International Journal on Magnetic Particle Imaging
Vol 10, No 1, Suppl 1, Article ID 2403034, 3 Pages

Infinite Science Publishing

Proceedings Article

Microwave-assisted high-speed synthesis of superparamagnetic iron-oxide nanoparticles

T. Knickrehm[a] · K. Lüdtke-Buzug[a,*]

[a]Institute of Medical Engineering, University of Lübeck, Lübeck, Germany
[*]Corresponding author, email: kerstin.luedtkebuzug@uni-luebeck.de

Abstract

In this work, the microwave-assisted synthesis of superparamagnetic iron oxide nanoparticles (SPIONs) for MPI is presented. Compared to conventional coprecipitation, microwave-assisted synthesis in specially designed microwave reactors enables good yields while reaction times can be reduced to a few minutes. To find the best synthesis route, various parameters such as the base used, reaction temperature, heating and cooling time were analysed. Various dextrans (molecular weight 10,000-100,000) were used to assess whether the methods can also be applied to other coating materials. The first results of this evaluation study are presented here.

I. Introduction

Nanoparticles, which are synthesized from a variety of materials, are of great use in medical, biological, and technical fields [1,2]. Their optimal morphology, which depends on the specific application, exhibits considerable diversity in terms of shape and size. The synthesis process forms these nanoparticles in a complex way, resulting in different structures such as chains, aggregates, spheres, rods, or tubes that are tailored to the requirements of the specific application.

Magnetic nanoparticulate systems play a crucial role in the field of magnetic medical imaging [3], particularly in techniques such as magnetic resonance imaging (MRI) and the new magnetic particle imaging (MPI). In these applications, these nanostructures act as key components, serving either as contrast enhancers in the case of MRI or as direct imaging tracers in the context of MPI. Their ability to influence and improve imaging processes emphasizes the importance of magnetic nanoparticles for progress in medical diagnostics.

High-speed synthetic chemistry [1,2,3] is a novel way to optimize synthesis for different chemicals. The goals of synthetic high-speed chemistry include improving the overall speed and efficiency of chemical synthesis, shortening reaction times, increasing yields, and minimizing resource consumption.

While the traditional synthesis routes often take several hours or even days to perform reactions, special designed synthesis reactors can significantly reduce reaction times from hours to a few minutes with excellent results. One reason for the efficiency of this method is the fast overheating of the reaction mixtures to temperatures far above the boiling point of the used solvents.

This approach will be applied here to optimize nanoparticulate, magnetic particle systems as tracers for MPI. In high-speed synthetic chemistry, cutting-edge technologies such as flow chemistry [4,5], microwave-assisted synthesis [6,7,8] and automated systems are often used to streamline and accelerate the synthesis of target structures.

Here, the microwave-assisted high-speed synthesis of superparamagnetic iron oxide nanoparticles (SPIONs) is proposed for efficient exploration of different nanoparticular structures for MPI.

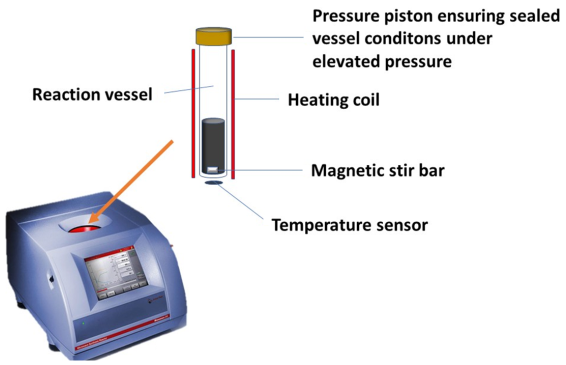

Figure 1: Microwave set up with Anton Paar MW400.

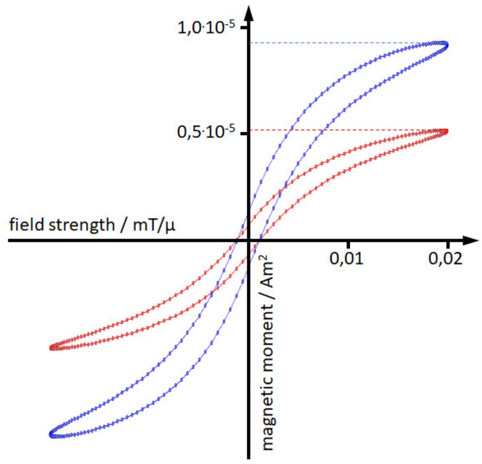

Figure 2: Hysteresis curve of magnetic nanoparticles produced via the microwave-assisted synthesis route (blue) in comparison to the hysteresis of Resovist (red). An increase in saturation magnetization (see dashed lines) by a factor of 1.6 was achieved here.

II. Material and methods

In the presented project the different parameters for the synthesis of the SPIONs have been varied. Two different bases (NaOH and NH_3) were used. Furthermore, the influence of temperature on the properties of the products was investigated. Also, the influence of the heating and cooling time was analyzed. Different dextrans (molecular weights from 10,000 to 100,000) were used as coating material for the synthesis.

A microwave reactor is used for direct heating (see Fig. 1). Sealed reaction vessels undergo a transformative process, reaching temperatures surpassing the boiling point of the reaction mixture.

Microwave irradiation stands out as an energy-efficient method, achieving internal heating by directly coupling microwave energy with dipoles and/or ions within the reaction mixture. Despite the vessels being nearly transparent to microwaves, these waves permeate the vessel wall, instigating molecular-level heating through direct interactions with key components like solvents, reagents, and catalysts. For the experiments presented here, the Anton Paar MW400 was used [9].

Table 1: Used chemicals for the nanoparticle synthesis.

Chemical	***Quantity***
Iron(II)chlorid($FeCl_2$ $4H_2O$)	500 mg/10 mL
Iron(III)chlorid($FeCl_3$ $6H_2O$)	1,000 mg/10 mL
Ammonia(NH_3, 7.5 %)	2 mL
Sodiumhydroxid(NaOH, 1M)	2 mL
Dextran (MW, 10,000, 40,000. 70,000, 100,000)	500 mg/10 mL - 2,000 mg/10 mL

The products of the different synthesis were investigated by Magnetic Particle Spectroscopy (MPS, Institute of Medical Engineering [10]) and Photon Correlation Spectroscopy (PCS, Zetasizer Nano S, Malvern Panalytical). The magnetic properties and the hydrodynamic diameter were used as quality criteria of the produced SPIONs. The results of this studies were evaluated.

All used solutions must be cooled in an ice bath before synthesis. Further, before cooling, the solutions must be degassed for 30 minutes in an ultrasound bath. In Table 1 the amount of the used iron salts and coating materials for the syntheses are listed.

The next step is to combine the cooled dextran and iron solutions. Then, the cooled ammonia is added and the tube is sealed airtight with a septum. The mixture is homogenized with the vortex lab mixer.

The reaction tube is then placed in the Anton Paar MW400 microwave device and the reaction is started with the predefined parameters. Table 2 shows the various reaction parameters that have been optimized during the synthesis campaign.

After completion of the synthesis, the reaction vessel is cooled down to 55 °C and the particle suspension is transferred to a 10 ml vial. The vial is placed in the center of a permanent magnet and left there for approximately 12 to 14 h to remove undesiredly formed larger particles.

The quality of the particles is assessed based on the MPS and PCS measurements. To analyze the produced SPIONs, the solution is carefully separated from the large particles by pipetting off the supernatant.

III. Results and discussion

Figure 2 shows the comparison of the hysteresis curve of magnetic nanoparticles produced via the microwave-assisted synthesis route (indicated in blue) in comparison to Resovist (indicated in red). The particles of high-speed synthesis route show a significant higher saturation magnetization.

Microwave chemistry is based on the sophisticated

10.18416/ijmpi.2024.2403034

Table 2: Parameters used for the nanoparticle synthesis.

Synthesis with Dextran (MW 100,000)	Variation of the parameters	Optimized parameter for presented SPIONs
Temperature range	30 – 180 °C	70 °C
Heating rate	2 – 6 min	2 min
Volume	4 mL	4 mL
Stirrer speed	200 – 1200 RPM	600 RPM
Base (NH_3 or NaOH)	NH_3 1-30 % NaOH 1–5M	2 mL 7.5 % NH_3

heating of materials, especially solvents, by utilizing dielectric heat effects. Essential to the generation of heat under microwave irradiation is the dipolar nature of the substance. This implies that the molecular structure possesses both negative and positive charges. As the microwave field oscillates, these dipoles align with the oscillations, prompting rotation. This rotational movement results in friction, culminating in the efficient conversion of microwave energy into heat. We assume that the dipolar polarization is the major mechanism due to the polarity of dextran. In Fig. 2, the results for dextran MW100,000 are presented.

IV. Conclusions

Crucially, microwave irradiation employs in-core heating, bypassing the initial heating of the vessel surface. This distinctive feature creates inverted temperature gradients, setting it apart from conventionally heated systems. Such inversion signifies a novel and efficient temperature distribution, emphasizing the profound impact of microwave energy on the reaction mixture at a molecular scale.

This way, the synthesis times can be reduced enormously, which makes the search for optimal reaction parameters much easier. Furthermore, we found that the coating material seems to play a greater role than in the conventional synthesis route. However, the results are still too rudimentary, and the studies are continuing, so that no reliable statements can currently be made about the optimum parameters for the synthesis.

Acknowledgments

The presented work is part of the Master Thesis of T. Knickrehm.

Author’s statement

Conflict of interest: Authors state no conflict of interest. Informed consent: Informed consent has been obtained from all individuals included in this study. Ethical approval: n/a

References

[1] A. Nikitin et al.: *Synthesis of iron oxide nanorods for enhanced magnetic hyperthermia*, J. Magn. Magn. Mater., 469, 443, 2019, doi.org/10.1016/j.jmmm.2018.09.014

[2] S. Kalyani, J. Sangeetha, and J. Philip: *Microwave Assisted Synthesis of Ferrite Nanoparticles: Effect of Reaction Temperature on Particle Size and Magnetic Properties*, Journal of Nanoscience and Nanotechnology, Vol. 15, pp. 5768–5774, 2015, doi:10.1166/jnn.2015.10274.

[3] K. Lüdtke-Buzug: *Magnetische Nanopartikel - Von der Synthese zur klinischen Anwendung*, Chemie in unserer Zeit, 46(1), 32-39, 2012, DOI: 10.1002/ciuz.201200558.

[4] A. Malhotra, A. von Gladiss, A. Behrends, T. Friedrich, A. Neumann, T. M. Buzug, and K. Lüdtke-Buzug: *Tracking the Growth of Superparamagnetic Nanoparticles with an In-Situ Magnetic Particle Spectrometer (INSPECT)*, Scientific Reports, 9(10538), 2019, DOI: https://doi.org/10.1038/s41598-019-46882-6.

[5] A. Malhotra, M. Graeser, and K. Lüdtke-Buzug: *Analysis of nucleation and Growth using INSPECT II for co-precipitation methodology-based synthesis*, International Journal on Magnetic Particle Imaging, 2024.

[6] D. Obermayer, B. Gutmann, C. O. Kappe: *Microwave Chemistry in Silicon Carbide Reaction Vials: Separating Thermal from Nonthermal Effects*, Angew. Chem., Vol. 121 Issue44, pp. 8471-8474, 2009, doi.org/10.1002/ange.200904185.

[7] C. O Kappe, A. Stadler, D. Dallinger: *Microwaves in Organic and Medicinal Chemistry*, 2nd Edition. Wiley-VCH, Weinheim, 2012.

[8] M. A. Herrero, J. M. Kremsner, and C. O. Kappe: *Nonthermal Microwave Effects Revisited: On the Importance of Internal Temperature Monitoring and Agitation in Microwave Chemistry*, J. Org. Chem. 2008, 73, pp. 36-47, 2008, doi 10.1021/jo7022697.

[9] https://www.anton-paar.com/de-de/produkte/details/mikrowellensynthese-reaktor-monowave-400200/

[10] S. Biederer, T. Knopp, T. F. Sattel, K. Lüdtke-Buzug, B. Gleich, J. Weizenecker, J. Borgert, T. M. Buzug: *Magnetization response spectroscopy of superparamagnetic nanoparticles for magnetic particle imaging*, Journal of Physics D: Applied Physics, 42(20), 205007, 2009, DOI: 10.1088/0022-3727/42/20/205007.

