Supplementary Information

Phosphonium Polyelectrolyte Complexes for the Encapsulation and Slow Release of Ionic Cargo

Tristan D. Harrison,† Olga Yunyaeva,† Aneta Borecki,† Cameron C. Hopkins,‡ John R. de Bruyn,‡ Paul J. Ragogna,*† and Elizabeth R. Gillies*†§

†Department of Chemistry and the Centre for Advanced Materials and Biomaterials Research
‡Department of Physics and Astronomy and the Centre for Advanced Materials and Biomaterials Research
§Department of Chemical and Biochemical Engineering, The University of Western Ontario,
1151 Richmond St., London, Ontario, Canada N6A 3K7

Table of Contents

1. NMR spectra .............................................................................................................S2-S5
2. Size exclusion chromatograms................................................................................S6
3. Debye plots.............................................................................................................S6
4. Thermal characterization data for polymers..........................................................S7-S8
5. Digital images of networks....................................................................................S9
6. Thermal characterization data for networks.........................................................S10
7. Calculations of network phosphorus content.......................................................S11-S12
8. SEM images...........................................................................................................S13-S14
9. Additional rheology data.......................................................................................S15
10. Self-healing in DI water.......................................................................................S16
11. Drug release model fitting....................................................................................S17
12. References.............................................................................................................S18
**Figure S1.** $^1$H NMR spectrum of P-Hp-P polymer (400 MHz, D$_2$O).

**Figure S2.** $^{31}$P$^{1}$H NMR spectrum P-Hp-P polymer (161.8 MHz, D$_2$O).
Figure S3. $^1$H NMR spectrum of P-Ph-P polymer (400 MHz, D$_2$O).

Figure S4. $^{31}$P{$^1$H} NMR spectrum P-Ph-P polymer (161.8 MHz, D$_2$O).
Figure S5. $^1$H NMR spectrum of P-Bu-P polymer (400 MHz, D$_2$O).

Figure S6. $^{31}$P$(^1$H) NMR spectrum P-Bu-P polymer (161.8 MHz, D$_2$O).
Figure S7. $^1$H NMR spectrum of P-Et-P polymer (400 MHz, D$_2$O).

Figure S8. $^{31}$P($^1$H) NMR spectrum P-Et-P polymer (161.8 MHz, D$_2$O).
Figure S9. Size exclusion chromatograms for A) P-Ph-P and B) P-Bu-P.

Figure S10. Light scattering Debye plot for A) P-Hp-P; B) P-Et-P.
Figure S11. Thermogravimetric analysis of A) P-Hp-P ($T_o = 290 \, ^\circ\text{C}$); B) P-Ph-P ($T_o = 325 \, ^\circ\text{C}$); C) P-Bu-P ($T_o = 344 \, ^\circ\text{C}$); D) P-Et-P ($T_o = 330 \, ^\circ\text{C}$). The two-step decomposition for P-Hp-P and P-Ph-P is hypothesized to be either Hoffman elimination or reverse Menschutkin (nucleophilic) degradation which can been seen in related ammonium systems.¹

Figure S12. Thermogravimetric analysis of HA ($T_o = 220 \, ^\circ\text{C}$).
Figure S13. Differential scanning calorimetry thermogram of A) P-Hp-P; B) P-Ph-P; C) P-Bu-P; D) P-Et-P.

Figure S14. Differential scanning calorimetry thermogram of HA.
Figure S15. PEC networks of polyphosphoniums mixed with either 30 - 50 kg/mol or 1000 - 2000 kg/mol HA. A) P-Et-P-(HA 30 - 50 kg/mol); B) P-Bu-P-(HA 30-50 kg/mol); C) P-Hp-P-(HA 30 - 50 kg/mol); D) P-Et-P-(HA 1000 – 2000 kg/mol); E) P-Bu-P-(HA 1000 - 2000 kg/mol); D) P-Hp-P-(HA 1000 - 2000 kg/mol).
Figure S16. Thermogravimetric analyses of lyophilized networks: A) P-Hp-P-HA; B) P-Ph-P-HA; C) P-Bu-P-HA; D) P-Et-P-HA.

Figure S17. Differential scanning calorimetry thermograms of A) P-Hp-P; B) P-Ph-P; C) P-Bu-P; D) P-Et-P.
Calculation of phosphorus content in the PEC networks from SEM-EDX.

Following a previously reported procedure, \(^2\) P-Hp-P-HA, P-Ph-P-HA, P-Bu-P-HA and P-Et-P-HA networks were washed with water for 24 h to remove salts, and dried overnight at 25 °C in a vacuum oven. The dry PEC networks were mounted on carbon tabs and coated with 5 nm of osmium. SEM-EDX analysis was used to measure the carbon and phosphorus atomic %, in triplicate.

Knowing that each phosphonium monomer contains \(x\) C (with \(x\) depending on the specific polymer) and 1 P atom, while the carboxylate monomer contains 14 C atoms, the measured atomic % of P relative to that of C could be converted to a carboxylate:phosphonium ratio. For example, the expected atomic P % relative to C for different ratios is summarized in the following table for complex P-Et-P-HA:

<table>
<thead>
<tr>
<th>Stoichiometry of carboxylate: phosphonium monomers</th>
<th>Total C &amp; P atoms in the given ratio</th>
<th>Atomic % of P relative to P and C</th>
</tr>
</thead>
<tbody>
<tr>
<td>1:3</td>
<td>62</td>
<td>4.84</td>
</tr>
<tr>
<td>1:2</td>
<td>46</td>
<td>4.35</td>
</tr>
<tr>
<td>1:1</td>
<td>30</td>
<td>3.33</td>
</tr>
<tr>
<td>2:1</td>
<td>44</td>
<td>2.27</td>
</tr>
<tr>
<td>3:1</td>
<td>58</td>
<td>1.72</td>
</tr>
<tr>
<td>4:1</td>
<td>72</td>
<td>1.39</td>
</tr>
</tbody>
</table>

Example calculation for P-Et-P-HA:

\[
2.8 \text{ atomic } % \text{ P relative to P and } C = \left( \frac{1 \text{ P atom}}{x \text{ total C and P atoms}} \right) 100\%\
\]
\[ x = \frac{100}{2.8} = 35.7 \text{ total C and P atoms in the ratio of monomers} \]

For one P atom in the ion pair, we have 16 total atoms attributable to the phosphonium monomer (1 P and 15 C atoms).

\[ 35.7 - 16 = 19.7 \text{ carbon atoms attributable to the carboxylate monomer} \]

\[ \frac{19.7 \text{ atoms}}{14 \text{ carbon atoms per carboxylate monomer}} = 1.4 \]

Therefore the ratio of carboxylate:phosphonium ions in \textbf{P-Et-P-HA} is 1.4:1. The same procedure was used to calculate the ionic ratios for the other networks.
Figure S18. SEM images of PECs: A) P-Hp-P-HA; B) P-Ph-P-HA; C) P-Bu-P-HA D) P-Et-P-HA. Samples were prepared by the lyophilization of gels that were swelled in DI water for 24 h, followed by coating with 5 nm of osmium.
Figure S19. SEM images of PECs A) P-Hp-P-HA; B) P-Ph-P-HA; C) P-Bu-P-HA D) P-Et-P-HA. Samples were prepared by the lyophilization of gels that were swelled in PBS for 24 h then soaked in DI water for 1 min to remove surface salts, followed by coating with 5 nm of osmium.
Figure S20. $G'$ and $G''$ for P-Bu-P-HA, measured using small amplitude oscillatory shear at different shear stress amplitudes at a constant angular frequency of 1 rad/s.
Figure S21. Digital images of PECs damaged by a 0.5 mm diameter hole self-healing over 18 h in DI Water at 37 °C. A) P-Hp-P-HA; B) P-Ph-P-HA; C) P-Bu-P-HA & D) P-Et-P-HA.

<table>
<thead>
<tr>
<th>Time (h)</th>
<th>P-Hp-P-HA</th>
<th>P-Ph-P-HA</th>
<th>P-Bu-P-HA</th>
<th>P-Et-P-HA</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td><img src="image1.png" alt="Image" /></td>
<td><img src="image2.png" alt="Image" /></td>
<td><img src="image3.png" alt="Image" /></td>
<td><img src="image4.png" alt="Image" /></td>
</tr>
<tr>
<td>2</td>
<td><img src="image1.png" alt="Image" /></td>
<td><img src="image2.png" alt="Image" /></td>
<td><img src="image3.png" alt="Image" /></td>
<td><img src="image4.png" alt="Image" /></td>
</tr>
<tr>
<td>4</td>
<td><img src="image1.png" alt="Image" /></td>
<td><img src="image2.png" alt="Image" /></td>
<td><img src="image3.png" alt="Image" /></td>
<td><img src="image4.png" alt="Image" /></td>
</tr>
<tr>
<td>18</td>
<td><img src="image1.png" alt="Image" /></td>
<td><img src="image2.png" alt="Image" /></td>
<td><img src="image3.png" alt="Image" /></td>
<td><img src="image4.png" alt="Image" /></td>
</tr>
</tbody>
</table>
Figure S22. Fitting to the linearized version of the Korsmeyer-Peppas equation: $\ln\left(\frac{M_t}{M_\infty}\right)$ versus $\ln(t)$ up to $M_t/M_\infty = 0.6$ for the release of A) fluorescein and B) diclofenac from the PEC networks in PBS at 37 °C. The slopes of the graphs (indicated from the equations $y = mx + b$ provided above) correspond to the diffusional exponent $n$. Note that the release of ATP was not fitted due to its rapid release and consequent absence of sufficient data points for $M_t/M_\infty < 0.6$. 
References
