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Original Research Paper

Impact of precursor solution concentration to form superparamagnetic $MgFe_2O_4$ nanospheres by ultrasonic spray pyrolysis technique for magnetic thermotherapy

Harinarayan Das [a,b,*], Nipa Debnath [a], Atsushi Toda [a], Takahiko Kawaguchi [c], Naonori Sakamoto [c,d], Hiromichi Aono [e], Kazuo Shinozaki [f], Hisao Suzuki [a,c,d], Naoki Wakiya [a,c,d]

[a] Graduate School of Science and Technology, Shizuoka University, 3-5-1 Johoku, Naka-ku, Hamamatsu 432-8561, Japan
[b] Materials Science Division, Atomic Energy Centre, Dhaka 1000, Bangladesh
[c] Department of Electronics and Materials Science, Shizuoka University, 3-5-1 Johoku, Naka-ku, Hamamatsu 432-8561, Japan
[d] Research Institute of Electronics, Shizuoka University, 3-5-1 Johoku, Naka-ku, Hamamatsu 432-8561, Japan
[e] Graduate School of Science and Engineering, Ehime University, 3 Bunkyo-cho, Matsuyama 790-85770, Japan
[f] School of Materials and Chemical Technology, Tokyo Institute of Technology, 2-12-1 O-okayama, Meguro-ku, Tokyo 152-8550, Japan

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ABSTRACT

The superparamagnetic magnesium ferrite ($MgFe_2O_4$) dense nanospheres are synthesized by ultrasonic spray pyrolysis (USP) method from different concentrations of the initial precursor solution. The effect of precursor solution concentration on the particle's size, morphology, and superparamagnetic behavior has been investigated. XRD results confirm that studied precursor concentration (0.06, 0.12 and 0.24 M) exhibited single phase cubic structure. The mean crystallites size (called as primary particles) of 0.06, 0.12 and 0.24 M samples are 9.6, 11.5, 11.0 nm, respectively but the entire nanosphere's diameter (called as secondary particles) increases from 206 to 340 nm with increasing precursor concentration. TEM analysis also reveals that nanospheres consist of densely aggregated crystallites of spherical shape and smooth surface. The value of polydispersity index (PDI) shows narrower size distribution for lower concentration. Magnetic properties indicate the superparamagnetic nature for all samples. Herein, the appropriate induction heat generation rate with better morphology was obtained for 0.06 M concentration. Ion release in the aqueous solution of the composition (about 95% for Mg; 99% for Fe) indicating better stability has been confirmed by ICP-OES test. In this approach, as-synthesized nanospheres are suitable for using as a heating agent in magnetic thermotherapy application.

1. Introduction

Magnetic thermotherapy or hyperthermia is a clinical therapeutic treatment where body tissues are exposed to an elevated temperature level of the range of 41–46 °C. Cancer cells are damaged and killed by high temperature because of its heat sensitivity but healthy cells can survive in this temperature range [1–6]. When AC magnetic field is applied, superparamagnetic sized nanoparticles can generate heat and be used as the heating agent in thermotherapy. Magnetic spinel ferrite nanoparticles are the most effective heating agent for hyperthermia treatment because of their chemical stability, higher magnetic response and simple preparation process with appropriate size [7–10]. These nanoparticles should have some special requirements for clinical biomedical application such as high rate of heat generation, non-agglomeration, high biocompatibility in living cells [11]. It has reported that magnesium ferrite ($MgFe_2O_4$) has highest heat generation ability in AC magnetic field compare to other spinel ferrites (MFe_2O_4; M = Mg, Mn, Fe, Co, Ni, Cu, and Sr) [12–14]. However, the frequency level with the magnetic field is also an important factor to generate heat in the human body, because higher magnetic field and frequency may produce eddy current that can damage the normal healthy cell [5]. Therefore, investigation of the magnetic materials having better efficiency in minimum magnetic field strength, frequency, and operation time should be ultimate objective in hyperthermia research. Konishi et al. reported that $MgFe_2O_4$ response of higher heat generation in the minimum frequency than Cu, Ni or Fe ferrites [15]. Synthesis of the nanoparticles in appropri-

* Corresponding author at: Materials Science Division, Atomic Energy Centre, Dhaka 1000, Bangladesh.
E-mail address: hn_das@baec.gov.bd (H. Das).

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ate superparamagnetic size with narrow size distribution is better to generate heat in the AC magnetic field [16]. Barati et al. have calculated theoretically that the particle size of $MgFe_2O_4$ is up to 15 nm for superparamagnetic to ferromagnetic transition, but they found 13 ± 0.5 nm experimentally at room temperature [17].

From last decade, $MgFe_2O_4$ nanoparticles have been fabricated by various methods such as coprecipitation method [18], sol–gel method [19], mechanochemical processing [20], combustion method [21], microwave hydrothermal method [22] and polymerization method [23]. Single crystalline nanoparticles synthesized by above methods have the tendency to agglomerate to minimize the surface energy. Such agglomeration of nanoparticles may block the capillary blood flow and is threatening for *in vivo* use of magnetic nanoparticles [24–26]. A dense nanocluster consists of single crystallite nanoparticles is suggested where the amount of agglomeration is very low. Ultrasonic spray pyrolysis (USP) is one of the suitable techniques where a large variety of micro to nano size spherical particles can be generated by droplet to particle formation mechanism with high purity, controlled composition and good crystallinity in short reaction time [27–33]. Here, the resulting nanospheres are named as secondary particles which arises through the growth and aggregation of nano-assembles (single crystallites) called primary particles.

Most of the solid tumors exhibit a vascular pore whose size is between 380 and 780 nm [34]. It is necessary to control the size of the secondary particles under this limit. In the one-particle-per-droplet mechanism of spray pyrolysis, the relationship between the diameter of obtained particle (D_p) and the precursor droplet (d) can be expressed by the following equation

$$D_p = d\left(\frac{C \cdot \rho_s}{\rho_p}\right)^{\frac{1}{3}} \quad (1)$$

where C, ρ_s and ρ_p are the precursor solution concentration, density of the precursor solution and density of the final particles, respectively [35]. According to the above relation, the diameter of synthesized particles is directly proportional to the cube root of the concentration of precursor solution used for synthesis ($D_p \propto \sqrt[3]{C}$). For the present case, the average size and the size distribution of the final synthesized nanoparticles are controlled by the concentration of initial precursor solution by implementing above mechanism. In this study, we use the different concentration of precursor solution with a view to achieve/tune the appropriate nanoparticle size with optimum superparamagnetic and heat generation properties for magnetic thermotherapy treatment.

2. Experimental details

2.1. Materials and method

Magnesium ferrite of composition $MgFe_2O_4$ was prepared by USP method using metallic nitrate salt. We used metallic nitrate salt because of its higher aqueous solubility. The starting reagents were magnesium nitrate hexahydrate ($Mg(NO_3)_2{\cdot}6H_2O$) and iron (III) nitrate nonahydrate ($Fe(NO_3)_3{\cdot}9H_2O$). Both analytical grades (purity >99%) were purchased from Kanto Chemical Co. Tokyo. The resultant nitrate salts were mixed with Mg:Fe molar ratio of 1:2 and then diluted with distilled water to prepare 0.06, 0.12 and 0.24 M solution concentration, respectively. Then the solution was atomized in the three-neck round flask on ultrasonic bath by the ultrasonic nebulizer (Model: MH-1630, Honda Electronics Co. Ltd., Japan) with the constant resonant frequency of 1.6 MHz and mist production rate was 575 ± 125 ml/h. The aerosol was delivered by the carrier gas to a horizontally oriented tubular quartz reactor zone maintained at 700 °C. N_2 gas was used as a carrier gas and the total gas flow rate was controlled at 3 L/min by a mass flow controller (Model RU-100, Lintec Co. Ltd., Japan). The mean residence time calculated from the carrier gas flow rate and the geometry of the heating zone (90 cm long and 30 mm diameter) was about 0.6 s. The atomized droplets underwent nucleation, evaporation, and crystallization in the hot reactor. Finally, the generated magnesium ferrite nanoparticles were stored on a filter paper (No. 5C, 60 Ø mm, Kiriyama Glass Co. Japan) connected to a water-jet air pump with a funnel. The sample holder was wrapped by a ribbon heater (FHU-8, Die Casting Electrical Co. Ltd. Japan) and the temperature was always maintained at 70 °C to keep the powder as-dried condition. Several K- type thermocouples (Model: K-2, Toho Electronics Ltd. Japan) were used to measure the temperature of atomizer surface, the different axial point of reactor zone and sample holder by digital temperature indicator. When whole precursor solution had atomized or enough product was stored, then the system was turned off and the product on the filter paper was collected as the powder. The as-prepared particles were directly used for further characterizations.

2.2. Characterization techniques

2.2.1. XRD spectroscopy

The crystal structure of as-synthesized nanospheres was examined using an X-ray powder diffractometer (D8 Advance; Bruker Analytik, Germany). The X-ray generator was operated at an accelerating voltage of 40 kV and the tube current of 40 mA with Cu $K\alpha_1$ radiation (λ = 0.1542 nm). XRD patterns were collected in step scan mode with the scanning rate of 0.01 s^{-1}. The phase composition and mean crystallite size were directly determined using TOPAS software utilizing the ICSD-PDF database [36].

2.2.2. FE-SEM observation

The external surface morphology of the powder samples was examined by field emission scanning electron microscopy (FE-SEM) (Model: JSM-700F, JEOL Ltd., Japan). The accelerating voltage of the electron gun was 15 kV with a medium probe current and a working distance of 10 mm. FE-SEM samples were prepared by dispersing the $MgFe_2O_4$ powders in ethanol with ultrasonically disagglomerated for 10 min in an ultrasonic bath. This suspension was disposed on an aluminum stub to dropwise and allowed the ethanol to dry. Then the samples were coated with nano osmium by sputtering to prevent surface charging.

2.2.3. TEM analysis

The internal crystal structure with aggregated nature was investigated using scanning transmission electron microscopy (STEM) (Model: JEM-2100F; JEOL Ltd. Japan) operating at an accelerating voltage of 200 kV. To prepare the TEM samples, powder samples were dispersed in ethanol using ultrasonic for 10 min and one droplet was dropped on a carbon-coated copper grid, then allowed to dry in the oven before analysis.

2.2.4. DLS measurement

The particle size distribution of nanospheres in the solvent was measured using an electrophoretic scattering photometer (Photal SELS-800Y; Otsuka Electronics Co. Ltd., Japan) by the principle of dynamic light scattering technique (DLS). Before this measurement, powder samples were dispersed in the ethanol solvent and sonicated for 10 min for homogeneous distribution. All measurements were repeated three times to verify the reproducibility of the results.

2.2.5. VSM measurement

The magnetic properties of the samples were examined using vibration sample magnetometer (VSM) (BHV-35; Riken Denshi Co. Ltd. Japan) measured at room temperature with a maximum

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