Thermoplastic Silicone-Polyurethane Copolymers for Medical Devices and Prosthetic Implants

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Outline
I. Vertical Integration of Biomaterials & Device Development
II. Introduction to Polyurethanes and Silicone-urethanes
III. History of Silicone-Urethanes as Biomaterials
IV. Silicone-Urethane Synergy in Biomedical Applications
   • Thromboresistance
   • Biostability
V. Production of Silicone-Urethane Copolymers
VI. Device Fabrication Methods

Polymer Development Process

Potential Advantages of Silicone-urethane Copolymers

Chemistry of Conventional Polyurethanes and Silicone-Polyurethane Copolymers

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**Urethane and Urea Formation**

\[ R - NCO + HO - R' \xrightarrow{} R - N - C - O - R' \text{ urethane} \]

\[ R - NCO + NH_2 - R' \xrightarrow{} R - N - C - N - R' \text{ urea} \]

\( R' = \) polyester, polycarbonate and/or polydimethylsiloxane (PSX)

**Chain Extenders & Soft Segment Used in Many Biomedical Polyether Urethanes:**

Polyether, Biomax, BioSpan®, SPU, Tecoflex, etc.

Urethane: Butane Diol  \( HO\cdot CH_2\cdot CH_2\cdot CH_2\cdot OH \)

Urea: Ethylene Diamine  \( H_2N\cdot CH_2\cdot CH_2\cdot NH_2 \)

\( H_2[O(CH_2\cdot CH_2\cdot CH_2)],OH \)  \( MW = 200 \text{ to } 2000 \)

Polytetramethylene oxide (PTMO)

a.k.a. polytetramethylene ether glycol (PTMG)

**Diisocyanates Commonly Used in Biomedical Polyurethanes**

- Methylene bis(p-phenyl isocyanate)
- Diphenylmethane diisocyanate
- Methylene bis(cyclohexyl isocyanate)
- Hydrogenated MDI \( H_2MDI \)

**Hydrogen Bonding Among Adjacent Hard Segments in TPU:**

Thermally-Reversible “Crosslinks”

- Blackwell & Gardner, Polymer, 2012, 1979

**Polydimethylsiloxane End Group:**

\( MW = 2000 \text{ daltons} \)

\( 6\AA \)

\( \approx 75 \text{ Å} \)

Area Per Molecule \( \approx 675 \quad \text{Å}^2 \)

Area Per Mole \( \approx 4 \times 10^{10} \text{ cm}^2 \)

**Segmented Polyurethane with Silicone Surface Modifying End Groups (SME)**

- R.S. Ward © 2001, The Polymer Technology Group, Berkeley, CA
Hydroxyalkyl-Terminated PSX Fluid:
Reacts with -NCO to form silicone-urethane with hydrolytically-stable Si-C bonds

Continuous Synthesis of Reactive Silicone Oligomers

Incomplete History of Silicone-Urethane Biomaterials

Some Clinical Devices and Prostheses Made from Silicone-Urethanes
- Intraaortic Balloons
- VADs
- Vascular Grafts
- Vasc. Access
- A-C Bypass
- Pacemaker Leads
- Orthopedic Implants
- Urological Implants

Examples of Silicone-Urethanes in Biomedical Applications: 1970 to present

CarboSil® TPU: Thermoplastic Silicone-polyether-urethane w. SME
PurSil® TPU: Thermoplastic Silicone-polyether-urethane w. SME
BioFlex® S SPU: Solvent-Cast w. PSX Surface Modifying End Groups™ (SME)
RiboForm® Cast on Silicone: Solvent-cast SPU w. PSX from substrate
Thoraco®: Solvent-Cast SPU w. PSX®PU Surface Modifying Additive (SMA)
Biemer & Re-dissolved Lucor® Spandex: Solvent-cast SPU w. PSX "contaminant"
Avcothane-811 / Cardiothane™-81: Solvent-Cast PSX-urethane hybrid (ca. 1970)

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Avcothane-51 / Cardiothane 51:
The First Silicone-Urethane Biomaterial ca. 1970
"...stability of polyether urethane is enhanced by the silicone."
- A blend of silicone and polyurethane
- Silicone molecular weight determines morphology
- Opaque to visible light
- Fabricated from a moisture-sensitive solution

Ventricular Assist Devices:
- BioSpan or Biomer Cast on Silica-free Silicone
- Thoralon™ (Polyurethane with Silicone SMA)

Thoratec Vascular Grafts:
- Thoralon™ (SPU w. Silicone SMA)
Clinical Uses: Vascular Access & CABG

Manufacture of Thermoplastic Silicone-Polyurethanes:
Batch and Continuous Processes

Typical Batch Synthesis of Thermoplastic (Silicone)Polyurethanes
Continuous Polymerization Process for Thermoplastics Polyurethanes

PTG Continuous Synthesis of Thermoplastic Polyurethanes

**PurSil™ Thermoplastic Silicone-Polyether Urethanes (TSPU)**

- **PurSil™ TSPU**
  - "Aromatic TSPU"
  - Aromatic Hard Segment:
  - PTMO Soft Segment
  - Silicone Co-Soft Segment
  - Silicone End Groups*

- **PurSil™-AI TSPU**
  - "Aliphatic PurSil TSPU"
  - Aliphatic Hard Segment:
  - PTMO Soft Segment
  - Silicone Co-Soft Segment
  - Silicone End Groups*

* Can be varied

**CarboSil™ Thermoplastic Silicone-Polycarbonate Urethanes**

- **CarboSil™ TSPU**
  - "BioniSil-Silicone Copolymer"
  - Aromatic Hard Segment:
  - 'Carbonate' Soft Segment
  - Silicone Co-Soft Segment
  - Silicone End Groups*

- **CarboSil™-AI TSPU**
  - "Aliphatic CarboSil TSPU"
  - Aliphatic Hard Segment:
  - 'Carbonate' Soft Segment
  - Silicone Co-Soft Segment
  - Silicone End Groups*

* Can be varied

Thromboresistance of Silicone-Polyurethanes

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Reduced In Vivo Platelet Adsorption via Silicone Modification of Polyurethane

IABs at Explant: 7 Days In Cows

Without Silicone SMA
With Silicone SMA

VAD Bladders: 30-day Calf Explant

SPU with Silicone SMA
SPU without Silicone SMA

Biostability of Silicone-Polyurethanes

Factors Affecting the In Vivo Degradation of Polyurethanes

- Hard Segment: Chemistry and Content
- Soft Segment Chemistry and SMEs
- Initial Molecular Weight and Purity
- Device Manufacturing Process: Residual Stresses and Thermal History
- Device Design and Function
- Sterilization Method
- Implant Site: Blood, Muscle, Soft Tissue, etc.
- Adjacent Materials: e.g., Cobalt Alloys

Cardiothane-51 IAB After 327 Day Implant *(1981)*


R.S. Ward © 2001, The Polymer Technology Group, Berkeley, CA
ATR Infrared Analysis of Cardiolthane-51 IAB* Explanted @ 327 days

Change in GPC Chromatogram Due to In Vitro Degradation

Intra-muscular Explants:
12 month unstressed (200X SEM)

Accelerated In Vivo Biostability Testing:
Segmented Silicone-Urethane Copolymer:
18 month Rabbit Implants @ 150% Strain (1000X)

Accelerated In Vitro Biostability Testing of a Thermoplastic Silicone-Urethane Copolymer:
12 Week Exposure in 'Solution A' (MIO Solution)

'Stores Test' Results:
ESC Resistance of PurSil™ 10-60A TSPU (500X SEM)

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Optimization of Silicone Content of Copolymers for Specific Applications

Maximizing Biostability of Soft Polyurethanes
0. Increase Hard Segment Content to Phase Inversion Pt.
1. Add Backbone Silicone + SME
2. Add Silicone SME
3. Reduce Residual Stresses in Parts
4. Increase / Maintain Polymer MW Before Implant
5. Increase Alkyl Chain Length Between Ether Oxygens
6. Increase (Conventional) Stabilizer Content
* CAUTION: Ranking based on author's opinion and limited data

Structure and Properties of New Thermoplastic Silicone-Polyurethanes: CarboSil™ and PurSil™ TSPUs

GPC Molecular Weight of PurSil® 80A Thermoplastic Silicone-Polyurethane Copolymers After One Extrusion*

<table>
<thead>
<tr>
<th>Silicone Content [wt%]</th>
<th>Mw</th>
<th>Mn</th>
<th>Mw/Mn</th>
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<tr>
<td>10</td>
<td>108000</td>
<td>182100</td>
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<td>20</td>
<td>115000</td>
<td>186000</td>
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<tr>
<td>37</td>
<td>92700</td>
<td>145300</td>
<td>1.6</td>
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* Polymethylsiloxane Mixed Soft Segment and PSX Surface Modifying End Groups

Tensile Strength of PurSil® 80A Aromatic Thermoplastic Silicone-Polyurethane Copolymers: Solvent-Cast Films

<table>
<thead>
<tr>
<th>Silicone Content [wt%]</th>
<th>Tensile Strength [psi]</th>
<th>Ultimate Elongation [%]</th>
<th>Initial Modulus [psi]</th>
<th>Optical Clarity</th>
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<tbody>
<tr>
<td>10</td>
<td>6200</td>
<td>720</td>
<td>3200</td>
<td>Water-clear</td>
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<tr>
<td>20</td>
<td>5900</td>
<td>690</td>
<td>2750</td>
<td>Water-clear</td>
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<tr>
<td>37</td>
<td>4810</td>
<td>600</td>
<td>4300</td>
<td>Water-clear</td>
</tr>
</tbody>
</table>

* Polymethylsiloxane Mixed Soft Segments + PSX Surface Modifying End Groups

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Tensile Properties* and MW of 80A Thermoplastic Silicone-Polyurethanes: Aromatic Polymer

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<tbody>
<tr>
<td>Aromatic</td>
<td>MDI-BO</td>
<td>PTMO</td>
<td>0</td>
<td>2150</td>
<td>615</td>
<td>2150</td>
<td>994600</td>
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<tr>
<td>PurSil™ 88 PPU</td>
<td>MDI-BO</td>
<td>PTMO</td>
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<td>6515</td>
<td>265</td>
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<td>133130</td>
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<tr>
<td>PurSil™ 88 PPU</td>
<td>MDI-BO</td>
<td>PTMO</td>
<td>15</td>
<td>6170</td>
<td>585</td>
<td>5170</td>
<td>119578</td>
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<tr>
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<td>10</td>
<td>6170</td>
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<td>119578</td>
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* Lab-Synthesized

Stress-Strain Curves of PurSil™ Silicone-Polyether-urethane Copolymers: Compression-Molded Plaques

Tensile Strength vs. Silicone Content: CarboSil™ and PurSil™ Aromatic TSPUs

Possible Optimization of Silicone Content for Specific Applications

Processing and Fabrication Methods for (Silicone-Urethane) Thermoplastics

Processing of Thermoplastic Silicone-Polyetherurethanes:
All methods suitable for soluble thermoplastics
- Extrusion
- Injection Molding
- Heat Sealing
- RF Welding
- Solution Casting
- Dipping
- Solvent Bonding
- Other
Conclusion

- Strong, optically-clear, thermoplastic silicone-urethane copolymers have been developed.
- Hardness, silicone content and surface chemistry can be varied (over a wide range) to optimize polymers for specific applications.
- Ongoing accelerated biostability testing of soft polymers shows significant improvements over silicone-free polycarbonates and polyether urethanes; (Additional improvements are possible with SME™ technology)
- Thermoplastic processing and solvent solubility increase the range of device fabrication methods.