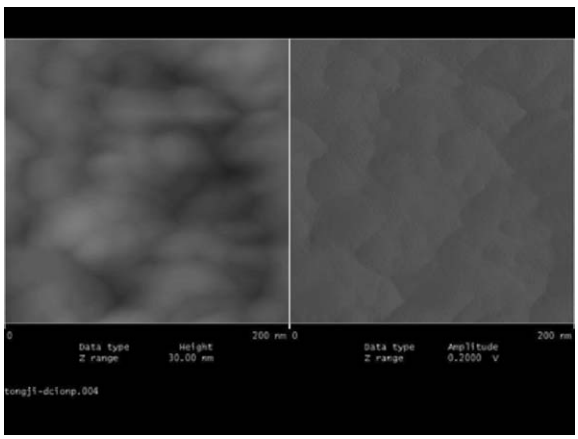

Fig. 3. Representative AFM micrograph of magnetite–dextran microspheres (DX3).

As to the saturation magnetization (M_s) of the magnetite–dextran microspheres in a certain magnetic field, the total iron quantity and the initial ratio of Fe/dextran are the most effective parameters. The other two parameters, dextran concentration and water bath temperature, were not significantly effective. The effect of the iron quantity on the M_s of the microspheres is demonstrated in Fig. 6, with higher iron content being more magnetic. The trend of the initial ratio of Fe/dextran to the M_s is also shown (Fig. 7). The M_s turns stronger along with the increase of the Fe/dextran initial ratio. It means that more iron and less dextran can get better magnetic property of the resulted particles as claimed [16] before.

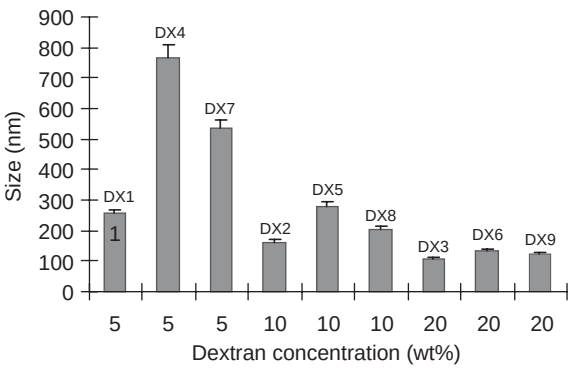

Fig. 4. Effect of dextran concentration on the particle size.

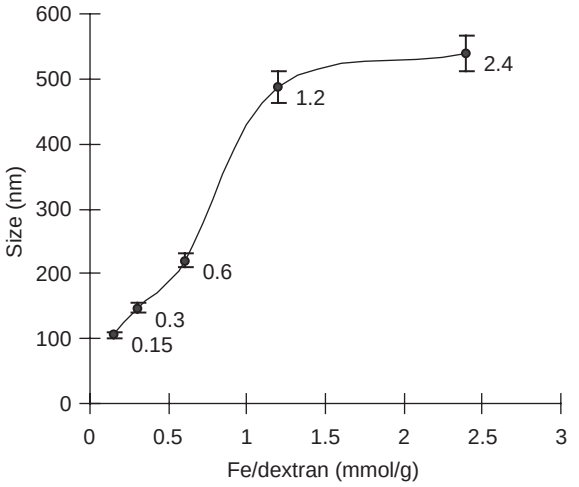

Fig. 5. Correlation between the Fe/dextran and the size.

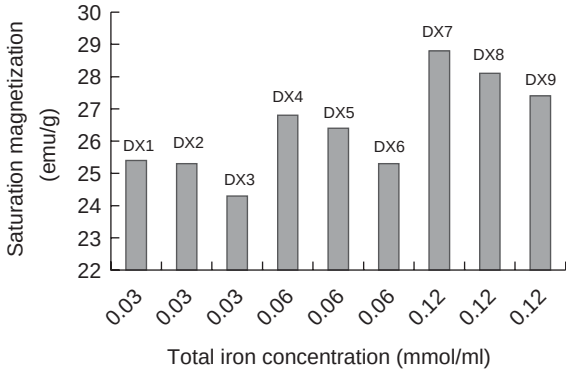

Fig. 6. Effect of iron quantity on the saturation magnetization.

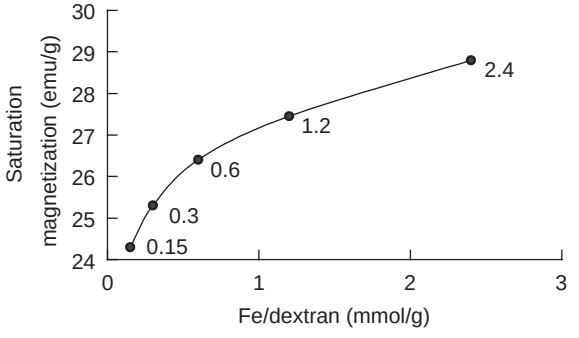

Fig. 7. Correlation between the Fe/dextran and the saturation magnetization.

In conclusion, the initial ratio of Fe/dextran is of importance to both the size and the magnetic properties of the magnetite–dextran microspheres. Higher ratio results in stronger magnetic susceptibilities but larger size (Figs. 5 and 7). This ambivalence makes it important to choose a proper ratio of Fe/dextran to reach better saturation magnetization and smaller size particles for further application.

Acknowledgements

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Further reading

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