

## Synthesis of Nano-magnetite coated with chitosan for MRI contrast agent by Sonochemistry

Huiping Shao<sup>1,2</sup>, HyoSook Lee<sup>2\*</sup>, Yuqiang Huang<sup>1</sup> and ChongOh Kim<sup>1</sup>

<sup>1</sup>Department of materials engineering, ChungNam National University, Daejeon 305-764, Korea

<sup>2</sup>Korea Institute of Geoscience & Mineral Resources, Daejeon 305-350, Korea

**Introduction** Superparamagnetic iron oxide (SPIO) nanoparticles have been developed for clinical applications in magnetic resonance imaging (MRI) contrast enhancement [1-3]. The SPIO nanoparticles have the advantage of producing an enhanced proton relaxation in MRI, especially useful for T2-weighted images. Different methods have been used to prepare nano-magnetite particles, such as high-temperature ceramic method, co-precipitation [4], spray drying [5] and microemulsion processes [6], etc. Recently, the sonochemical method has been used to fabricate stable ferromagnetic colloids [7]. In this paper, the nano-magnetite particles were synthesized by using a sonochemical method. The particles were coated by chitosan to ensure that it was in noxious and biocompatible. Also, the multiple binding of chitosan coated onto particles ensure a firm autoclave-resistant attachment and storage stability. The particle size properties were characterized with particle size analysis (PSA), and the structural properties by X-ray diffraction (XRD). The synthesized magnetic fluids were applied for MRI enhancement into the New Zealand rabbit.

**Experimental method** A mixed solution of 4.86g  $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$ , 1.99g  $\text{FeCl}_2 \cdot 4\text{H}_2\text{O}$ , water 100 ml and ammonia 10ml were reacted under ultrasonic for 1 hour. The precipitates were washed with distilled water until solution pH is 7, then the precipitates slurry in 100 ml water was coated with 16 ml 1% chitosan under ultrasonic for 45 minutes. At last, the nano-magnetite fluids were centrifuged at 5000 rpm for 13 minutes.

To compare the variety of particle size, the ultrasonic time, ultrasonic power and coating chitosan quality were examined, and their particle sizes were characterized by PSA (particle size analysis).

**Results and Discussion** The particle size is a key factor for contrast agent; the diameter of the drops with SPIO in the core is suitable in range of 30~100 nm for diagnoses. Figure 1 shows that the time of ultrasonic affects the drop size obviously. From 15 minutes to 60 minutes, the larger drops decreased obviously and these sizes distribution becomes narrow. For the same reason, the ultrasonic power of 30% is selected to prepare the magnetic

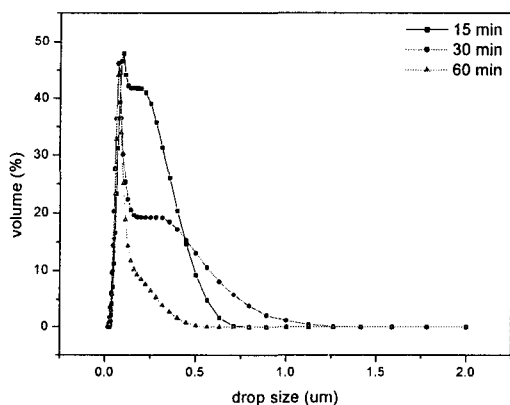


Fig. 1. Drop size under different ultrasonic times.

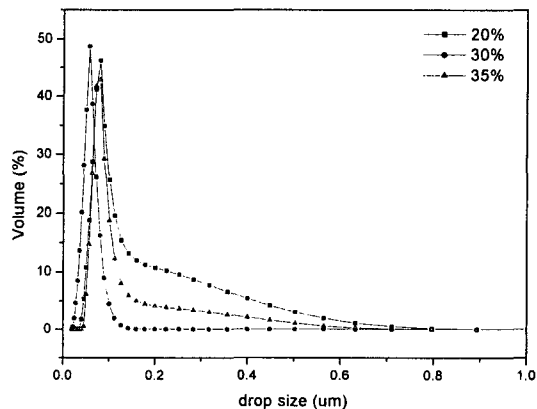


Fig. 2. Drop size under different ultrasonic powers.

Corresponding author: Tel: 042-868-3603 Email: [hslee@kigam.re.kr](mailto:hslee@kigam.re.kr).

drops according to the Figure 2. The coating chitosan quality has a little effect on drop size, however, it is important for dispersing the particle successfully. As the result, the ultrasonic power 30%, the ultrasonic time 60 minutes and coating chitosan quality 15ml were the optimum experimental conditions. The result of PSA analysis shows that the average drop size is in the range from 50 nm to 80 nm. Figure 4 is the X-ray diffraction pattern of magnetite fluid nanoparticles and it shows that ultrasonic time 30 min has better crystal structure than 15 min. Also, from the X-ray pattern, it indicates the particle size is smaller in the case of ultrasonic 30 min than 15 min. We have the effect on the MRI enhancement in the MRI T2 images of the rabbit liver.

**Conclusion** The nano-magnetite particles (SPIO) were synthesized by sonochemical method for MRI contrast agent. The drop size with the synthesized SPIO in the core were controlled in the range 40~80 nm with the chitosan at such conditions: the ultrasonic time 60 min, ultrasonic power 30% and coating chitosan quality 15 ml. The prepared particles have a perfect crystal structure to ensure that the clear image can be gained in diagnoses. Such SPIO coated with chitosan can be used in medical diagnostic techniques.

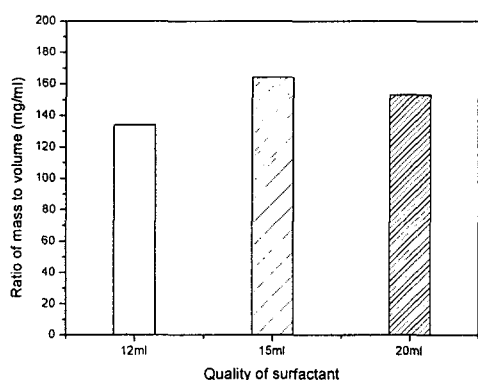


Fig. 3. Dispersing effect under different chitosan quality.

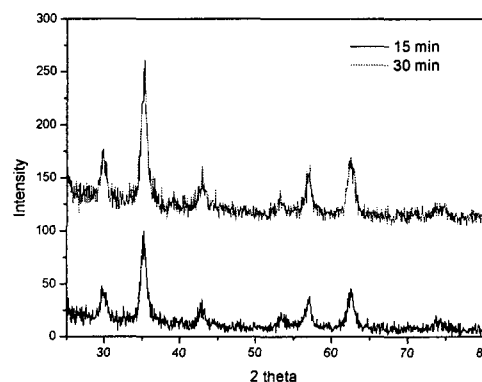


Fig. 4. X-ray diffraction pattern of particles.

## Reference

- [1] A. Moore, J. P. Babilion, E. A. Chiocca, R. Weissleder, *Biochim. Biophys. Acta* 1402(1998) pp239.
- [2] D.K. Kim, Y. Zhang, J. Kehr, T. Klason, B. Bjelke, M. Muhammed, *J. Magnetism and Magnetic Materials*, 225 (2001), 256.
- [3] M. P. Morales, O. Bomati-Miguel, R. Perez de Alejo, et al, *J. Magn. Magn. Mater.* 226 (2003) pp102.
- [4] A. Bee, R. Massart and S. Neveu: *J. Magn. Magn. Mater.* Vol. 149 (1995) pp6.
- [5] H. F. Yu and A. M. Gadalla: *J. Mater. Res.* Vol. 11, No. 3(1996), pp663.
- [6] N. Moumen, P. Veillet and M. Pl Pileni: *J. Magn. Magn. Mater.* Vol.149 (1995) pp67.
- [7] K. S. Suslick, M. Fang and T. Hyeon: *J. Am Chem. Soc.* Vol. 118 (1996) pp11960.