Nanoparticle System to Entrap and Deactivate Vesicants

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Abstract

Throughout history, terrorism and warfare have motivated the development of weapons in the form of chemical agents. Specifically, mustard gas has maintained a history as a harmful and potentially life-threatening vesicant. Prior products used to combat the threat of mustard gas have been insufficient as a prophylactic approach. This research sought to provide a solution by designing a nanoparticle (NP) system to absorb, entrap, and deactivate mustard gas into safe byproducts. Material selection and methods for the synthesis and testing of the system were developed based on the functional decomposition of previously explored technologies. The nanoparticles were then synthesized using the emulsion-solvent evaporation technique and characterized, which proved that particles with a diameter of approximately 200 nanometers were produced. Using a pH meter, a calibration curve was developed and used as a comparison for the loaded nanoparticle solution to determine an 83% entrapment efficiency. The reaction was tested by measuring the pH change after introduction of the vesicant with free deactivating chemical, blank nanoparticles, and nanoparticles loaded with deactivating chemical. The pH was chosen as an indicator of the deactivation reaction because the hydrolysis of the vesicant produces hydrochloric acid. The nanoparticles proved to be a better deactivator than free chemicals, however the difference between blank and loaded nanoparticles was minimal.

Background

- Mustard agents are easy to make and a widely used type of chemical warfare agent.
- Potential users include researchers and first responders such as firefighters, emergency medical technicians, police, and military personnel.

Prior Products	Drawbacks
Boots, gloves, protective suits	Areas of concern: neck, wrists, ankles
Topical lotions/creams	Application issues
Povidone Iodine (PI)	Antidote, not prophylactic
Anti-inflammatory medication	Reduces swelling, but not skin damage
Fuller's earth	Dust problems with military equipment
Decontaminating Solution 2 (DS2)	Corrosive

Objectives

- To provide a safe, yet more efficient method of protection from vesicants that improves the operational effectiveness of first responders and soldiers .
- Design a nanoparticle system that will absorb, entrap, and deactivate the target vesicant.

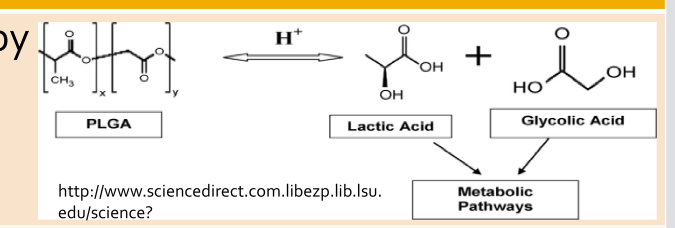
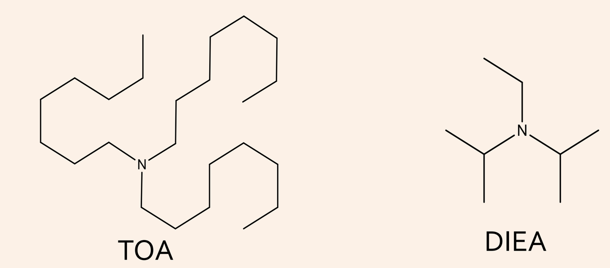
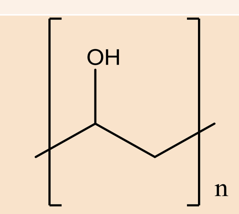
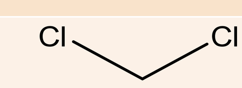
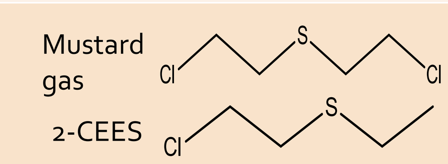
Show *in vitro*:

1. The synthesis of nanoparticles loaded with a deactivating chemical.
2. The model vesicant was absorbed by the designed nanoparticle system.
3. The vesicant reacted with deactivating chemical in the nanoparticle system to form non-toxic byproducts.

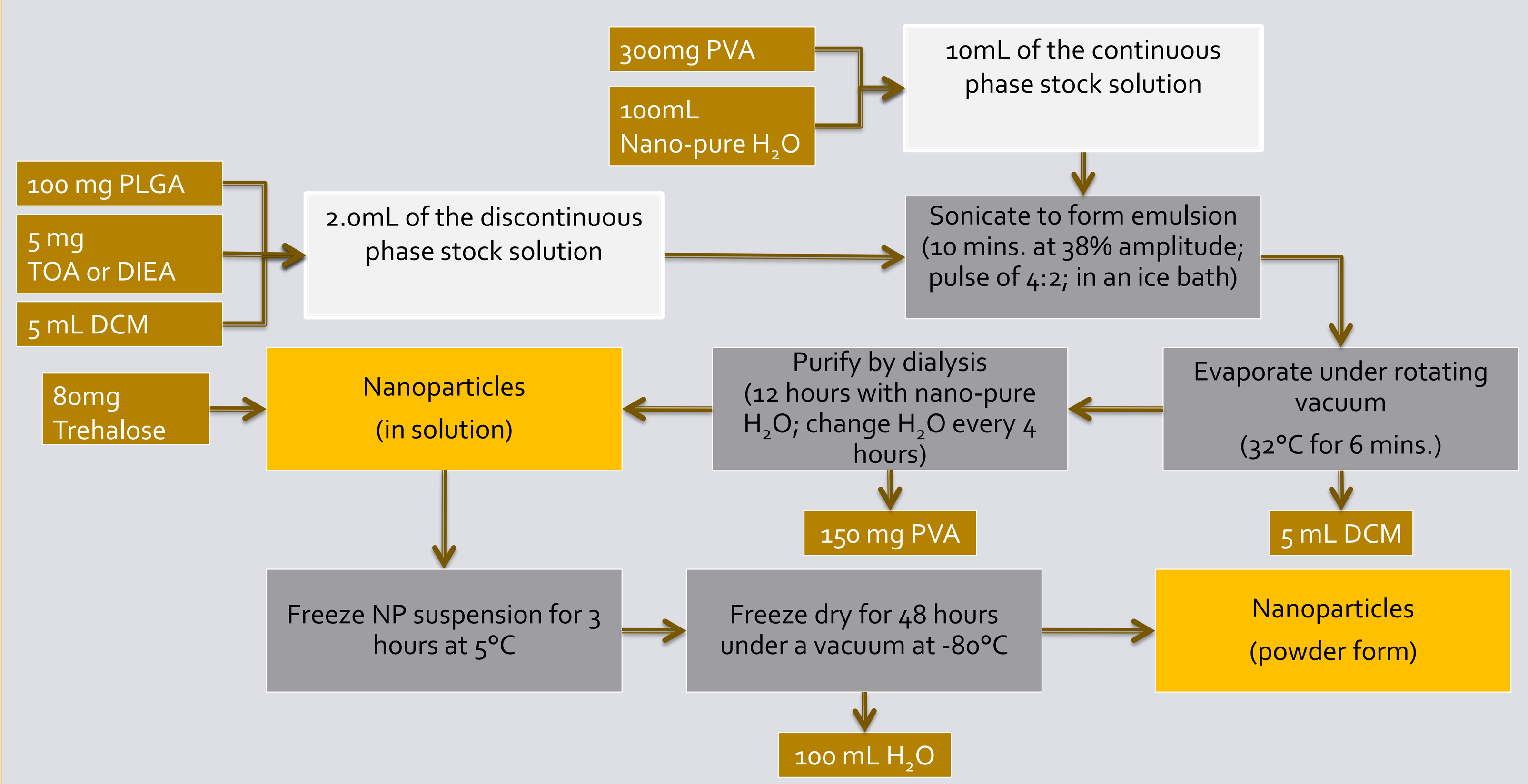
Measurable Objectives

Characterization	Entrapment Efficiency	Reaction Testing
•Size: >200 nm to prevent endocytosis •Polydispersity Index (PDI): Monodisperse <0.1 •Zeta Potential: ±30 mV for moderate stability	•Successfully entrap >70% of the deactivating chemical in the nanoparticles	•NP instantaneous response to presence of 2-CEES •Entrapment and deactivation of 2-CEES •Loaded NP deactivation occurs faster than free chemical reaction with 2-CEES

Materials and Methods

NP System Component	Justification
Polymer: poly D, L-lactide-co-glycolide (PLGA)	FDA approved for human therapy Well-characterized polymer Biocompatible Biodegradable 
Deactivating Chemical: -Trioctylamine (TOA) -Diisopropyl ethyl amine (DIEA)	Hydrophobic amine Reactive for our purposes; Non-nucleophilic base Will not bond with the polymer 
Surfactant: Polyvinyl alcohol (PVA)	Water soluble Excellent emulsifying properties Reduces surface tension Aids in the solubility of vesicant 
Solvent: Dichloromethane (DCM)	Not reactive with deactivating chemical Ability to dissolve all other NP synthesis components Evaporates easily due to its relatively low boiling point (39.6°C) 
Model vesicant: 2-chloroethyl ethyl sulfide (2-CEES)	Comparable analog to mustard gas, but has weaker blistering effects 

Nanoparticle System Synthesis: Emulsion-Solvent Evaporation Technique

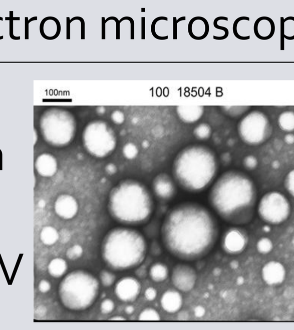


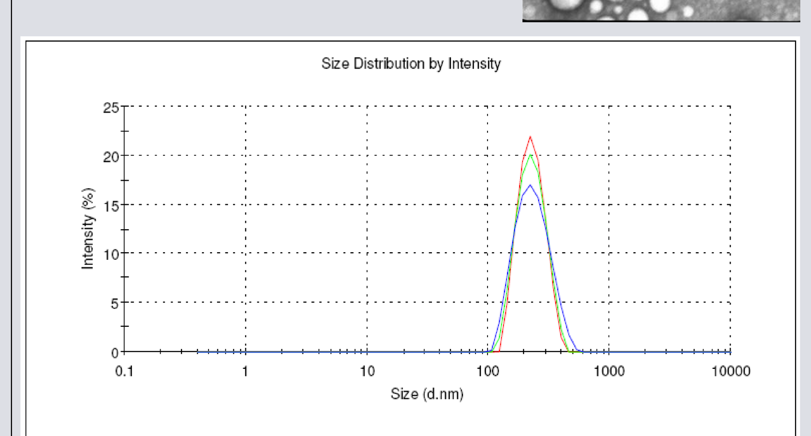
Characterization

- Visually confirm that nanoparticles were produced as designed using:
  - Dynamic light scattering
  - Transmission electron microscopy

Blank Nanoparticles

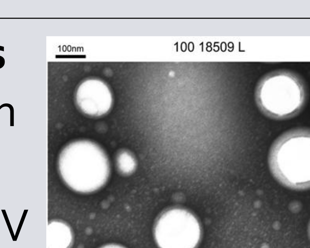
- Average Size: 216.3 nm
- PDI: 0.098
- Zeta Potential: -21.7 mV

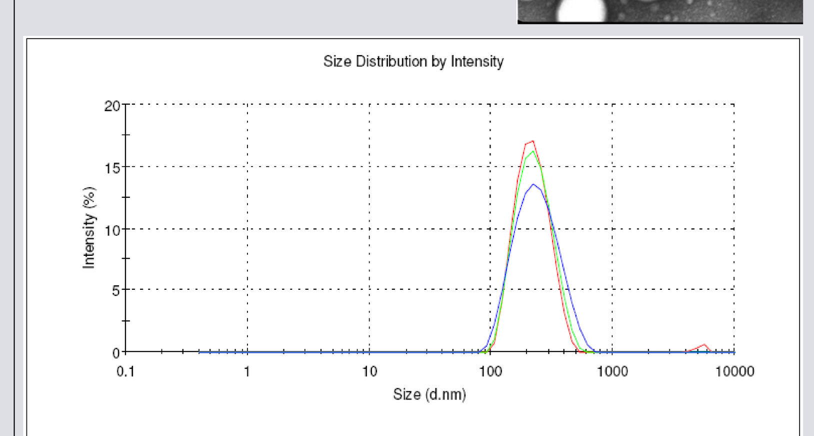




Loaded Nanoparticles

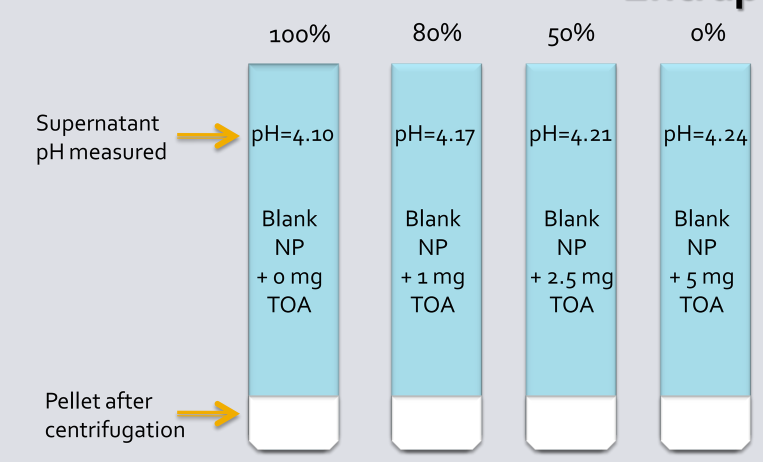
- Average size: 213.1 nm
- PDI: 0.142
- Zeta Potential: -8.4 mV





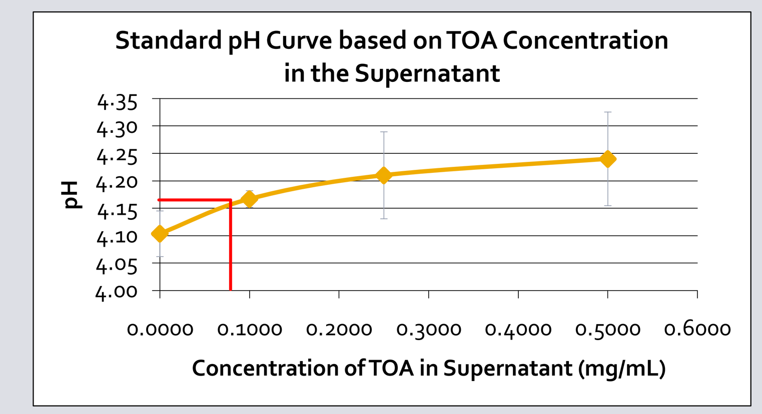
Results

Entrapment Efficiency



Procedure:

- Four batches of blank NPs synthesized
- Different amounts of deactivating chemical added to the NP solutions simulating varying entrapment efficiencies
- NP system centrifuged for 25 minutes at 35,000 rpm to separate nanoparticles (pellet) from solution (supernatant)
- Steady state pH of supernatants was measured

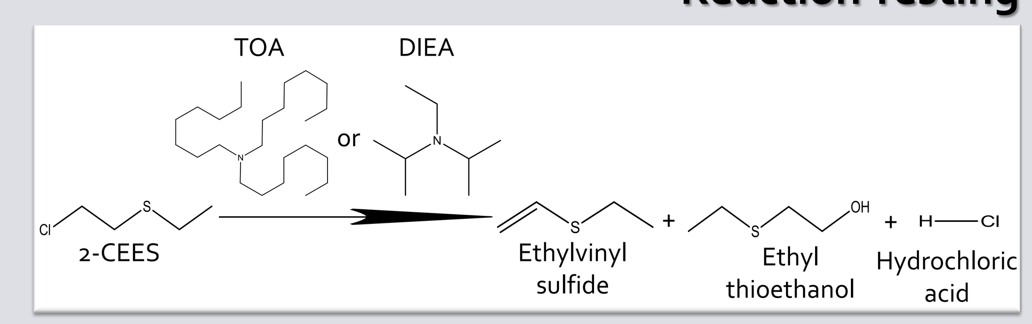


Standard curve used to determine the entrapment efficiency of the deactivating chemical, TOA, loaded inside the nanoparticles.

Results:

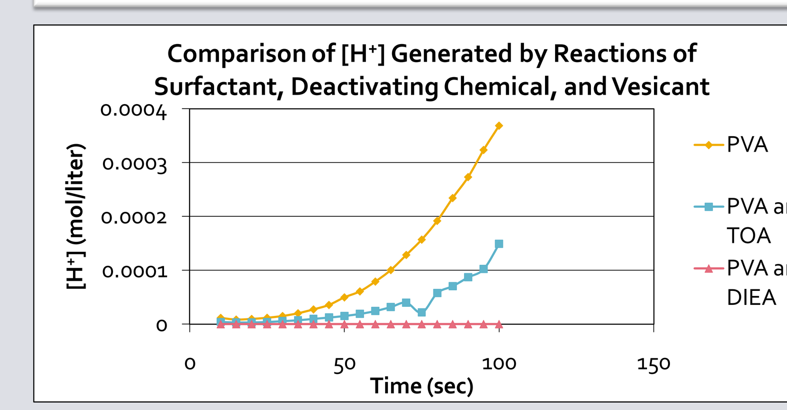
- pH of loaded nanoparticle supernatant= 4.16
- Interpolation from standard curve used to determine a concentration of 0.0857 mg/mL
- The concentration corresponded to an entrapment efficiency of 82.86%
- Consistent with measureable objectives

Reaction Testing

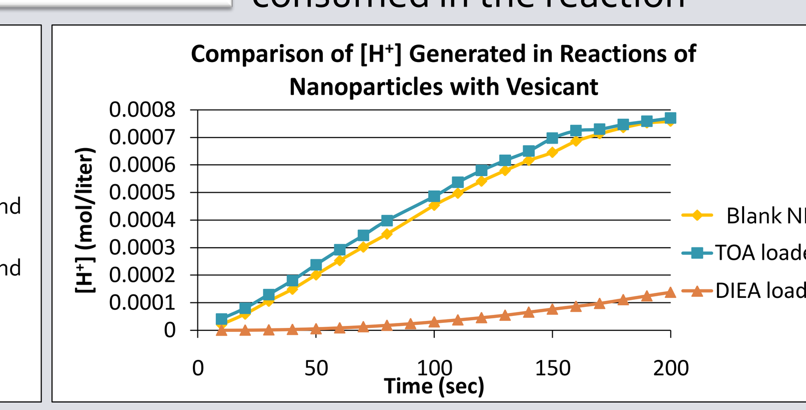


Deactivation reaction:

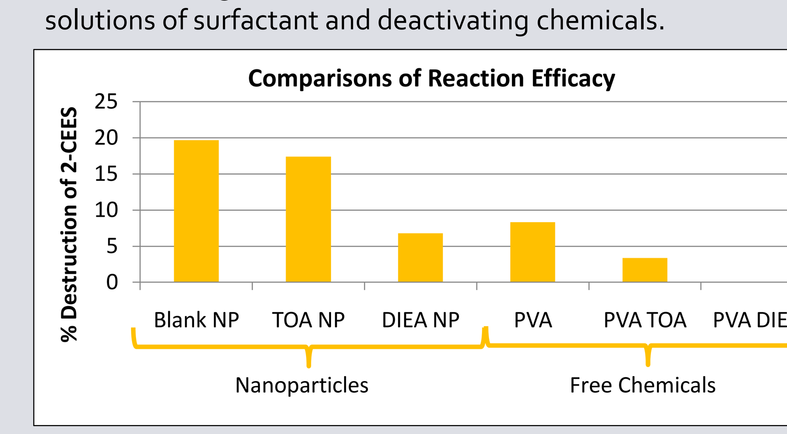
- Vesicant undergoes hydrolysis producing HCl, which causes a measurable decrease in pH
- Deactivating chemical is not consumed in the reaction



Profile of [H+] generated after introduction of vesicant to solutions of surfactant and deactivating chemicals.



Profile of [H+] generated after introduction of vesicant to solutions of nanoparticles loaded with deactivating chemicals.



Comparison of percent destruction of vesicant after introduction to various chemical and nanoparticle solutions.

Procedure:

- 5 µL of vesicant reacted with 10 mL free deactivating chemical, blank NPs, and loaded NPs
- pH change measured and recorded over time

Results:

- NPs deactivate vesicant better than free deactivating chemicals
- Percent destruction of vesicant by blank and loaded NPs was similar

Conclusions

- Nanoparticle characterization showed successful synthesis results
  - Consistent with measurable objectives for size, polydispersity index, and zeta potential
- Entrapment efficiency of deactivating chemical was successfully determined
  - Consistent with measurable objectives
- Although no significant change was observed between the loaded and blank nanoparticles, reaction testing showed that nanoparticles reacted faster than free deactivating chemicals
  - Consistent with measureable objectives

Acknowledgements

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