Biodegradable thiol-modified poly(vinyl alcohol) hydrogels

Yuri Svirkin, Adam Kozak, Gavin Braithwaite

MRS 2013

Cambridge Polymer Group,
56 Roland Street, Suite 310
Boston, MA 02129
www.campoly.com
Introduction

• PVA biocompatible
• Well respected biomaterial

• Not readily injectable and in situ crosslinkable
• Not intrinsically biodegradable
• Not sufficiently mucoadhesive

• This presentation will talk about
  – New method of making an injectable PVA hydrogel that is mucoadhesive and degradable
Synthesis of Thiolated Poly(vinyl alcohol)

- Conversion of some OH groups to thiol groups adds thiol pendant groups directly to the PVA backbone.
Synthesis of TPVA/PEGDA Hydrogels

- TPVA crosslinking with difunctional poly (ethylene glycol) thiol-reactive molecules forms a hydrogel via Michael-Type addition reaction
  - Thiol groups control crosslink density
  - PEGDA chain length control molecular weight between crosslinks

\[
\text{TPVA} \quad + \quad \text{PEGDA} \quad \xrightarrow{\text{pH 7.4 1xPBS}} \quad \text{Hydrogel}
\]
1H NMR of TPVA

- 1H NMR of converted product indicate presence of mercaptopropionic ester fragment
  - Degree of modification ~3%
Molecular Weight Distribution of PVA and TPVA

• Gel Permeation Chromatography indicates a small fraction of higher molecular weight species
Gelation kinetics of TPVA/PEGDA (concentration)

- Rheology provides a sensitive tool for tracking gelation kinetics as a function of concentration

Effect of concentration at 25 °C:
- green (3%);
- red (4.5%)
Gelation kinetics of TPVA/PEGDA (temperature)

- Temperature also controls gelation kinetics

Effect of temperature at 3.0%
green (25 °C); red (37 °C)
Kinetics and Properties of TPVA/PEGDA Hydrogels

<table>
<thead>
<tr>
<th>Polymer concentration, % [w/v]</th>
<th>Temperature, °C</th>
<th>25 °C</th>
<th>37 °C</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.0</td>
<td>23.3</td>
<td>803</td>
<td>5</td>
</tr>
<tr>
<td>4.5</td>
<td>9.2</td>
<td>6440</td>
<td>133</td>
</tr>
</tbody>
</table>

Gelation point

MRS 2013
Swelling kinetics of TPVA hydrogels

- Tracking unconfined swelling of the hydrogels in 1xPBS suggests no steady state is achieved

Swelling of 4.5 % w/v TPVA/PEGDA hydrogel in 1xPBS as a function of degradation time. Swelling percent=\((W-W_0)/W_0\);
Degradation of TPVA Hydrogel

- The use of the mercaptopropionic and acrylate results in hydrolysable ester bonds within the crosslinks.
**TPVA Degradation Products by GPC Analysis**

- Cleaving of ester bonds yields species with TPVA and PEGDA molecular weights

![Graph showing TPVA and PEGDA degradation products](image)
TPVA Mucoadhesive Properties

- Thiol groups known to be mucoadhesive
- Mixing of TPVA with mucin and tracking rheology response proves molecular interactions
  - Complex viscosity of TPVA (red), mucin (blue) and TPVA combined with mucin (red) measured at 25 °C.
Features and applications of TPVA/PEGDA Hydrogels

• TPVA/PEGDA hydrogels formed through Michael-Type addition reaction
  – physiological conditions from low viscosity TPVA and PEGDA
  – well suited for in situ applications
• Hydrolysable ester bonds in crosslinks
  – inherited biodegradability
  – degradation results in formation PVA and PEGDA
  – products are biocompatible and low molecular weight to allow for easy elimination by passing through kidneys
• Unreacted thiol groups,
  – not used in crosslinking reactions result in mucoadhesive properties
• Potential applications
  – percutaneous, temporary tissue bulking and scaffolding