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One-step hydrothermal synthesis of highly water-soluble secondary structural Fe_3O_4 nanoparticles

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ABSTRACT

Magnetite nanoparticles (MNPs) were prepared using the ferric acetylacetonate as the sole iron source in a facile hydrothermal route, while poly(acrylic acid) (PAA) was chosen as the stabilizer via one-step functionalized MNPs for better hydrophilic properties. The orthogonal was used in the paper for the experimental parameters optimization, including the solvent, the reaction time, the amount of stabilizer and the presynthesis. The obtained highly water dispersible MNPs with uniform size from about 50 to about 100 nm was individually composed of many monodisperse magnetite crystallites approximately 6 nm in size. And the MNPs show high magnetic properties, whose magnetite content was up to 76.76% and the saturation magnetization was 39.0 emu/g. Later the formation mechanism of MNPs was also discussed. Thus the MNPs proved to be very promising for biomedical applications.

1. Introduction

In the last decade, superparamagnetic nanoparticles have proved to be very promising for biomedical applications [1–3] as they are not subject to strong magnetic interactions in dispersion. Iron oxide nanoparticles (mostly Fe_3O_4 and γ-Fe_2O_3) have received the most attention because of their compatible and stability under physiological conditions, among which magnetite is a very promising candidate for its biocompatibility has already proven [4]. Besides the primary superparamagnetic nanoparticles, the efficient preparation of lager secondary structural superparamagnetic Fe_3O_4 particles have been attracted increasing attention because some of their properties are much more fit for biomedical applications, such as magnetic separation [5], and magnetic-targeted substrate delivery [6]. Some approaches have been developed to synthesize the aqueous secondary Fe_3O_4 nanoparticles, such as hydrothermal synthesis [7], self-assembly [8] and thermal decomposition [9].

Many NPs are stabilized in physiological conditions by functionalized with negatively charged groups (carboxylated, sulfate, phosphate, etc.) resulting in a negative ζ-potential of about 30–50 mv in physiological buffer [23]. In iron oxide, the surface iron atoms act as Lewis acids (L.A.) and coordinate with molecules that donate long-pair electrons, while in aqueous solutions, the iron atom coordinate with water, which dissociates to leave the iron oxide surface with hydroxyl functionalized. These hydroxyl groups are amphoteric and could react with both acids and bases. The Fe_3O_4 functionalized with carboxyl would be in the Scheme 1. Generally, despite their negative surface charge, these NPs are binding more conformational charges of the proteins on the NPs [23].

The naked Fe_3O_4 MNPs tend to aggregate and flocculate because of their high surface energy. So it is necessary to stabilize the nanoparticles in the biological medium. A number of stabilizers have been in research including monomeric stabilizers [10–12], inorganic materials [13,14] and polymer stabilizers [15–18] and so on. However the aqueous MNPs coated with dextran and PVA both have failed the test of long-term stability, pH or electron tolerance [15,16]. Be proper in biomedical applications, the coating of MNPs should satisfy the following requirements: (i) low or nontoxic [19], (ii) biocompatible and must also allow for a targetable delivery with particle localization in specific area, (iii) avoiding agglomeration of SPIONs in biological medium, (iv) achieving the desired surface charge for the SPIONs' main task, (v) preserving the functionalities of the nanomaterials, (vi) exhibiting the protein absorption on the SPIONs' surface and their corresponding denaturation [20]. Such MNPs can bind to drugs, proteins, enzymes, antibodies, or nucleotides and can be directed to an organ, tissue, or cancer using an external magnetic field. Cytotoxicity of the bare and coated SPIONs(–COOH and $–NH_2$) has been assessed via various methods, such as the MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) assay, and several in vivo models [20,21]. Besides the conventional physicochemical effects [22], other important factors such as the sedimentation of SPIONs, absorption of proteins [23], the interface of nano-bio and the effect of cell "vision" (i.e., cell type)

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[24,25]. The results confirm the biocompatibility of both bare and coated SPIONs at the applied doses, which were much higher than currently approved dose (i.e., 0.56 mg/kg) in humans [20,26].

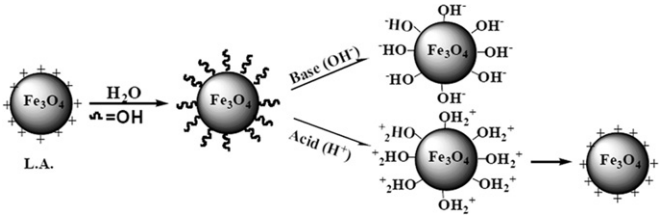
Several approaches have been developed into coating MNPs, including in situ coating and post-synthesis coatings [27,28]. One step synthesis of carboxylate functionalized MNPs in this paper will be simpler and much more economical for larger scale, while the coatings of PAA increases the stability and biocompatible of the MNPs and also helps in bioadhesion [29]. Moreover in our work, hydrothermal synthesis of MNPs in the autoclaves will bring us the pressure higher than 200 psi and the temperature above 200 °C which would be good for the nucleation of primary MNPs. Compared with the hydrothermal synthesis, secondary structural MNPs prepared by Jianping Ge et al. [8,31] is more complex with three steps resulted in lower efficiency.

In this work, a facile hydrothermal method was developed to construct a series of secondary structural Fe_3O_4 MNPs using PAA as stabilizer in situ functionalized the particles to get better hydrophilic properties. The optimization of experimental parameters is used the controlled clinical trials and mainly characterized with TEM. The obtained carboxyl MNPs would be amination and then combined with biological ligand and the protocol demonstrated to be feasible in our later work.

2. Experiment

2.1. Chemicals

Iron(III) acetylacetonate ($Fe(acac)_3$), poly(acrylic acid) (PAA) was purchased from Sigma-Aldrich and used as supplied. Ethylene glycol (EG), diethylene glycol (DEG), Triethylene glycol (TREG) were received from Chemical Company, China. All chemicals were of analytical grade and used without further purification.



Scheme 1. Procedure of Fe_3O_4 MNPs reacted with base or acid as L.A.

2.2. Synthesis of Fe_3O_4 nanoparticles

An amount of $Fe(acac)_3$ was dissolved in the solvent (40 mL) under stirring for about 30 min to fully dissolve the solids and then slowly dropped PAA with stirring for another minutes. The obtained red homogeneous solution was transferred to a Teflon-lined stainless-steel autoclave and sealed to heat to the boiling point of the selected solvent (the approximate boiling point of EG/DEG/TREG is 200 °C/250 °C/290 °C) for several hours. Carboxylate ions from the PAA chemically adsorbed onto the particle surface, yielding a stable sterically stabilized dispersion of nanparticles in water. Subsequently the magnetic nanoparticles were rinsed with water and ethanol (3 or 4 times) to effectively remove the solvent and unbound PAA. During each rinsing step, the nanoparticles were separated from the reaction system by a strong NdFeB Magnet ((BH)max=30 MG Oe). Larger particles created by aggregation during the preparation and stabilization in the dispersion were removed by centrifugation which was also used to get better size-dispersion. The experimental details and parameters of the controlled clinical trials are described as the Table 1.

2.3. Characterization

The magnetic nanoparticles were characterized by several techniques including TEM, FTIR, TGA, XRD, XPS and VSM.

The size and the morphology of nanoparticles were investigated by transmission electron microscopy (TEM, Model Tecnai 12, Philips Co. Ltd., Holland). Morever, in this paper the characterization of TEM is used to choose better experimental parameters. Feurier transform infrared (FTIR) spectroscopy of dry powders of the coated MNPs were recorded in KBr pellets on a Vector 22 spectrometer (Bruker Co. Ltd., Germany), and blank scanning was performed before measurements to eliminate the influence of vapor and CO_2 in air. Thermogravimetric analysis (TGA,) of dried samples was carried out using a TA Instruments TGA apparatus (Model TA2100, TA Instruments, USA) under an inert atmosphere (N_2) at a heating rate of 20 °C/min up to 800 °C. Furthermore X-ray diffractometer (XRD, D/max 18 kV, Bruker D8 Super Speed) with Cu Kα radiation and X-ray photoelectron spectroscopy (XPS, Thermo, ESCALAB250) were used to ensure the MNPs structure.

Table 1
Experimental details and parameters of the controlled clinical trials.

Batch	$Fe(acac)_3$ (mmol)	Solvent (40 mL)	PAA(wt%)	Strring	Temperature (°C)	Time (h)	Average particle size of primary MNPs (nm)	Average particle size of secondary structural MNPs (nm)
1	1.5	EG	1.00	Ultrasonic agitation	200	16	9.3	120
	1.5	DEG	1.00	for 30 min	250	16	8	–
	1.5	TREG	1.00		280	16	7	–
2	1.5	EG	1.00	Ultrasonic agitation	200	5	20	–
	1.5	EG	1.00	for 30 min	200	8	7	90
	1.5	EG	1.00		200	12	10	126
	1.5	EG	1.00		200	16	6	50
	1.5	EG	1.00		200	24	5	137
	1.5	EG	1.00		200	32	5	130
3	1.5	EG	0.00	Ultrasonic agitation	200	16	8	75
	1.5	EG	0.25	for 30 min	200	16	8	150
	1.5	EG	0.50		200	16	5	137
	1.5	EG	0.75		200	16	5	120
	1.5	EG	1.00		200	16	–	–
	1.5	EG	2.00		200	16	–	–
4	1.5	EG	1.00		200	16	6	120
	1.5	EG	2.00	Agitation for 30 min	200	16	6	110
	1.5	EG	3.00		200	16	6	100