POLYMER THERAPEUTICS: POLYMERS FROM BIOACTIVES AND AS BIOACTIVES

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AIMDN: Nanomedicine
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Polymers from Bioactives

Polymers as Bioactives
PolymerDrugs

PolyAspirin

\[\text{H}_2\text{O}\]

salicylic acid

sebacic acid

Versatility of Formulations

- Disks
- Microspheres
- Coatings
- Electrospun mats
- Hydrogels
- Adhesives
Periodontal treatments
- **Controlling bone growth**
- Wound care
- Medical device coatings
- Cardiac stents
- Dermatology indications
- Personal care & cosmetic products
- Biofilm prevention/mitigation
- Steroid-sparing joint pain-injectables
- Controlled release of opiates
- Nerve guide conduits
- Urinary catheters
Formulation and sample preparation

SA-adipic Polymer

Bone allograft + Polymer + Mineral Oil (light)

Wada, K; Yu, W; Elazizi, M; Barakat, S; Ouimet, MA; Rosario-Meléndez, R; Fiorellini, JP; Graves, DT; Uhrich, KE, *J Control Rel*, **171** (1) 33-37 (2013)
Representative micro-CT images of mineralized bone formation in defect region

SA-PAE/bone graft

Bone graft alone

Diabetic

Normoglycemic

4 weeks

12 weeks

Wada, K; Yu, W; Elazizi, M; Barakat, S; Ouimet, MA; Rosario-Meléndez, R; Fiorellini, JP; Graves, DT; Uhrich, KE, *J Control Rel*, **171** (1) 33-37 (2013)
Encapsulation and dual delivery: salicylic acid and insulin

Insulin suspended in PBS

SAPAE dissolved in DCM

Homogenize insulin/PBS and SAPAE/DCM

Add drop-wise to PVA solution while homogenizing

Stir to evaporate DCM

Wash to remove PVA

Lyophilize to remove water

1% PVA solution

poly(vinyl alcohol): PVA

Microfluidic-based insulin encapsulation in SA-based polymer microspheres

1% PVA

SA-based polymer in DCM

Insulin solution

SA-based polymer in DCM

1% PVA

Insulin-encapsulating SA-based polymer droplet

polymer droplet

Insulin droplets

With J Zahn
Advantages of microfluidic-based microsphere formation

- Size uniformity

- Easily tuned microsphere size

- Smaller batch-to-batch variation
- Better controlled loading

flow rate ratios between PVA and polymer solution at (left) 5 and (right) 20

Scale bar = 100 µm

With J Zahn
Polymers from Bioactives

Polymers as Bioactives
• **Amphiphilic macromolecules (AMs):**
  – Based on sugar backbone, hydrophobic arms, and a hydrophilic polymer tail

• **Original design criteria:**
  – Self-assemble to solubilize hydrophobic APIs
  – Hydrolytically degradable
  – Range of physicochemical properties

**Tunable Structures**
- Branch number (2 to 4)
- Branch length (6 to 16)
- PEG length (2K or 5K)

**1cM**
- CMC ~ 1.3x10⁻⁷ M (or 8x10⁻⁷ g/ml)
- Micellar size ~ 15-20 nm
Monocyte
Macrophage
Foam Cell Formation
Foam Cells Explode = Plaque Formation
LDL
oxLDL
Free radicals
Inflammatory Cytokine Secretion
Iverson, N; Sparks, S; Demirdirek, B; Uhrich, KE; Moghe, PV *Acta Biomater*, 6 (8) 3081-3090 (2010)
AMPHIPHILIC MACROMOLECULES

Iverson, N; Sparks, S; Demirdirek, B; Uhrich, KE; Moghe, PV Acta Biomater, 6 (8) 3081-3090 (2010)
Modification of Hydrophobic Chains: Esters versus Ethers

Faig, A; Petersen, LK; Moghe, PV; Uhrich, KE. *Biomacromolecules*, in press (2014)
Role of Branching of Hydrophilic Domains

Abdelhamid, D; Arslan, H; Yingyue, Z; Uhrich, KE Polym Chem, 5 (4), 1457-1462 (2014)
Role of Branching of Hydrophilic Domains

<table>
<thead>
<tr>
<th>AM</th>
<th>Thermal Properties (°C)</th>
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<tbody>
<tr>
<td></td>
<td>$T_g$</td>
</tr>
<tr>
<td>M12(P25)</td>
<td>-52</td>
</tr>
<tr>
<td>T12(P25)</td>
<td>-50</td>
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<tr>
<td>M12(P10)</td>
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<td>M12P5</td>
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<td>T12P5</td>
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Abdelhamid, D; Arslan, H; Yingyue, Z; Uhrich, KE Polym Chem, 5 (4), 1457-1462 (2014)
Stereochemistry

Hydrophobicity

Backbone architecture

Rigidity

Heteroatom

Hehir, S; Plourde, NM; Gu, L; Poree, DE; Welsh, W; Moghe, PV; Uhrich, KE, Acta Biomat, 8, 3956-3962 (2012). Poree, DE; Zablocki, K; Faig, A; Moghe, PV; Uhrich, KE, Biomacromolecules, 14, 2463-2469 (2013)
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- Prof. Pat O’ Connor (UMDNJ, Orthopedics)
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