Proposal Number:	
Proposal Title:	Genzer - Decomposition of organophosphates using functional coatings on top of polypropylene nonwoven mats
Technical topic ID#:	2021-RT-03
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Summary

We propose designing and testing functional fiber coatings that capture and degrade organophosphate-based chemical warfare agents in fluid media. We will deposit the coating on top of polypropylene (PP) nonwoven mats to create highly effective organophosphate degradation systems. The coating will comprise copolymers featuring maleic anhydride units (commercially available) to anchor functional groups such as hydroxamic acid and quaternary amine moieties. The high surface area of the nonwoven fibers, the fiber mat's high porosity, and the presence of the aforementioned chemical functionalities will ensure that organophosphates degrade both inflow and static conditions. We will initially prime the fibers' surface with poly(octadecene-*alt*-maleic anhydride) (POMA) and subsequently modify the maleic anhydride in the copolymer coating using small-molecule modifiers featuring functional units, such as hydroxyamide or quaternized tertiary amine. We will also utilize functional silica particles to do the same. This process will result in functional coatings that contain hydroxamic acid (HA) and quaternary ammonium (QA) moieties. Both HA and QA are known to decompose organophosphates efficiently. Of great interest will be to study the synergetic effect of HA and QA, which is currently unknown, and capitalize on such impact to ensure the excellent removal of chemical warfare agents.

Specific aims

1. Coat PP nonwovens with POMA monolayers. Create functional coatings featuring (1) hydroxamic acids (HA) or (2) quaternary amines (QA). Concurrently, prepare functional coatings featuring both HA and QA moieties in different ratios.
2. Prepare high-surface-area fibers by anchoring silica nanoparticles modified with maleic anhydride to POMA. Alter the chemistry of the particles to deliver HA (or QA) functionality.
3. Optimize the coating properties (*i.e.*, thickness, the concentration of HA, QA). Study the effect of HA and QA loading (individual and synergetic) on the decomposition of organophosphate chemical warfare agent simulants – use dimethyl nitrophenyl phosphate (DMNP) as a model system.

1. Literature Review Summary (Scientific literature)

Organophosphate compounds are an industrially important class of chemicals. The non-specific action of these chemicals on living organisms constitutes a significant threat to modern society because of their potential use as chemical warfare agents.[1] Aside from their immediate lethality, they can also have more subtle effects on human health, even in trace amounts.[2,3] For these reasons, effective means of removing these compounds from the environment are needed.

The chemical basis for the high activity of these compounds in living organisms derives from the fact that a leaving group on a phosphate entity is conducive to a reaction with the serine residues in the active site of the acetylcholinesterase enzyme found in the nerve synapses of animals. The inhibition of synapse downregulates the enzyme production, leading to paralysis and death, making these compounds effective poisons.[4] Additionally, the substituents' variability on the phosphorous atom can modify the organophosphate behavior to produce a different broad range of toxicities.[5] This chemical route forms the basis for the use of organophosphates as warfare agents. It also enables a valuable avenue of their elimination from the environment by employing chemical strategies that lead to controlled hydrolysis of the bond between the phosphate and the preferred leaving group making organophosphates compounds harmless.

Davies and Green reported on organophosphate degradation by breaking the phosphoester bond after recognizing organophosphates as potential chemical warfare agents.[6] The first effective treatment for organophosphate poisoning involved oximes. Pralidoxime has been the most commonly studied therapeutic agent.[7] The therapeutic agents negating the organophosphate's action, while capable of degrading unbound compounds, must also perform the same reactions.[8] Pyridinium is an example of a compound capable of this action. It helps target the negatively-charged cleft of acetylcholinesterase.[9] One would expect that this would limit the ability of the drug to cross the blood-brain barrier. However, this is not the case.[10] Hydroxamic acids, or more appropriately hydroxamate anions, were also active in these degradation reactions.[11] One finding of importance to this work was that the hydroxyimide form does not have the same reactivity level as the hydroxamic acid form.[12] More recent work has shown that hydroxamic acid can have improved performance when used in a micellar form.[13,14,15]

Small nucleophile molecules are not the only systems employed effectively for organophosphates decontamination. Though the organophosphate compounds will naturally degrade in the environment over time, the reaction rates are low, leading to an acute threat to the field combatants. The need for a system that allows for immediate degradation of these compounds requires high specificity/selectivity chemistries to speed the process is imminent.[16] The selection of chemistries capable of efficient degradation must satisfy several criteria, including the simplicity of use/application, high stability under various conditions (heat and humidity), ability to regenerate in-situ and overall cost. The novel approaches in designing nonwoven-based materials capable of degrading chemical warfare agents can be drawn from chemistries used in converting pesticides that belong to the same chemical family. Several naturally occurring chemicals satisfy initial design criteria, *i.e.*, low-cost bentonite-based sorbent systems.[17,18] Non-targeted proteins can react with organophosphates and can play a role in their degradation.[19] Cyclodextrins can also get modified for use in degrading organophosphates using hydroxamate groups.[20]

An alternative approach is to utilize chemically active macromolecular systems. Specifically, a study reported using a dendrimer with one oxime group at each branch's terminus as a possible replacement for the biomolecule-based approach.[21] Another example involves conventional linear polyacrylamides, which are modified to bear the amidoxime group. The degradation half-lives of chemical warfare agents range from 5 minutes to several hours.[22] Hydrogels with pyridine moieties are also capable of promoting the hydrolysis of organophosphates and mustard gas agents.[23] A recent paper reported on using quarternary amines to degrade organophosphates.[24] The authors did not comment specifically on the role of the quaternary amines. We attribute the ability to degrade organophosphates in that study to the increased local pH within the macromolecular architecture.

In recent years, metal-organic frameworks (MOFs) have garnered much interest as catalysts for various reactions; several studies have shown that some MOFs can rapidly degrade organophosphates.[25,26]

2. Prior Art Search (Patent literature)

The usage of fabrics for the degradation of chemical warfare agents (CWA) is a relatively new technological area. The type of contaminant in waste streams defines the mechanism employed in the separation process, which must lead to pollutant-free outgoing streams by design. Current fiber mat-based technologies can be divided broadly into the following categories: a) incorporation of active chemical functionalities on the fabric surface capable of continuous catalytic degradation with the regeneration in-situ; b) ion-exchange technologies enabling reversible capturing of chemical species possessing an opposite to the mat non-zero-net charge (primarily biological warfare agents), and c) irreversible capturing of chemical compounds that could be trapped due to its high affinity toward a nonwoven mat coating.

Below we list relevant patents in this domain that reflect the commonly used methods to purify the CWA contaminated environment using nonwoven/woven fiber technologies. Many public domain methods leading to the formation of functionalized nonwovens mats fabrication cannot be used directly to produce mats capable of continuous in-situ organophosphates degradation, and material self-regeneration.

Title	Patent No.
Method for making a functionalized membrane.	WO2009086347A1
Protective material in two-dimensional or three-dimensional form against chemical poisons and warfare agents comprises nano-crystals permanently fixed to the surface of a carrier element	DE10051647A1
Adsorption filter material with integrated particle- and/or aerosol-filtering function and its use.	US8366816B2
Nanophase Mn(VII) oxide (NM70) and nanophase Mn(III) oxide (NM30) incorporated nonwovens	US8163036B1
Polymeric composition for the neutralization of noxious agents	US8920825B2
Adsorption filter material for producing protective materials, particularly protective clothing and covering for the civilian or military sector, filter material and filters for removing pollutant, has integrated particle and aerosol protection	DE102007033178A1
Breathable chemical, biological, radiation, and/or nuclear protection fabric or material	US9475263B1
Protective garments	US20200015529A1
Activated protective fabric	US8501644B2
Sorption filter material and use thereof	US8647419B2

We have searched the patent databases extensively using the various combination of the following keywords: "nonwoven," "phosphates," "phosphate degradation," "active nonwoven fibers," "CWA and nonwoven," "organophosphate toxins," "phosphate supported degradation," and "in-situ degradation." We could not identify any relevant patents/patent applications that can fully capture the research objectives/the final product composition of the proposed research.

Title	Patent No.
Filterized fabric for protecting against toxic substance, manufacturing method therefor, and special clothes made thereof	WO2018199405A1
Chemical Protective Fabric	US20100319113A1
Protective article and methods of manufacture thereof	US20120135658A1
Functionalized nonwoven article	US8328023B2

3. Proposed research

3.1 Overview

We propose to use chemically-functionalized maleic anhydride copolymers for organophosphate degradation due to their ability to undergo diverse post-polymerization reactions.[27,28] These contrast with the studies involving anhydride-based drug delivery systems.[29] The diversity of functional groups that can be chemically employed to modify maleic anhydride combined with alternating backbone motifs allows for the construction of diverse catalytic degradation systems. The modified maleic anhydride copolymers are used in the form of coatings on top of nonwoven mats. The method gives these systems a unique ability of direct contact with the contaminated stream to produce a purified effluent while still maintaining its structural integrity. The proposed approach is an alternative to other methods, such as coatings with MOFs, to improve organophosphates' degradation efficiency.[30] An additional attractive aspect of maleic anhydride alternating copolymers as effective catalytic systems for organophosphates degradation is their wide commercial availability and low cost.

We plan to accomplish the task under **3 Aims** that are detailed below.

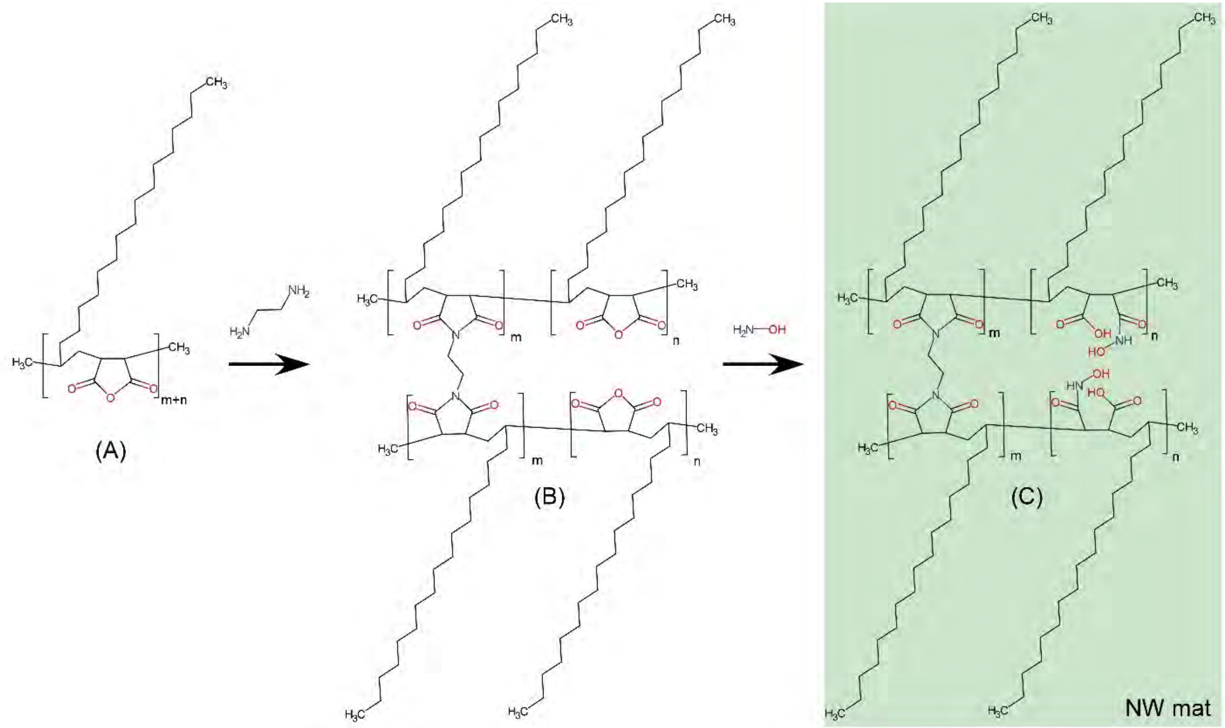

Figure 1. Schematic depicting the formation of functional layers on top of PP fibers. POMA precursor (A) is crosslinked with ethylenediamine (b) and subsequently functionalized with hydroxylamine (C).

3.2 Aim 1

In this aim, we will form a polymer primer on top of PP fibers, crosslink it, and generate hydroxamic acid and quaternary amines as the active species in monolayer polymer coatings. We will do so by exploring their individual contributions and well the combined effect.

3.2.1 Preparing primer layer on top of PP nonwovens

We will use a commercially available poly(octadecene-*alt*-maleic anhydride) (POMA, **Figure 1A**) polymer (also synthesized readily in the laboratory) to create functional coatings on top of polypropylene (PP) nonwoven fiber mats. The deposited POMA primers will serve as sites to deliver functionalities. Specifically, POMA will be deposited by either spin-coating or dip-coating from an acetone solution (0.5 – 10 mg/ml). POMA anchors to the PP substrate via hydrophobic interactions between the octadecene and PP surface.[31] Washing the coating with acetone will remove any unbound polymer and leave a thin POMA layer attached to the fiber mat. A brief wash with ethylenediamine solution (concentrations 0.01-0.1 wt%) will crosslink the coating by reacting primary amines with anhydrides (**Figure 1B**). We will keep the ethylenediamine solution concentration low. Only a small fraction of anhydride groups in POMA are consumed in crosslinking while maintaining the significant portion of anhydrides available for functionalization (*cf.* sections 3.2.2 and 3.2.3). We will confirm POMA's presence on the surface via FTIR (vibrations at 1860 and 1780 cm^{-1} correspond to the anhydride) and XPS (binding energy ~520 eV). Any unreacted anhydride units will serve as reaction sites for chemical functionalization.

3.2.2 Preparing coatings containing hydroxamic acid

We will immerse the POMA-modified fiber mats into hydroxylamine hydrochloride solutions in DMSO (concentrations 1-5 wt%) for various times (1-5 mins) at ambient conditions. Adding a small amount of Et_3N, we will form forms hydroxylamine, which reacts with maleic anhydride units to create hydroxamic acid sites in the coating (**Figure 1C**). We will confirm the reaction by monitoring the disappearance of the anhydride vibration signals in FTIR (*cf.* section 3.2.1) and the appearance of new vibrations at 1640 and 1550 cm^{-1}. Tracking the increase in the latter two vibrations intensities relative to the anhydride absorbance peak decrease will provide qualitative means of assessing the reaction progress.

3.2.3 Preparing coatings containing tertiary amines

We will immerse the POMA-modified fiber mats into dimethyl aminoethyl amine (**Figure 2D**) (or dimethyl amino propyl amine, **Figure 2E**) solutions (concentrations 1-5 wt%) for various times (1-5 mins) to create tertiary amine sites in the coatings (**Figure 2F**). Subsequent reaction with methyl iodide (vapor deposition or wash with methyl iodide solution in acetone at concentrations 1-5 wt%) will quaternize the tertiary amine (**Figure 2G**). We will confirm the reaction by monitoring the disappearance of the anhydride vibration signals in FTIR (*cf.* section 3.2.1) and the appearance of a new vibration at 1550 cm^{-1} corresponding to the presence of a quaternary amine. We will monitor the increase in the intensity of the 1550 cm^{-1} vibration relative to the anhydride signal disappearance will provide qualitative means of assessing the reaction progress. Heating the functionalized fiber mat above 100°C for 30 mins will promote the formation of imides, thus improving coating stability.

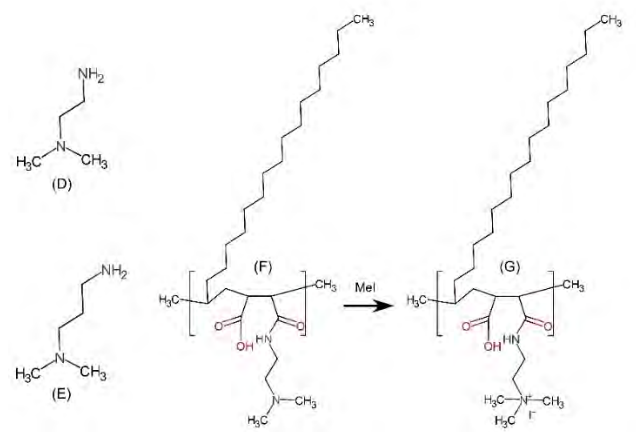

Figure 2. Dimethyl aminoethyl amine (D) or dimethyl aminopropyl amine (E) are used to functionalize POMA (A in **Figure 1**). The resulting polymer (F) is then reacted with methyl iodide (MeI) to produce the structure depicted in (G).

3.2.4 Preparing coatings containing hydroxamic acid and tertiary amines

We will prepare the coatings by combining the methods described in sections 3.2.2 and 3.2.3. The key in these experiments is to create coatings with variable concentrations of hydroxamic acid and the quaternized amine. We will examine the modification sequence's effect by starting with the modification described in section 3.2.2 and followed by the one outlined in section 3.2.3. We will also alter the sequence by first modifying the primer layer using the method described in section 3.2.3, followed by that outlined in section

3.2.2. Alternatively, we will immerse the POMA-modified fiber mats into solutions featuring hydroxylamine and the tertiary amine (*cf.* sections 3.2.2 and 3.2.3). We will vary the hydroxylamine concentrations and the tertiary amine systematically. Quaternization will follow the protocols outlined in section 3.2.3. The chemical analysis will follow the steps outlined earlier in sections 3.2.2 and 3.2.3.

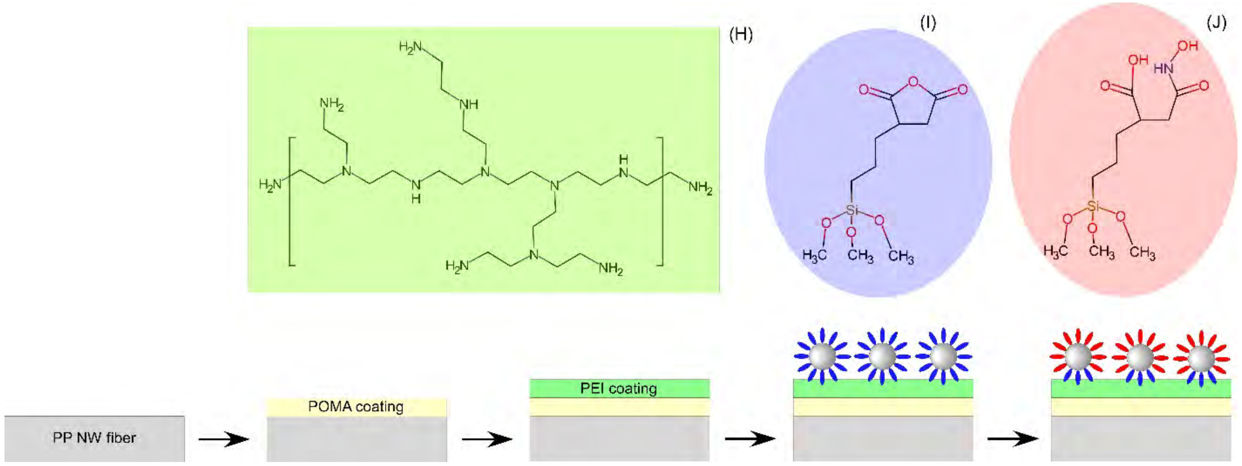

Figure 3. Nonwoven PP fiber is coated with POMA and subsequently overcoated with polyethyleneimine (PEI) (H). Silica nanoparticles are reacted with anhydride-based silanes and are anchored to the POMA coating on top of PP (I). Reaction with hydroxylamine creates active groups on top of silica particles (J). Structures not drawn to scale.

3.3 Aim 2

In this aim, we will first coat a POMA primer layer on top of PP fibers. Then we will deposit polyethyleneimine (PEI), which will crosslink POMA and immobilize it on top of the PP fiber. Concurrently, PEI will serve as an anchoring layer for maleic anhydride-functional silica particles. We will functionalize the anhydride groups on silica particles with hydroxylamine to create hydroxamic acid sites (*cf.* section 3.2.2). This method will create functionalized fiber mats with a large reactive surface area, enhancing the overall system performance.

3.3.1 Preparing functional primers on top of PP nonwovens

POMA primer will be deposited on top of PP fibers as described earlier (section 3.2.1). Following this step, we will coat the PP/POMA surfaces with an aqueous PEI solution (concentration 0.025-10 mg/mL). PEI will crosslink the POMA layer by reacting the anhydride groups in POMA and primary amines in PEI, thus forming a gel. We will confirm the reaction by monitoring the disappearance of the anhydride vibration signals in FTIR (*cf.* section 3.2.2) and the appearance of new vibrations at 1640 and 1550 cm^{-1}. Concurrently, PEI will serve as an anchoring layer for attaching functionalized silica particles (**Figure 3**).

3.3.2 Preparing functional silica particles

We will use silica particles (available from Aldrich and other sources; size ranging from 50 nm to 1 μm) and modify their surfaces with succinic anhydride silanes (available commercially from Gelest). We will prepare succinic anhydride silane solutions in ethanol (concentrations 1-10 mmol), load particles, and perform silane coupling at 50°C for 12 hours. After the reaction, we will remove the silica particles and let them dry at 150°C to remove any residual solvent and close succinic anhydride cycles that may have opened up during the coupling in the small presence of water.

3.3.3 Preparing functional coatings

We will redissolve the succinic anhydride silane functionalized particles in ethanol and deposit them onto the PP/POMA/PEI substrates by spray-/spin-/dip-coating. The particles will attach to the primer layer by reacting the succinic anhydride groups with primary amines in PEI. We will subsequently modify the succinic anhydride groups in silica particles by exposing them to hydroxylamine to create hydroxamic groups (see section 3.2.2). Concurrently, we will explore exposing such coatings to create additional quaternary ammonium units in the unreacted tertiary amines in PEI by following the procedures outlined in section 3.2.3.

3.4 Aim 3

In this aim, we will address the concentration of hydroxamic acid and the quaternary amine in decomposing DMNP.

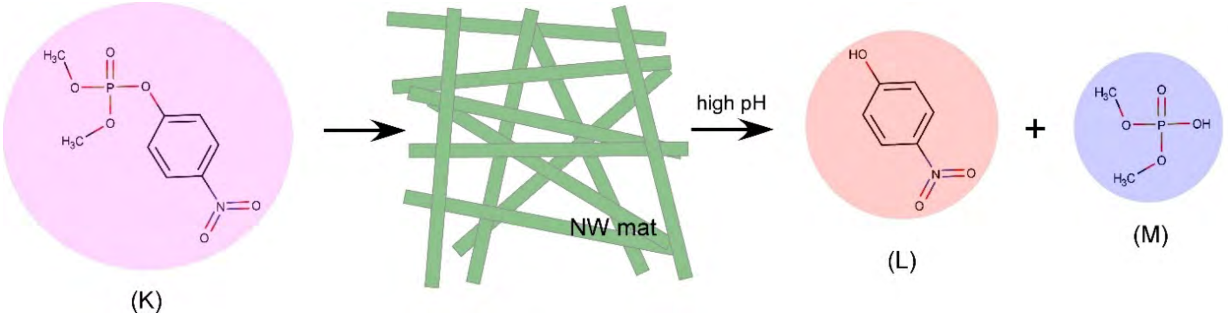

Figure 4. Degradation of dimethyl nitrophenyl phosphate (DMNP) (K) into 4-nitrophenol (L) and dimethyl phosphate (M).

3.4.1 Optimizing the properties of functionalized hydrogel layers on top of PP nonwovens (Aim 1)

In Aim 1, the hydrogel layer forms by crosslinking POMA with diamine will determine the absolute concentrations of hydroxamic acid and quaternized amine. Following the experiments described in sections 3.3.1-3.2.4, we will thus vary the hydrogel layer thickness by adjusting the gel-forming material's concentration, the density of ethylenediamine, and the reaction time. We will determine the thickness of the coating by mass balance. Specifically, we will weigh the fiber mat before and after the coating and use SEM to determine the fiber size before and after coating.

3.4.2 Optimizing the properties of hydrogel/silica particles on top of PP nonwovens (Aim 2)

In Aim 2, we use POMA as a primer and deposit PEI as a crosslinker and an active layer to deposit silica particles modified with succinic anhydride silanes. We will optimize the conditions for depositing POMA and PEI based on our recent work.[31] The succinic anhydride functionality in the silica particles enables hydroxamic acid unit formation; the tertiary amines in PEI can be further quaternized to create quaternized moieties. The presence of silica particles offers multiple advantages. First, it delivers the desired functionality (*cf.* section 3.2.2). Second, it offers improvement in the mechanical properties of the coatings and the resistance to damage. Third, the presence of a "rough" layer may act as an antifouling layer.

3.4.3 Testing the degradation of organophosphates

We will use dimethyl nitrophenyl phosphate (DMNP) to study the effectiveness of the coating to decompose DMNP into nitrophenol and a phosphoric acid residue (**Figure 4**). We adopt the testing procedure from the literature.[32] Specifically, we will test the organophosphate decomposition in solutions or N-ethyl morpholine (NEM, pH 10.29), 0.1 M Carbonate (pH = 9.0) and 1 M carbonate (pH =10.1). This step will help us establish the role of pH on degradation kinetics. The concentrations of DMNP will vary from 50 μM to 1 mM. We will record the kinetic measurements of DMNP degradation using a UV/Vis Thermo Evolution 300 spectrometer. In a typical experiment, we will collect the UV/Vis spectra between 200 and 700 nm with the step of 2.0 nm from the dry polymer coating (time 5-240 mins) on the fiber and compare them to those collected from DMNP solutions. The relative decrease in the signal corresponding to DMNP degradation (~280 nm) and the generation of 4-nitrophenol (~400 nm) provides evidence of organophosphate degradation. We will prepare standard solutions of 4-nitrophenol and analyze the intensity of the peak at 400 nm.

Using this calibration procedure, we will convert the UV/Vis absorbance intensity to the concentration of 4-nitrophenol in solution and evaluate the effectiveness of the decomposition of DMNP. The hydroxamic acid and the quaternized amine both degrade DMNP. The quaternized amine will locally increase the local pH in the coating. Varying the concentration of DMNP in mixed hydroxamic acid/ quaternized amine coatings would provide insight into the role of local increase of pH on the decomposition of DMNP. We will also adsorb DMNP onto PP nonwovens by directly spraying DMNP from DMSO solutions. We will assess the amount of adsorbed DMNP via TOF-SIMS and XPS. We will then spray solutions of different buffers onto the DMNP coated specimens, collect the solutions, and analyze the nitrophenol content via UV/Vis.

In preliminary experiments, we prepared poly(maleic anhydride-*alt*-methyl vinyl ether) gels and tested the degradation of DMNP in NEM solutions as a function of gel loading (**Figure 5**). Increasing the gel loading enhanced DMNP degradation, as expected. We will compare gel coating performance on top of PP nonwovens to bulk gels (with the same amount of gel in both cases).

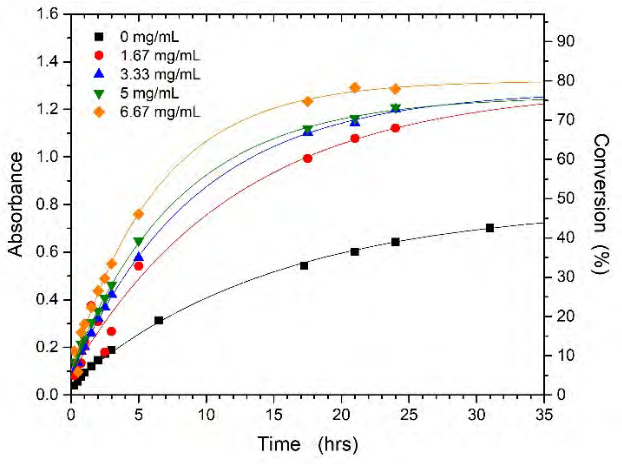

Figure 5. DMNP degradation as a function of poly(maleic anhydride-*alt*-methyl vinyl ether) (PMAMVE) gel loading in NEM buffer as compared with a NEM buffer solution (0 mg/mL). Increasing the HA (and QA) concentration in the coatings (due to the high surface area of the PP fiber mat) will significantly speed up DMNP degradation beyond the reported values for bulk gel.

Deliverables

Year 1

Adsorption of POMA to polypropylene fibers (before and after crosslinking). Chemical composition of the coating after modification with hydroxylamine and quaternary units. Performance of the coatings in decomposing DMNP organophosphate.

Year 2

Formation of POMA/PEI hydrogel coatings on top of PP nonwovens. Formation of silica particles functionalized with succinic anhydride. Decomposition of DMNP using hydrogel-modified coatings.

Year 3

The role of hydroxamic acid, a quaternary amine in POMA-based and POMA/PEI/silica particle-based coating and their synergetic effect on the decomposition of DMNP.

Milestones

Task	Year 1		Year 2		Year 3	
Anchor POMA to PP fibers. Crosslink the layer with diamines (**Aim 1**). and PEI (**Aim 2**). Test stability of the coating.	🟥	🟥				
Modify POMA with hydroxylamine and quaternary amine groups. Characterize the content of the functional groups (**Aim 1**).		🟥	🟥			

Perform degradation experiments of DMNP organophosphate (**Aim 3**).		🟥	🟥			
Prepare hydrogel coatings featuring POMA/PEI on top of PP nonwovens (**Aim 2**).			🟥	🟥		
Prepare functionalized silica particles and anchor them to the PP/POMA/PEI substrate. Modify the silica particles to create hydroxamic acid moieties (**Aim 2**).			🟥	🟥		
Perform degradation experiments of DMNP (**Aim 3**) using hydrogel coatings on PP nonwovens that have been functionalized with hydroxylamine and quaternary amine groups in POMA (**Aim 1**) and silica particles (**Aim 2**).			🟥	🟥	🟥	
Vary the loading of hydroxylamine and quaternary amine groups in the hydrogel coating (Aim 1) and functionalized silica particles (**Aim 2**).				🟥	🟥	🟥
Identify the effects of the role of hydroxamic acid and quaternary amine on the decomposition of DMNP (**Aim 3**).		🟥		🟥	🟥	🟥

Budget

We have made this budget as stringent bare-bones" as possible, taking into account the University, College of Engineering (COE), and Chemical & Biomolecular Engineering (CBE) Departmental rates over which the PIs have no control. We request sufficient funds to appoint 1 CBE Ph.D. student dedicated to the project over three years that covers his/her stipend, health insurance, and tuition. We request no salary support for the PIs.

Specifically, we request *(i)* student stipend of $35K for Year, $36.05K for Year 2, and $37.132K for year 3; *(ii)* fringe benefits (9.05% of the salary) plus health insurance (HI, $2,620); and *(iii)* tuition of $16,246 per student per year. ($9,094 in-state tuition + $4,332 Graduate Tuition Remission Match (GTRM) as required by the University). GTRM refers to 25% of the difference between in-state and out-of-state tuition. Under the GTRM, if an out-of-state student is hired, the University pays the difference between the sponsor's contribution per year and the actual cost of out-of-state tuition annually. If an in-state GRA is hired, the sponsor is not charged for the GTRM, only the actual tuition. Neither the tuition amount nor the GTRM carry the F&A cost. We apply a 10% inflation factor to calculate the tuition for subsequent years after Year 1. These rates (stipend, fringe, tuition, *etc.*) are consistent with the University, COE, and CBE policies.

We also request funds for materials and supplies ($8K/year), analytical services (*i.e.*, AIF) ($2k/year), and travel ($2K/year).

Item	**Amount**		
	Year 1	**Year 2**	**Year 3**
Graduate student	$35,000	$36,050	$37,132
Fringe benefits (@ 9.05%)+HI ($2,620)	$5,788	$6,014	$6,249
Total personnel	**$40,788**	**$42,064**	**$43,380**
Materials and supplies	$8,000	$8,000	$8,000
Services	$2,000	$2,000	$2,000
Travel	$2,000	$2,000	$2,000
Tuition	$16,246	$17,871	$19,658
Sub-total (S)	**$69,034**	**$71,934**	**$75,038**
Indirect Cost (I), 10% of sub total	$5,279	**$5,406**	**$5,538**
S+I TOTAL	$74,312	$77,340	$80,576
3 YEAR TOTAL	**$232,228**		

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