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Rapid Diagnostics with Nanoparticles

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CHEMICAL AND LIFE SCIENCE

Rapid Diagnostics with Nanoparticles

CAPSTONE DESIGN EXPO 2015

Objective

Background

More than 500,000 open heart surgeries are performed in the United States every year. The anticoagulant Heparin is used to decrease the likelihood of thrombosis or hemorrhaging in each surgery by bonding to the enzyme inhibitor antithrombin III (AT-III). However, anesthesiologists currently lack the ability to measure antithrombin levels in a patient quickly, making appropriate Heparin dosages difficult to determine and possibly resulting in thrombosis or hemorrhaging if thrombin levels move outside the allowable range. This could be prevented with a simple bedside test performed in minutes.

For this test it may be possible to use Super Paramagnetic Iron Oxide Nanoparticles (SPIONs), which are cheap and can be synthesized at the gram level in a continuous process.

Hypothesis

Super Paramagnetic Iron Oxide Nanoparticles surfaces can be functionalized using (3-Aminopropyl)trimethoxysilane (APTMS) to immobilize thrombin molecules for bedside testing.

Specific Aims

- Synthesize Super Paramagnetic Iron Oxide Nanoparticles in batch and continuous processes.
- Coat nanoparticles in (3-Aminopropyl)trimethoxysilane to functionalize surface.
- Develop control surface for both processes to produce consistent results.

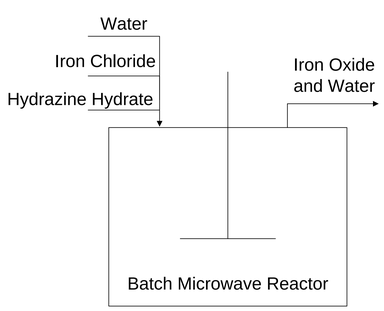

Figure 1. Microwave Reactor Synthesis Method

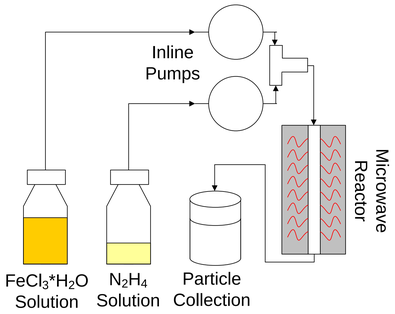

Figure 2. Continuous Microwave Reactor Synthesis

Results

Design of Experiments

In order to find the appropriate process parameters to control iron oxide core size in a microwave batch synthesis a 2x2 design of experiments was performed, varying reaction temperature and time. To allow for producing gram amounts of iron oxide cores, design of experiments was also performed in a plug flow reactor using microwave synthesis, varying flow rate and reactor temperature.

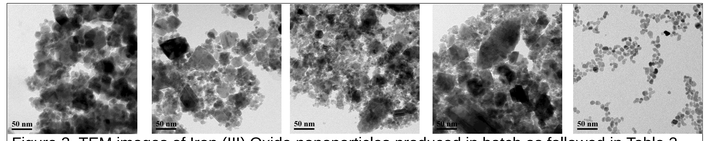

Figure 3. TEM images of Iron (III) Oxide nanoparticles produced in batch as followed in Table 3

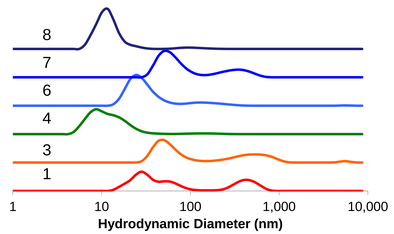

Figure 4. DLS For Flow Reactor runs numbered on figure.

Table 1. Dominant Nanoparticle Peak

	Size (nm)	Volume (%)
Run 1	29.77	86.4
Run 3	47.27	56
Run 4	11.38	94.4
Run 6	24.84	90
Run 7	56.04	71.5
Run 8	11.69	96.2

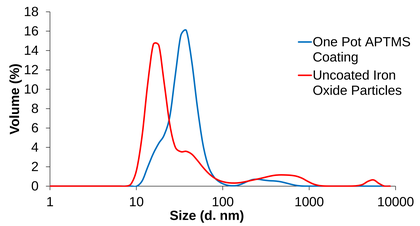

Figure 5. DLS results showcasing change in diameter size from uncoated to coated particles

Table 2. XRD Crystallite Size

Peak No.	Crystallite size [nm]
1	23.80
2	26.60
3	27.90
4	14.30
5	9.90
6	17.80
Average	20.05
Std. Dev.	7.21

Future Studies

1) Perfect control over nanoparticle size distribution for continuous process.
2) Functionalize amine group of APTMS coating to prepare for thrombin attachment.

Conclusion

Summary of results

1)Crystallite size for the batch process design of experiments midpoint as calculated by XRD is 20.05 nm.
2)The smallest particles in flow were generated using temperatures over 100° C, with a hydrodynamic diameter of approximately 11.54 nm.

Conclusion

1)For the DOE trials run by batch synthesis, TEM results showed that particle size was time dependent with less time resulting in smaller particle size.
2)For the DOE trials run by continuous synthesis, polydispersity was shown to be dependent upon temperature with a higher temperature resulting in better monodispersity.
3)Optimal process conditions in a continuous process are 115° C and 0.28 mL/min.
4)One desired effect of APTMS is stabilization of the particles, which could have reduced aggregation. The increase in the largest volume fraction of particles from uncoated to coated could support this, however further characterization is needed.

Table 3. Batch DOE Setup

Run	Temp. Level	Time Level
1	1	1
2	0	0
3	-1	-1
4	-1	1
5	1	-1

Level	-1	0	1
Temp (° C)	85	100	115
Time (min)	5	10	15

Table 4. Continuous DOE Setup

Run	Temp. Level	Flow Rate Level
1	-1	-1
2	-1	1
3	0	0
4	1	-1
5	1	1
6	-1	0
7	0	-1
8	0	1

Level	-1	0	1
Temp (° C)	85	100	115
Flow Rate (mL/min)	0.280	0.150	0.085

Acknowledgments

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References

Palimi, M., et al. "Surface Modification of Fe2O3 Nanoparticles with 3-aminopropyltrimethoxysilane (APTMS): An Attempt to Investigate Surface Treatment on Surface Chemistry and Mechanical Properties of Polyurethane/Fe2O3 Nanocomposites." Applied Surface Science 320 (2014): 60-72.

Osborne, E., et al. "Rapid Microwave-Assisted Synthesis of Dextran-Coated Iron Oxide Nanoparticles for Magnetic Resonance Imaging." *Nanotechnology* 23.21 (2012)

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