USE OF OLIGOMERIC END-GROUPS TO MODIFY SURFACE PROPERTIES OF BIOMEDICAL POLYMERS

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We have previously reported the use of surface-active multipolymers as surface-modifying additives (SMA) in biomedical polymers for improved thrombore sistence of blood pumps, vascular grafts and catheters. Small concentrations (≤ 5% wt/wt) of SMA used in admixture with base polymers modify the base polymer's surface properties without significant modification of base polymer bulk properties. Low bulk concentrations of SMA can produce essentially complete monolayer coverage on formed articles. Following fabrication of device components the surface 'develops' spontaneously by the surface-energy-reducing migration and orientation of SMA in the air-facing surface. Properly-designed amphipathic SMAs are also able to reorient to minimize interfacial energy in response to a change in environment, e.g. following blood contact. This is thought to reduce thrombogenicity, possibly by minimizing protein denaturation or otherwise affecting protein adsorption.

Although SMA-modified base polymers are presently in clinical use in successful devices, the approach has some shortcomings. The rate of approach to equilibrium surface composition can be very slow at temperatures at which the polymer's continuous phase is glassy or crystalline. This requires elevated temperature and/or long storage times to completely affect the surface modification. In material applications involving abrasion or erosion of the surface it is not clear how the surface layer can be replenished by the bulk SMA 'reservoir', particularly if the use temperature is below Tg or Tm of the polymer's continuous phase.

In order to overcome some of the limitations of SMAs we have developed a series of biomedical base polymers which have SMA-like properties "built in" and which do not rely on the use of additives to achieve the desired surface chemistry. We have accomplished this through the use of surface-active (oligomeric) end groups having a range of chemical structures and/or optional functional groups. By restricting the surface-modifying moieties to the termini of essentially linear base polymers, changes to the base polymer's bulk properties are minimized. The added mobility of end groups relative to backbone groups is thought to facilitate the formation of uniform overlayers by the surface-active (end) blocks. The fact that essentially all polymer chains carry the surface-modifying moiety eliminates many of the potential problems associated with additives.

Several investigators have proposed the modification of fully-reacted base polymers (e.g. polyurethanes) via the grafting of side chain structures, e.g. optionally sulfonated alkyl groups. In this approach urethane or urea groups in the hard segments are used as reactive sites for grafting. In general, the use of the hard segment groups for grafting weakens the base polymer by discouraging hard-segment/hard-segment interactions. In polyurethanes we couple end-groups to the backbone polymer during synthesis via a terminal isocyanate group, not via a hard segment. The use of the oligomeric end-groups, therefore, leaves the original polymer backbone intact so the polymer retains strength and processability.

Surface modification via oligomeric end-groups (SME) is easily adapted to the synthesis of polymers which normally incorporate a low molecular weight monofunctional end-group for molecular weight control. The use of dodecyl amine in place of diethyl amine in the synthesis of segmented polyurethanes is one example. Using this approach we have made polymers with tensile strengths exceeding 5000 psi which contain ~ 0.5 wt. % dodecyl groups. With higher molecular weight end-groups, total end-group concentration can be much higher. Using monofunctional 2000-MW polydimethylsiloxane-amine (PSX) we have prepared high-strength elastomers with nominal 6% (wt/wt) siloxane content. Using monofunctional polyethyleneoxide-amines or alcohols we have incorporated up to 16% ethyleneoxide into otherwise hydropobic polymers, with good strength retention.

In addition to the use of a single end-group chemistry, the SME approach allows mixed end-groups to be present in a single polymer. Use of hydropobic and hydrophilic end-groups gives amphipathic structures in which the hydropobic/hydrophilic balance may be easily varied. Suitable oligomeric reagents are readily available, and the synthesis procedure is quite straightforward. These considerations suggest that the use of surface modifying end groups will prove to be a useful method for the development and manufacture of a wide range of new biomaterials.

<table>
<thead>
<tr>
<th>Soft Segment</th>
<th>End Group</th>
<th>Tensile Strength (psi)</th>
<th>Ul. Elong. (%)</th>
<th>Init. Mod. (psi)</th>
<th>Surface Chem.</th>
</tr>
</thead>
<tbody>
<tr>
<td>PTMO</td>
<td>Dodecyl</td>
<td>6529 ± 391</td>
<td>926 ± 62</td>
<td>628 ± 118</td>
<td>hydrocarbon</td>
</tr>
<tr>
<td>PSX</td>
<td>5397 ± 287</td>
<td>926 ± 8</td>
<td>610 ± 24</td>
<td>652 ± 72</td>
<td>PSX</td>
</tr>
<tr>
<td>Carbonate</td>
<td>PSX</td>
<td>6055 ± 442</td>
<td>628 ± 16</td>
<td>652 ± 72</td>
<td>PSX</td>
</tr>
<tr>
<td>Mixed</td>
<td>PSX + PEO</td>
<td>4200 ± 1200</td>
<td>1200 ± 1500</td>
<td>1500 ± 5000</td>
<td>amphi/matic</td>
</tr>
</tbody>
</table>

Typical Properties of End-Group Modified Polyurethanes

REFERENCES
4. Graszi, T.G. & Cooper, S.L. U.S. Patent 5,017,664
5. Munro, M.S., et. al U.S. Patent 4,530,974

The 21st Annual Meeting of the SOCIETY FOR BIOMATERIALS
April 5-9, 1994, Boston, MA, USA