NIPAAm Co-DEAEMA Hydrogels Prolong Ketorolac Drug Release

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Introduction
Post-Surgical Pain Management
- 70-80% of approximately 50 million US post-surgical patients each year report moderate to extreme pain
- Poor pain management can lead to:
  - Higher rates of morbidity
  - Chronic postoperative pain
  - Impaired recovery
  - Prolonged opioid use/risk
  - Higher healthcare costs
- Rationale for ketorolac tromethamine
  - Fewer side effects than opioids
  - Equally as effective in relieving pain as opioids
- Sustained, local delivery of ketorolac via PNDJ hydrogels
  - Minimizes dosage
  - Reduces potential side effects

Research Purpose
Deliver sustained release of ketorolac using poly(NIPAAm-co-DBLAAm-co-JAAm) (PNDJ) gel formulation and to reduce the healthcare burden caused by adverse effects of opioid treatments

Methods and Materials
- 4 release studies over 7-14 days w/varing JAAm, DEAEMA content
- All release studies conducted at pH 7.4, 37°C
- 3 samples, 400 mg each per gel formulation
- Ketorolac released from gel was measured in phosphate buffer

<table>
<thead>
<tr>
<th>Study 1</th>
<th>Study 2</th>
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<tbody>
<tr>
<td>PNDJ 1.1 mol % JAAm</td>
<td>PNDJ 1.4 mol % JAAm</td>
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<tr>
<td>PNDJ 1.3 mol % JAAm</td>
<td>PNDJ 1.5 mol % JAAm</td>
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<tr>
<td>PNDJ 1.4 mol % JAAm</td>
<td>PNDJ 2.2 mol % JAAm</td>
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<th>Study 3</th>
<th>Study 4</th>
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<tr>
<td>1-3% Tobramycin incorporated into: PNDJ 1.4 mol% JAAm</td>
<td>NIPAAm, co-BMA, DEAEMA</td>
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Results
24-72 Hours Average Ketorolac Release

Discussion
- Study 1
  - 50-60% burst release within 1-6 hrs
  - Did not reach 100% burst release?
- Study 2
  - Extremely high burst release
  - Ketorolac release for more than 5 days is difficult in PNDJ hydrogels
- Study 3
  - Tobramycin decreased ketorolac release by a small amount
  - Release sustained only 7 days
- Study 4
  - NIPAAm co-DEAEMA gels prolonged release for 2+ weeks
  - LCST = 7 °C → needs to be 25-35 °C

Conclusion
- Initial ketorolac burst release is very high with PNDJ gels
- Incorporating tobramycin slows down ketorolac release (a little bit)
- NIPAAm co-DEAEMA hydrogels prolongs ketorolac release

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