

The Role of Water in Modulating Reactivity within Selectively Permeable Membranes

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ABSTRACT

A copolymer of poly(vinyl alcohol-co-vinylamine) called PVAam, has been demonstrated to be an effective self-decontaminating material for phosphonate nerve agents when placed in contact with a powder or a cast film of the co-polymer, but only after conditioning at high relative humidities. Studies on the effect of moisture on the reactivity of films of the M12 grade of PVAam revealed that at water activities (A_w) below 0.88, the M12 polymer showed no capacity to hydrolyze the G-agent surrogate diisopropyl fluorophosphate (DFP). The hydrolytic activity of M12 is limited to saturated moisture levels. In this paper, the effects of moisture content on the structure of M12 films are described by electron spin resonance features, by reaction rates from solid state NMR, and by molecular modeling. Structural alterations in the M12 membrane due to moisture uptake are related to the membrane's ability to hydrolyze DFP.

INTRODUCTION

In 2006, a new project was initiated with the support of the *Joint Service Technology* office to develop chemically reactive materials as self-detoxifying fabrics for protection against chemical and biological agent threats. The U.S. Army Natick Soldier Research, Development and Engineering Center's (NSRDEC) focus has been studying the properties of agent-reactive permselective membranes that have good moisture vapor transfer rates (MVTR).¹ One such candidate that meets these requirements is a commercially available copolymer of poly(vinyl alcohol-co-vinylamine), or PVAam from Celanese Corporation, shown in figure 1.

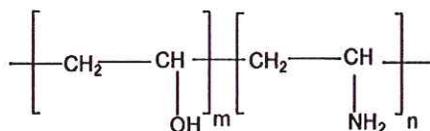


Figure 1. Empirical formula of PVAam copolymer

Celanese supplies a low molecular form (L12) that has a range of molecular weights (MW) from 30-50 KDa and a high molecular form (M12) with a MW of 80-130 KDa. Both forms are water soluble and films can be cast from aqueous solutions. Both co-polymers (L12 and M12) contain 12 mol% amine and have been shown to decontaminate G-agents and their simulants². Although the copolymer film is reactive with G-agents, it has to be conditioned with

water vapor at a water activity, $A_w = 1.0$ for maximum reactivity.¹⁻² The work reported herein examines structural changes that PVAam membranes undergo as a function of moisture level (A_w), and how these changes can be related to changes in reactivity.

EXPERIMENTAL

PVAam films were cast from aqueous solutions and crosslinked into thin films, as previously described.² The dry films were conditioned to the desired moisture content (A_w) by equilibration over saturated salt solutions.³ A solid state nuclear magnetic resonance (NMR) technique was developed by researchers at NSRDEC and the U.S. Army Edgewood Chemical Biological Center (ECBC) to monitor the extent of the decontamination of G-agent by reaction with PVAam films using phosphorus (^{31}P) NMR.² The ^{31}P signal (used to measure the extent of DFP hydrolysis by removal of the fluorine from the phosphorus atom over time) was monitored periodically over 24 hours. Pseudo 1st order and apparent 2nd order rate constants (k_{obs} and k_2) were obtained from plots of the integrals of the ^{31}P NMR peaks of DFP and DFP-OH as a function of time, using the method of Chen, et. al.⁴

For ESR experiments, M12 and L12 films were spin-labeled with 4-maleimide-TEMPO (Aldrich Inc.). Analysis of the ESR spectra was performed by a *Least-Squares Fitting of Slow Motional ESR spectra* program.⁵

RESULTS

The ^{31}P solid state NMR of DFP in its reaction with PVAam films at saturation moisture conditions ($A_w = 1.0$), shows three peaks in Figure 2 corresponding to DFP (~2.5 and ~8.3 ppm) and the hydrolyzed acid product of DFP (~15.2 ppm). By plotting peak area (integrals) as a function of time it is possible to estimate the kinetic parameters of the DFP degradation.⁴ The results are given in Table 1. Table 1 shows that L12 has a rate of decomposition one-half of the rate for M12 at $A_w = 1.0$ (saturated moisture conditions), but at $A_w = 0.98$ and below, M-12 shows no activity against DFP. L12 still exhibits hydrolytic activity, even at $A_w = 0.96$.

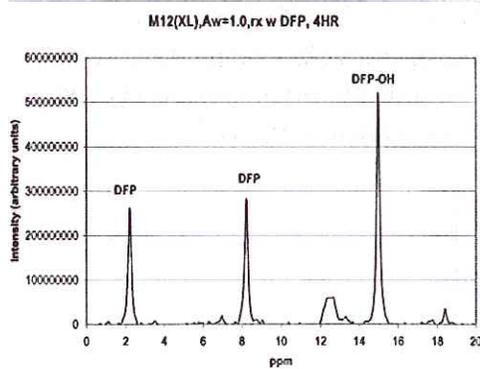


Figure 2. ^{31}P NMR of M-12 rx with DFP

Sample	A_w	$K_{\text{obs}} \text{ min}^{-1}$	$t_{1/2} \text{ (HR)}$
M-12	1.0	0.0088	1.31
L-12	1.0	0.0049	2.36
M-12	0.98	---	---
L-12	0.98	0.0024	4.81
M-12	0.96	---	---
L-12	0.96	0.0015	7.7

Table 1. Rate Constants for DFP hydrolysis by M-12 and L-12 at various A_w levels

In Table 2, the persistence of the spin label (attached to the polymer structure) is listed with corresponding moisture content within the polymer matrix. T_R is the rotational correlation

time (msec to nsec) which represents the length of time over which the maleimide spin label (MSL) rotation persists in a given orientation. These values indicate an increase in chain mobility as the polymer begins to hydrate. T_R increases by ~ 3 orders of magnitude as water content increases from A_w 0.94 to A_w 0.96. Examination of ESR spectra at these two moisture levels (data not shown) show a change from “rigid limit” to a partially mobilized (solution-like) spectrum. At $A_w > 0.96$, the ESR spectra (data not shown) exhibits a 3-line spectra which approximates the MSL-TEMPO free rotation in solution. The implication is that at $A_w > 0.94$ the M12 matrix is beginning to open up enough to allow rotation (i.e. swell). But even as the membrane structure is swelling at these higher humidities, corresponding NMR of M12 reactions shows no decomposition of DFP below A_w 1.0.

Table 2. Analysis of M12 ESR spectra by Least Squares Fitting of Slow Motional ESR

<i>Sample</i>	A_w	A_n (gauss)	R (radians/sec)	T_R
Labelled M12	0	16.4319	5.6	3 msec
‘	0.88	16.5197	65.7	2.5 msec
‘	0.94	16.5483	75.5	2.2 msec
‘	0.96	17.0202	167.5	10 nsec
‘	0.98	17.2466	97723.7	1.7 nsec
‘	1.0	17.0628	327340694	0.5 nsec

Molecular models of syndiotactic polymer M12 molecules and DFP with varying water concentrations were created using Amorphous cell module of Materials Studio (Accelrys, Inc.). We have used 10 chains of 25 monomers each. Density of the initial molecular structure was optimized using the NPT algorithm and several annealing steps. For the NPT runs, the pressure was controlled using Berendsen’s method with the pressure scaling constant set to 0.5 ps and system compressibility at 0.5 GPa. The equations of motion were integrated using the Verlet algorithm with a time step of 1fs. During these simulations the cutoff for the non-bond interactions was 9.5 Å with buffer width 0.5Å. We also used the group-based non-bond summation method to improve the computation time. After convergence was achieved, we equilibrated the system under the NVT conditions (Andersen thermostat). The resulting trajectory was analyzed by calculating structural properties such as the radial distribution function, $g(r)$ and coordination numbers $n(r)$. The results were averaged over at least 3 amorphous cell models.

We used Compass forcefield in the MD simulations carried out with the Materials Studio Discover program (Accelrys, Inc.). The COMPASS force field was developed to predict structural and thermophysical properties for many inorganic and organic fluids and also polymers, it was not tested in calculations for molecules including P-F bond, such as in the DFP molecule. Gaussian3 quantum mechanical calculations on DFP molecule using density functional theory (DFT) at the B3LYP/6311++G** level yield two conformers: non-symmetric (nS) and symmetric (S) of C_s symmetry. Both conformers are virtually degenerate and S is more stable by 0.2 kcal/mol. Including a water effect via the continuous electrostatic model PCM, leads to inversion of conformers stability with nS conformer more stable by about 0.6 kcal than S conformer. This effect is a consequence of a much higher dipole moment of nS conformer (4.5 Debye) as compared to the dipole moment of S (1.8 D). The Compass calculations in the gas phase predicts the nS conformer to be more favorable than S by about 1.3 kcal/mol. However, the meaningful application of Compass forcefield is the simulation of DFP in solution e.g. in water. The Compass-MD simulations of DFP in water find a broad distribution of dihedral

angles characteristic of the nS form of DFP, in overall agreement with the DFT-PCM calculations. We have calculated density of DFP liquid in 298K at 1.07 g/cm^3 in good agreement with experimental data of 1.05 g/cm^3 .

At first we attempted to characterize interactions between polymer chains as a function of water content. The interchain interactions were probed by comparing $g(r)$ function for intermolecular interactions of hydroxyl groups (O-O), amino groups (N-N) and hydroxyl-amino (O-N). The $g(r)$ functions for three models of dry polymer and in solution with water are displayed in Fig.3. We find that the hydroxyl groups of different chains interact through hydrogen bonding in a dry polymer and with water content of 0.5 water molecules per every monomer (0.5wm). When we increased the water content to 2 water molecules per monomer (2.0wm), the oligomeric chains became further apart resulting in the lost of the inter-chain interaction. The $n(r)$ values corroborate the qualitative analysis of $g(r)$ functions. The number of O-O contacts falls from 0.84 to 0.59 with the solvation of the polymer. The rapid swelling and saturation of polymer chains with water is a necessary step for decontamination functionality of a polymer. The total density of a polymer decreases from 1.155 to 1.154 and 1.112 g/cm^3 for a dry, 0.5wm and 2.0wm solvated polymer, respectively.

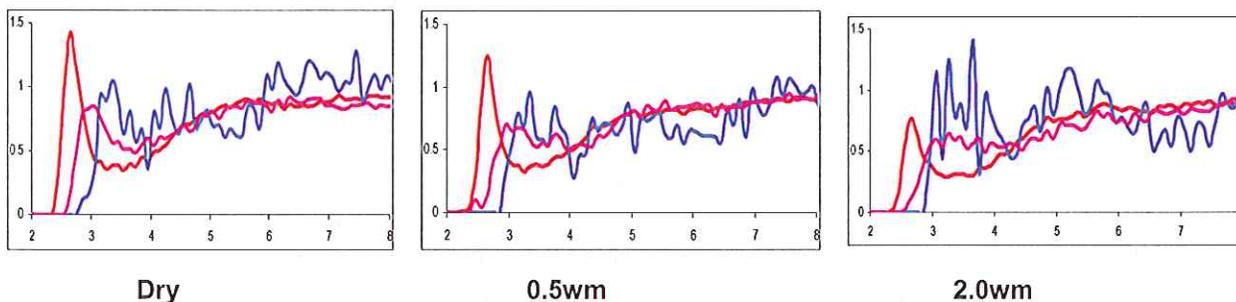


Fig 3. $G(r)$ functions of interchain interactions for hydroxyl (O-O)(red), amino (N-N) (blue) and hydroxyl-amino (O-N) (pink) groups of polymer.

The water molecules are strongly interacting with polar groups of polymer. Figure 4 shows $g(r)$ functions for hydroxyl-water (O-W) and amino-water (N-W) in the 0.5wm solution of a polymer.

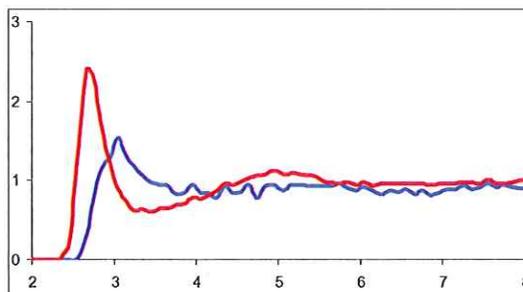


Fig 4. $G(r)$ functions of O-W (red) and N-W(blue) interactions in 0.5wm polymer solution

The $n(r)$ values calculated by integrating $g(r)$ functions to 4.0 \AA , which include completely both peaks, are 1.43, 1.45 for O-W and N-W interactions, respectively. In the case of 2.0wm solution, there is more water associated with polar groups of polymer, and the $n(r)$ values are 2.77, 3.04 respectively. The water molecules seem to be located *closer* to hydroxyl groups than to amino groups, however overall, amine groups attract *more* water than hydroxyls.

Fig 4. $G(r)$ functions of O-W (red) and N-W (blue) interactions in 0.5wdm polymer solution

Adding DFP significantly affects concentration of water molecules around the polymer polar groups. We have studied two solutions of polymer, containing 0.5 water and 0.5 DFP molecules per every monomer (0.5wdm) and also 2.0 water and 2.0 DFP molecules per monomer (2.0wdm). According to the coordination numbers, the water is being replaced by DFP molecules particularly close to amino groups. In the case of 0.5wdm solution there are 1.22 and 1.10 water molecules within the 4\AA radius of hydroxyl and amino groups, respectively. The corresponding values for the 2.0wdm solution are 1.74, 2.12, a significant drop in comparison with pure water solution (corresponding values are 2.77, 3.04, respectively). It is interesting to note that the DFP interacts mainly with the amino group already at the low level of DFP concentration, (0.5wdm).

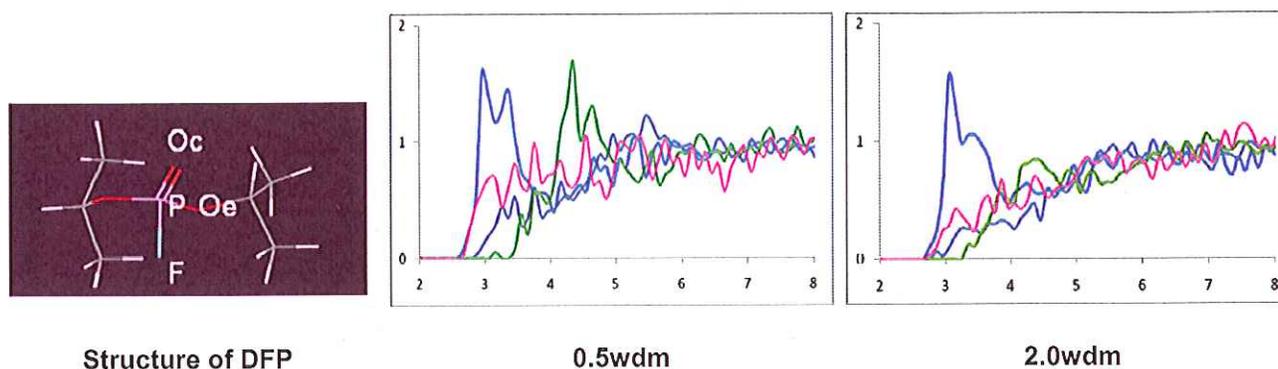


Fig. 5. Interaction of DFP atoms: Oc (blue), P (green), F (pink), Oe (cyan) with the N atom of polymer amine group for 2 solutions of polymer with water and DFP agent.

Figure 5 depicts $g(r)$ functions of amino and hydroxyl groups of the polymer with various atoms of DFP molecules. The $g(r)$ plot confirms that there is no correlation of DFP and hydroxyl groups of polymer. We do find correlation between amino group and phosphoryl oxygen of DFP (Oc) and, at low DFP concentration (0.5wdm), there is also evidence of a correlation between nitrogen and the phosphorous atom. These findings have implications in understanding the mechanism of hydrolysis of DFP by the polymer. We may assume that the preferable, initial configuration of polymer and DFP leads ultimately to a hydrolysis involving interaction of DFP phosphoryl oxygen atom with nitrogen atom of the polymer amine group.

The results of MD simulations are corroborated by the Quantum Mechanical study at the B3LYP and M05/6311++G** levels of DFT theory which found that amino groups interact more strongly with water molecules than hydroxyl groups do. The water molecules interact also more strongly with DFP molecules than either amine or hydroxyl groups. This fact was also noted in a strong water environment, modeled by a continuous electrostatic model of water (PCM in Gaussian program). *Based on these calculations, it appears that the increased water concentration around amino groups, as a result of stronger binding between amino groups and water, leads to an increased concentration of DFP close to amino groups. The mechanism of hydrolysis reaction of DFP might be either solely with amino groups in the copolymer, or concerted with water.* This is currently under investigation.

CONCLUSIONS

- Kinetic analysis of the hydrolysis of DFP by M12 and L12 shows that M12 reacts with DFP only at complete saturation ($A_w=1.0$); L12 has a slower reaction rate, but can react with DFP at lower A_w .
- Spin labeling the M12 membrane shows that below A_w of 0.94 the ESR spectra maintain a "rigid limit". Above A_w 0.94 there is evidence of water induced polymer chain mobility.
- M12 chain mobility may not be related to enhanced reactivity since M12 only hydrolyzes DFP at $A_w= 1.0$.
- Molecular dynamics simulations show higher concentrations of water and DFP molecules near amino groups than the hydroxyl groups of M12. This indicates that the concerted reaction of water and DFP involving amine group as a catalyst is responsible for a hydrolysis neutralization of DFP agent.

REFERENCES

1. Schreuder-Gibson, H., Gibson, P., et al., "Self-Detoxifying Materials for Chemically and Biologically Protective Clothing", Technical Report, NATICK/TR-08/008L, February 2008.
2. Schreuder-Gibson, H., Gibson, P., Yeomans, W., and Walker, J., Proceedings of the 2006 Scientific Conference on Chemical and Biological Defense Research, November 15 (2006).
3. Greenspan, L., 1977 Journal of Research of the National Bureau of Standards - A. Physics and Chemistry, 81A:89-96
4. Chen, L., Bromberg, L., Hatton, T.A., Rutledge, G.C., 2007 Polymer 48:4682
5. Budil, D. E., Lee, S., and Freed, J.H., 1996 J. Magn. Reson. Ser A, 120:155