Optimized Synthesis Method for Magnetic Nanoparticles Corporate with Radioactive Copper

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1. Introduction

The single-particle combine with both radioactive and magnetic properties can use PET-MRI contrast agents. This technique has been attracting attention as a next-generation nuclear medicine for the diagnostic device.

Generally, the research and development of PET-MRI contrast agents have focused on the synthesis of chemical labeling compounds, which have developed from synthesizing technology of nuclear medicine contrast agents by ligand binding between magnetic superparamagnetic iron oxide (SPIO) and radioactive labeling compounds.[1,2,3]

But, recently the development of a nanoparticle synthesis method with two different elements into a single-particle can be applied to bi-functional nano-particle manufacturing technology, which makes different single heteronuclear elements with radioactive and magnetic properties into a single particle. This type of new contrast agent technology is an excellent research area to have the leading role of technology development in nuclear medicine imaging for contrast agent market and securing the source technology through future R&D.

This present study is devoted to the synthesis of single-core nanoparticles combining heterogeneous elements by a cold model method using stable isotope material for optimized synthesis method. In this, The main conditions of the synthesis method are similar to those of the previous paper, and experiments were conducted to optimize the synthesis method and to construct a dedicated synthesis reactor to scale up the RMNP by more than five times.[4] In this study, the Fe element used as a magnetic component for MRI (Magnetic Resonance Imaging) imaging, and the stable isotope Cu ion used as the model for ^{64}Cu, ^{67}Cu radioisotope for PET (Positron Emission Tomography) imaging. The nanoparticles synthesized via hydrothermal reaction performed under 200 ° C with a mechanical mixer at 200 rpm. Then the recovered hydrophobic nanoparticles surface was converted to the hydrophilic surface using tetraethoxysilane coating agent. The size of the recovered RMNP confirmed to optimized to 6nm.

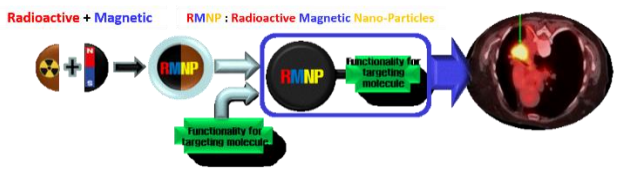


Fig. 1. The synthesis concept scheme of a bifunctional RMNP

2. Method and Results

2.1 Synthesis process of RMNP

Copper(II)acetylacetonate(2.61g, 10 mmol), Iron(III)acetylacetonate hydrate (3.52 g, 10 mmol), dodecylamine(7ml 30 mmol), lauric acid (6 g, 30 mmol) and 1,2-hexadecanediol(3.8g, 16mmol) were add in 200 ml benzyl ether. Then, the mixture was heated up to 200℃ and refluxed for 2 h under Ar(g) atmosphere.

After the reaction, the reactor was cool down to room temperature and precipitated by adding 50 ml of ethanol.

Then, the precipitates were collected by centrifuge under 15000rpm. And the collected pellet was dispersed in 15 ml hexane then centrifugated under 15000 rpm for 15 min for removing the residue solvent.

The centrifugation process repeated thrice, and the black-brown color nanoparticles were collected and used for further analysis.

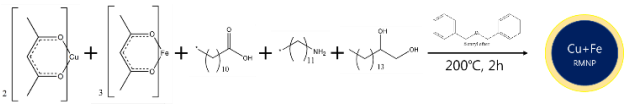


Fig. 2. The synthesis scheme of RMNP

2.2 Synthesis process of Core shelled RMNP

Cu-Fe RMNP (0.1g) and Cyclohexane (10mL) mixed by ultrasonication for 10 min, then to add the Igepal CO-520 (991 uL) mixture with 190 ml cyclohexane.

Then mixed cyclohexane solution was poured into baffle reactor, and added 2 ml ammonia solution, stirred for 10 min using agitator under 200 rpm then infused 400uL TEOS(tetra-ethyl-orthosilicate), and reacted for 2h at 50℃.

After polymerization, added 50 ml methanol into the reactor then recovered reactant. The collected solution centrifuged under 15000 rpm Then the precipitates were collected by centrifuge under 15000rpm. And the collected pellet was dispersed in 50 ml methanol then centrifugated under 15000 rpm for 15 min for removing the residue reactant.

The centrifugation process repeated thrice, and the black-brown color core-shell nanoparticles were collected and used for further analysis.

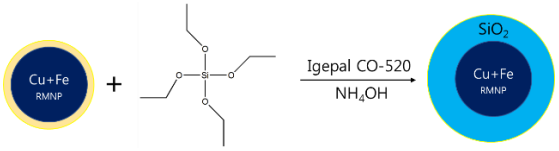


Fig. 3. The synthesis scheme of core-shell RMNP

2.3 Analysis

The particle size of recovered black-brown nanoparticles was analyzed using particle analyzer Figure 4 shows the distribution of synthesized RMNP particles. From this analysis, the size of nanoparticle was confirmed to be ~ 6 nm.

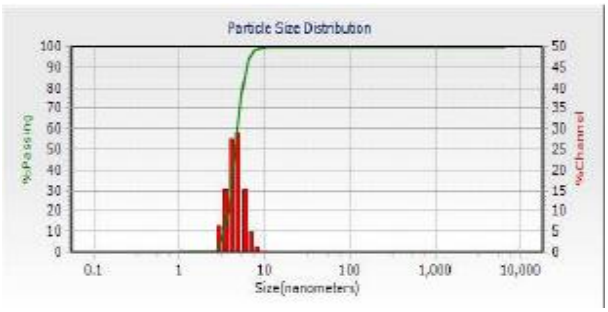
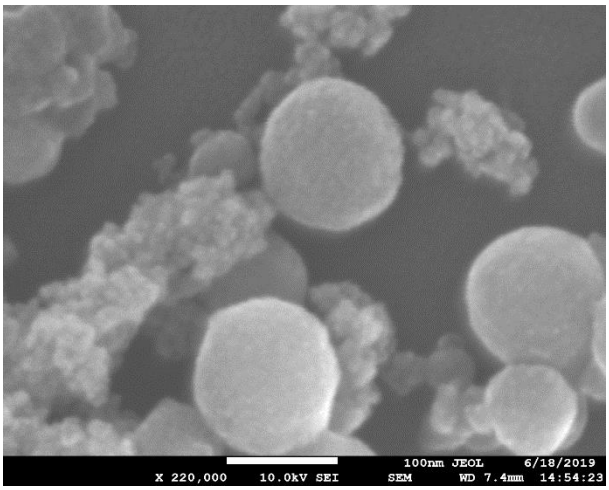
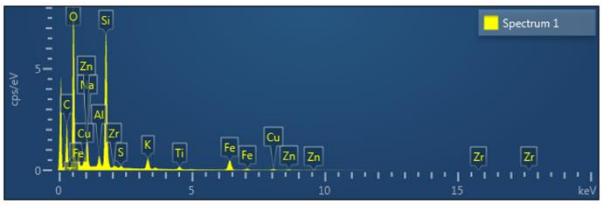


Fig. 4. Analyzed data of dispersed Cu+Fe RMNP in hexane

The presence of various components in the nanoparticles obtained through EDX analysis. Fig. 5 displays the EDX spectrum of nanoparticles confirming the presence of Cu and Fe element with the outer silica surface.





Element	Line Type	Apparent Concentration	k Ratio	Wt%	Wt% Sigma	Standard Label	Factory Standard	Standard Calibration Date
C	K series	0.35	0.00353	28.53	0.47	C Vit	Yes	
O	K series	1.82	0.00614	39.03	0.33	SiO2	Yes	
Na	K series	0.13	0.00054	2.65	0.09	Albite	Yes	
Al	K series	0.04	0.00031	0.97	0.04	Al2O3	Yes	
Si	K series	0.59	0.00466	12.36	0.12	SiO2	Yes	
S	K series	0.01	0.00011	0.28	0.03	FeS2	Yes	
K	K series	0.09	0.00079	1.82	0.04	KBr	Yes	
Ti	K series	0.03	0.00034	0.82	0.04	Ti	Yes	
Fe	K series	0.29	0.00286	6.94	0.13	Fe	Yes	
Cu	L series	0.06	0.00061	2.80	0.19	Cu	Yes	
Zn	L series	0.07	0.00071	3.26	0.21	Zn	Yes	
Zr	L series	0.02	0.00019	0.54	0.08	Zr	Yes	
Total:				100.00				

Fig. 5.SEM-EDX image of Cu+Fe RMNP@TEOS

Fig. 6 shows the SQUID measurement results of Cu + Fe RMNP @ TEOS. Although the outside of the RMNP accumulated as silica particles, it confirmed that the Cu + Fe RMNP @ TEOS particles were magnetic at room temperature

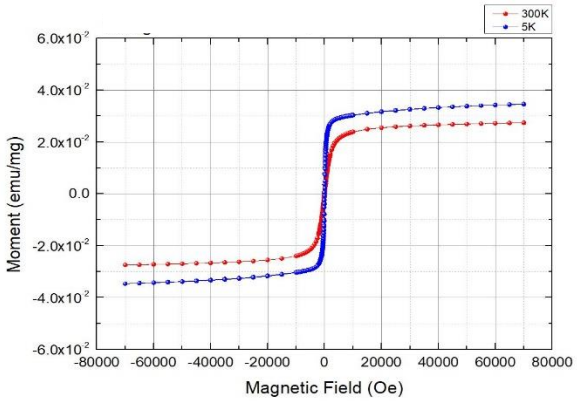


Fig. 6. SQUID data of RMNP, RMNP@TEOS

3. Conclusions

The nanoparticles in this optimization experiment synthesized by reaction using a baffled reactor at 200˚C. The synthesized RMNP was produced homogeneously in 6 nm size. In repeated experiments, the size of the nanoparticles was constant at 6 nm.

In the case of core-shell synthesis, agglomeration occurred when the amount of TEOS was high. Core-shell loading conditions well synthesized in the 00% range of nanoparticle weight.

It found that the ratio of synthesized core-shell Cu element could contain up to 30%.

The magnetic properties of the synthesized RMNP confirmed by squid analysis in the RMNP composed of heterogeneous elements.
It confirmed that the synthesized RMNP was well taken up intracellularly in the cytotoxicity test. Therefore, it confirmed that RMNP having both radioactive and magnetic properties could use as a PET-MRI contrast agent.

4. Acknowledgments

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