

Optimization of synthesis conditions to prepare desired shell thickness of superparamagnetic $\text{MgFe}_2\text{O}_4@\text{SiO}_2$ core-shell nanosphere for biomedical applications

H. Das*, N. Debnath*, T. Arai*, N. Sakamoto**, K. Shinozaki***, H. Suzuki*, N. Wakiya*

*Graduate School of Science and Technology, Shizuoka University, 3-5-1 Johoku, Naka-ku, Hamamatsu 432-8561, Japan, das.harinarayan@cii.shizuoka.ac.jp

**Research Institute of Electronics, Shizuoka University, 3-5-1 Johoku, Naka-ku, Hamamatsu 432-8561, Japan

***Department of Metallurgy and Ceramics Science, Tokyo Institute of Technology, 2-12-1 O-okayama Meguro-ku, Tokyo 152-8550, Japan

ABSTRACT

We have described here a simple way for the fabrication of superparamagnetic $\text{MgFe}_2\text{O}_4@\text{SiO}_2$ core-shell spherical nanoparticles with controlled shell thickness. First, core MgFe_2O_4 dense nanospheres were directly synthesized by ultrasonic spray pyrolysis (USP) technique from the aqueous metal nitrate precursor solution. Afterward, silica was coated on the obtained nanosphere for various desired shell thickness (10, 20 and 30 nm) by using theoretically calculated amount of tetraethyl orthosilicate (TEOS, as SiO_2 precursor) and appropriate ratio of HCl (as acidic catalyst) via modified sol-gel approach. The effect of different shell thickness on the structural and morphological properties of core-shell nanospheres were detail studied by various characterization techniques. These results demonstrate that core-shell structure have only a single core MgFe_2O_4 which is homogeneously covered by dense amorphous silica layer with appropriate thickness. The measured shell thickness (~10, 20 and 30 nm) by TEM image is almost same as our proposed shell thickness. TGA curves shows the better thermal stability of coated nanosphere and have shows higher monodispersibility for thin shell (~10 nm) due to less agglomeration.

Keywords: Nanosphere, Core-shell, Superparamagnetic, Hyperthermia

1 INTRODUCTION

Superparamagnetic magnesium ferrite (MgFe_2O_4) nanoparticles hold much promise for application in biomedical fields specially magnetically induced hyperthermia in cancer therapy because of its higher heating ability compare to other ferrites [1-3]. In addition, the elements of this composition are present in human body for bioactivity [4]. Due to the potential applications, different methods have been explored to synthesize MgFe_2O_4 nanoparticles. In this case, we have directly synthesized superparamagnetic MgFe_2O_4 as-dried nanoparticles by ultrasonic spray pyrolysis method, which could be produced

solid spherical shape particles with high purity and good morphology in short reaction time [5]. However, due to the inter-particle attraction of magnetic nanoparticles, it have tend to agglomeration and thus lose their specific properties. Furthermore, the surface reactivity of these particles are increase greatly as their dimension are reduced and they may cause rapid biodegradation when exposed biological systems [6-7]. Highly biocompatible nonmagnetic materials such as polymer, silica or carbon etc. encapsulating the surface of the nanoparticles can solve the above problems [8-9]. It is well-admitted that silica is a very good surface modifier, because of its excellent biocompatibility, nontoxicity, thermal stability and easily further conjugation with various functional groups [9-10]. In the last few years, silica coating of magnetic nanoparticles via sol-gel approach has been extensively investigated through systematic monitoring of the reaction parameters. However, most of the previous work was focused on silica shell formation by using base catalyst which influence to form branch clusters and porous silica [11]. But for higher biocompatibility, it is necessary to coat by amorphous dense silica layer. Acid catalyst is proposed to form such linear polymers because of its electrophilic reaction [11]. So that, at first we choose acidic catalyst that is to favor formation of homogeneous amorphous silica mono layer on core particles to obtain the desired morphology. For practical applications, it is required that every magnetic nanoparticles should be coated with a uniform silica shell without core free silica particles which lead to reduce the magnetization value and heating ability of hyperthermia. According to La Mer theory, hydrolysis of SiO_2 precursor concentration is key parameter to form appropriate silica coating NPs with controlled shell thickness [12].

Therefore this work has its main focus on the synthesis of superparamagnetic $\text{MgFe}_2\text{O}_4@\text{SiO}_2$ core-shell nanosphere for various desired shell thickness (10, 20 and 30 nm) by using theoretically calculated amount of tetraethyl orthosilicate (TEOS, as SiO_2 precursor) and appropriate ratio of HCl (as acidic catalyst) via modified sol-gel approach, we study systematically the formation of appropriate silica shell and influences of shell thickness on the structural, and morphological properties by various characterization

techniques such as XRD, FESEM, TEM, DLS and DT-TGA etc.

2 EXPERIMENTAL

The synthesis of MgFe_2O_4 nanospheres was done according to our previous reported work of one-step ultrasonic spray pyrolysis method with the schematic diagram of this system is given elsewhere [5]. From the obtained core MgFe_2O_4 nanopowders, we can easily derived corresponding size distributions from the SEM images and have determined mean size of the particles by Gaussian fitting of the curve and it is ~ 206 nm. Considering the spherical shape and assuming equal volumes of core, one to one silica coating with appropriate shell thickness can be realized by using the required amount of TEOS. The calculated amount of TEOS have been obtained using the following relation which is schematically illustrated in Fig. 1.

We consider a core-shell nanosphere with R , radius of core and t , thickness of shell, thus the volume of shell, $V_s = V - V_c$.

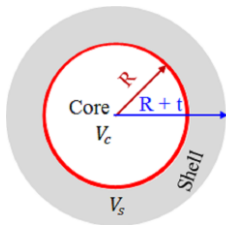


Figure 1: Schematic diagram of core-shell geometry

We know the density of core MgFe_2O_4 nanosphere and silica, then we have easily calculated amount of TEOS precursor for certain shell thickness which have shown in Table 1.

| Proposed SiO_2 shell thickness t (nm) | TEOS (μL) | Concentration of TEOS (mol/L) | HCl/TEOS (mol/mol) |
|--|------------------------|-------------------------------|--------------------|
| 10 | 57.95 | 0.1 | 0.01 |
| 20 | 127.15 | | |
| 30 | 208.51 | | |

Table 1: Calculated various volumes of reagents to form different thickness of silica shell for $\text{MgFe}_2\text{O}_4@SiO_2$ core-shell nanospheres.

The final step, freshly formed MgFe_2O_4 nanospheres were used as core and silica coating was obtained by using TEOS as a precursor of silica and HCl as a catalyst according to the sol-gel process. using the appropriate amount of reagent (see table 1), for successively proposed shell thickness (10, 20 and 30 nm) of core-shell $\text{MgFe}_2\text{O}_4@SiO_2$ nanosphere have been achieved. The resulting silica coated MgFe_2O_4 nanospheres were denoted as ST-10 nm, ST-20 nm, ST-30 nm, according to the silica shell thickness and ST-0 nm used some where instead of core nanospheres.

3 RESULTS AND DESCUSTION

To compare the X-ray intensity for uncoated and silica coated nanosphere is assigned to the main peak (311) crystal plane which have shown in Fig. 2. The diffraction peaks intensity decreases with increasing the shell thickness due to the presence of amorphous SiO_2 matrix, but all samples have same FWHM. The average crystallite size of all samples are same and it was 9.6 nm which have determined by TOPAS software. The equality of average crystalline size in all coated samples shows that surface modification process have no any detrimental effect on core MgFe_2O_4 nanospheres, such as dissolution or growth of crystals [13].

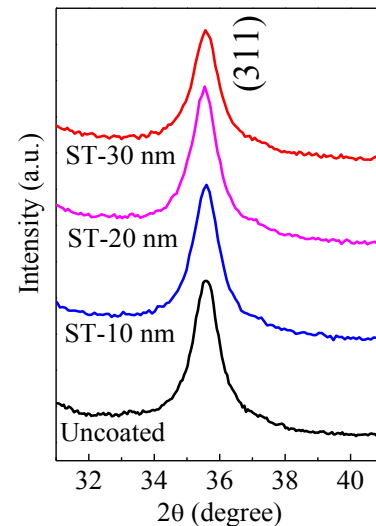


Figure 2 : Compare of X-ray (311) peak intensity of uncoated and $\text{MgFe}_2\text{O}_4@SiO_2$ core-shell nanospheres with various thickness of silica shell.

The morphological features of uncoated and $\text{MgFe}_2\text{O}_4@SiO_2$ core-shell nanospheres with 10 nm shell thickness were observed using FESEM image which have shown in Fig. 3. All individual particles have demonstrated with extremely smooth surface and regular spherical in shape without formation of any neck like dissymmetry. Average nanospheres diameter is larger than the uncoated core nanospheres for external silica shell. Fig. 3b shows that the core-shell nanospheres still keep the spherical morphology.

The various thickness of $\text{MgFe}_2\text{O}_4@SiO_2$ core-shell nanospheres have observed by transmission electron micrograph (TEM). In Fig. 4a-c, the observed core-shell structure exhibit dense ideal sphere where dark region indicate crystalline core and bright region indicate amorphous silica shell which enwraps closely around the core nanosphere. The average shell thickness ~ 10 nm can be observed from the Fig. 4a, which is good match with our predicted value. We have also obtained another appropriate shell thickness from the TEM image in Fig. 4b and Fig. 4c, which is about ~ 20 nm and ~ 30 nm, respectively. The

surface of 20 nm and 30 nm shell thickness is quite rough but dense homogeneous silica layer have observed without core less extra silica. Moreover, the TEM analysis clearly shows that the silica shell thickness could be conveniently controlled and predetermined by using the calculated volume of TEOS in our experimental process.

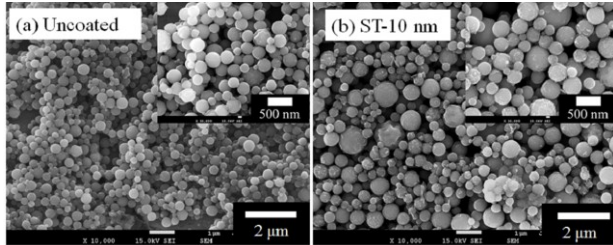


Figure 3: FESEM image of as synthesized (a) uncoated and (b) $\text{MgFe}_2\text{O}_4@\text{SiO}_2$ core-shell nanospheres with 10 nm thickness of silica shell.

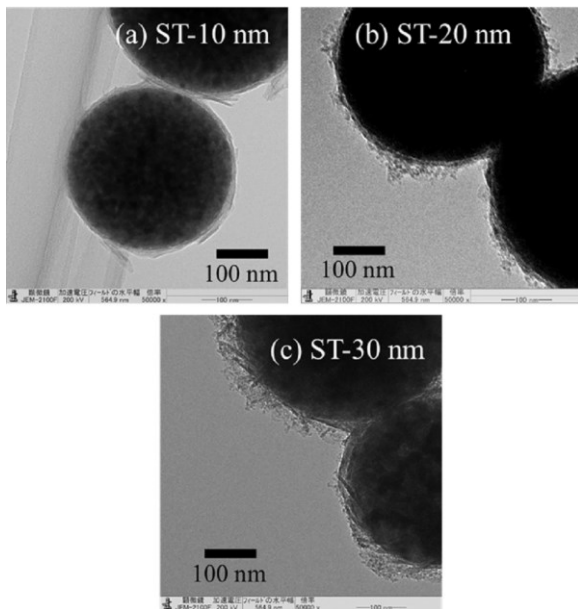


Figure 4: STEM images of $\text{MgFe}_2\text{O}_4@\text{SiO}_2$ core-shell nanospheres prepared by experimental condition of Table 1 for different shell thickness.

For further experimental evidence in support of the elemental evolution of the created shell on core nanosphere was obtained through the EDX spectra. Fig. 5 shows the EDX spectrum of 10 nm shell thickness nanosphere. It is clear that core MgFe_2O_4 contain only Mg, O and Fe elements whereas another extra peak of Si have observed for confirms that the synthesized core-shell nanospheres is composed of MgFe_2O_4 and SiO_2 . As impurity, Cl or other any trace elements have not present which have possibility from catalyst during coating processes [14].

The dispersibility of pure MgFe_2O_4 and $\text{MgFe}_2\text{O}_4@\text{SiO}_2$ core-shell nanospheres in liquid media (ethanol) were

measured by dynamic light scattering technique. The measurements were performed three times for each sample to verify the reproducibility of the results and plotted a graph of polydispersity index (PDI) as a function of silica shell thickness which have shown in Fig. 6. The PDI was calculated by using the formula, $\text{PDI} = (\sigma/d)^2$, where σ represents the standard deviation [15]. Among the various shell thickness, the diameter of core-shell nanosphere with 10 nm shell thickness have shown highly monodisperse with narrower size distribution. In our study, we found that concentration of SiO_2 does not affect the only shell thickness but also control the monodispersity.

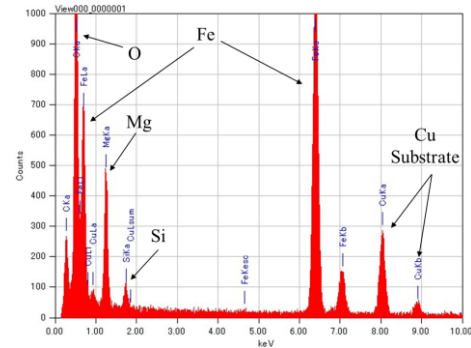


Figure 5: EDX spectra of $\text{MgFe}_2\text{O}_4@\text{SiO}_2$ core-shell nanospheres with 10 nm thickness of silica shell.

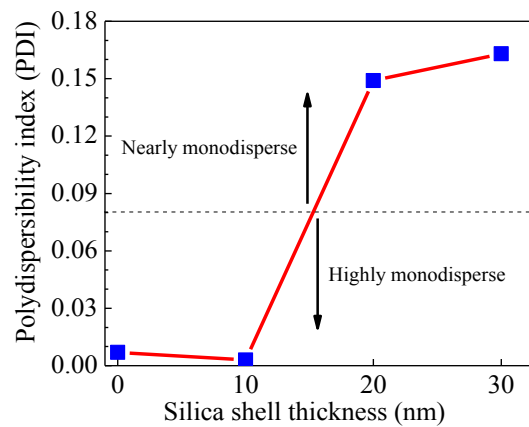


Figure 6: Polydispersity index (PDI) as a function of silica shell thickness of $\text{MgFe}_2\text{O}_4@\text{SiO}_2$ core-shell nanospheres measured in ethanol solvent by electrophoretic scattering photometer.

The thermal stability of pure MgFe_2O_4 core and $\text{MgFe}_2\text{O}_4@\text{SiO}_2$ core-shell nanospheres are shown in Fig. 7. In the initial step, all TG curves were identified by two regions of weight loss up to 200 °C, which can be attributed to the evaporation of residual solvents, mainly to the evaporation of surface adsorbed and interlayer water from the template. In the core-shell samples, it is higher and weight loss increases with the increase of silica shell thickness due to decomposition of hydroxyl groups and the

process of connecting the silanol groups with the core MgFe_2O_4 nanospheres [16]. The most important weight loss occurring of core MgFe_2O_4 nanospheres in the range from 300 to 400 °C, which was accompanied with simultaneous evolution of CO_2 gas. In case of core-shell structure, negatively charged $-\text{COO}-$ was negligible during the coating process, because of its electrostatic attractive force between the positively charged core MgFe_2O_4 nanosphere in acidic solution. Therefore, the weight loss rates of the core-shell samples were lower due to their better thermal stability. In core MgFe_2O_4 , a slight weight gain exhibit in the final stage owing to the oxidation in air at elevated temperatures. After coating with a silica shell, the oxidation could not occur in the experimental temperature range for all coating samples which further confirms the protective behavior of the silica shell [17].

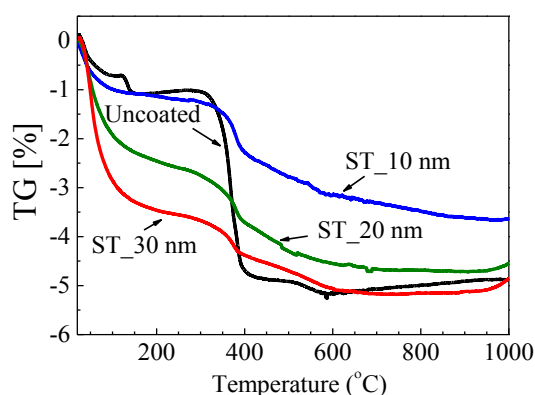


Figure 6: Thermogravimetric analysis of as-synthesized uncoated MgFe_2O_4 and $\text{MgFe}_2\text{O}_4@\text{SiO}_2$ core-shell nanospheres with different thickness of shell.

CONCLUSION

In summary, a process for the preparation of silica coated superparamagnetic MgFe_2O_4 nanospheres with controlled shell thickness was developed and optimized. The present study showed that silica shell thickness can be predicted and accurately tailored by using the calculated volume of SiO_2 precursor for particulate nanosphere in acidic solution which leads to the formation of homogeneous dense silica layer with uniform morphology and have no any additional detectable crystalline phase. In addition, pristine MgFe_2O_4 nanoparticles have produced by USP technique has dense sphere and highly monodisperse. In this case, the desired shell thickness have observed from TEM image and there is no any change in the shape of the particles through coating processes. However, thin shell (~10 nm) silica layer thickness to an almost homogeneous monolayer and narrower size distribution due to the low concentration of TEOS precursor. The present approach could also be applied to the preparation of other core-shell nanoparticles with ultrathin silica layer.

ACKNOWLEDGEMENT

This work was supported by Nippon Sheet Glass Foundation for Materials Science and Engineering, Japan (Grant no. 43), and research project of Research Institute of Electronics of Shizuoka University, Japan (Grant no. H27-10 and H27-11).

REFERENCES

- [1] T. Maehara, K. Konishi, T. Kamimori, H. Aono, H. Hirazawa, T. Naohara, S. Nomura, H. Kikkawa, Y. Watanabe and K. Kawachi, *J. Mater. Sci.* 40, 135-138, 2005.
- [2] S. Verma, P.A. Joy, Y.B. Kholam, S.B. Potdar, *Mater. Lett.* 58, 1092-1095, 2004.
- [3] A. Franco, Jr, M.S. Silva, *J. Appl. Phys.* 109, 07B505-3, 2011.
- [4] H. Hirazawa, H. Aono, T. Naohara, T. Maehara, M. Sato, Y. Watanabe, *J. Magn. Magn. Mater.* 323, 675-680, 2011.
- [5] H. Das, N. Sakamoto, H. Aono, K. Shinozaki, H. Suzuki, N. Wakiya, *J. Magn. Magn. Mater.* 392, 91-100, 2015.
- [6] D. Ma, T. Veres, L. Clime, F. Normandin, J. Guan, D. Kingston, B. Simard, *J. Phys. Chem. C* 111, 1999-2007, 2007.
- [7] G.A. Sotiriou, M.A.V. Onufrak, A. Teleki, E.J. Juan, A.M. Hirt, S.E. Pratsinis, C. Rinaldi, *Chem. Mater.* 25, 4603-4612, 2013.
- [8] S. Kralj, D. Makove, S. Campelj, M. Drogenik, *J. Magn. Magn. Mater.* 322, 1847-1853, 2010.
- [9] H. Setyawan, F. Fajaroh, W. Widiyastuti, S. Winardi, I.W. Lenggoro, N. Mufti, *J. Nanopart. Res.* 14, 807-9, 2012.
- [10] J. Zhu, S. Wei, N. Haldolaarachchige, D.P. Young, Z. Guo, *J. Phys. Chem. C* 115, 15304-15310, 2011.
- [11] C.J. Brinker, G.W. Scherer, *Sol-gel Science*, Academic Press, New York, 1990.
- [12] H.L. Ding, Y.X. Zhang, S. Wang, J.M. Xu, S.C. Xu, G.H. Li, *Chem. Mater.* 24, 4572-4580, 2012.
- [13] M.H. R. Farimani, N. Shahtahmasebi, M.R. Roknabadi, N. Ghows, A. Kazemi, *Physica E*, 53, 207-216, 2013.
- [14] R. Ullah, B.K. Deb, M.Y.A. Mollah, *Inter. J. Comps. Mater.* 4, 135-145, 2014.
- [15] J.P. Lachataignerais, R. Pons, P. Panizza, L. Courbin, J. Rouch, O. Lopez, *Chem. Phys. Lipids* 140, 88-97, 2006.
- [16] M.E. Khosroshahi, L. Ghazanfari, *Mater. Sci. Engr. C* 32, 1043-1049, 2012.
- [17] J. Zhu, S. Wei, N. Haldolaarachchige, D.P. Young and Z. Guo, *J. Phys. Chem. C* 115, 15304-15310, 2011.