EXPLORING ORAL INSULIN DELIVERY VIA MICROENCAPSULATION

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What is Insulin?
What does it do?
Research Methods
Results
Future Research
INSULIN

- Naturally-secreted peptide hormone
- Insulin hexamers are the storage form in the system
- Used for the treatment of diabetes mellitus types 1 and 2
MODES OF ADMINISTRATION

Current
- Insulin Pen
- Continuous subcutaneous insulin infusion
- Vial and Syringe

Future
- Inhalation
- Nasal
- Oral
MATERIALS

- Use natural biomacromolecules as materials to make the nanoparticles

- Biomacromolecules are advantageous because they have higher biocompatibility as well as biodegradability
METHOD I

- Dissolving Ins into HCL and adjusting pH to 8.
- Mix Ins into CaCl2 and Alginate (pH 5.1) in different ratios utilizing the sonicator.
- Mix previous solution into Chitosan solution (pH ~5.6) and sonicate.

Adapted from Chen et al. 2018
ENCAPSULATION EFFICIENCY METHOD 1

Beer's Law
Absorbance = εLc

- Extinction coefficient
- Concentration
- Pathlength
Method 2 SANS Measurements
3111_Algnate: Colloidal Aggregates
3111_Algnate_Chitosan: Polymer Networks

SANS Analysis
- Insulin is in the hexameric form
- Insulin, alginate and calcium form colloidal particles which further form branched aggregates
- Addition of chitosan leads to the formation of polymeric networks
Gastrointestinal Tract

Targeted Delivery System:
- No release (protected state) of insulin in acidic stomach environment
- Release of insulin in small intestine

Method 1 release results

![Graph showing cumulative release of insulin over time for different conditions.](image)
METHOD 2

Adapted from Zhu et al 2019
**PARAMETER OPTIMIZATION (METHOD 2)**

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<thead>
<tr>
<th>Sample Content (all incl. Ins)</th>
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- Increased turbidity/Decreased Transmittance = Increased nanoparticle formation
- Zein, Zn and a polysaccharide are important factors to increased nanoparticle formation/stabilization
- Determination that 2/10mg Pectin and .25/.75mg Alginate are best test samples
A lack of Zinc leads to the defragmentation of Insulin

Less intense bands indicating higher encapsulation efficiency rates

Multiple bands indicating defragmentation

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<tr>
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<td>Encapsulation efficiency (%)</td>
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<td>89.45</td>
<td>81.20</td>
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<td>10.49</td>
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<td>94.78</td>
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<tr>
<td>Sample</td>
<td>Insulin+Zn into Buffer as Control</td>
<td>Insulin+Zn into 2 mg/ml Pectin</td>
<td>Insulin+Zn into 10 mg/ml Pectin</td>
<td>Insulin+Zn into 0.25 mg/ml Alginate</td>
<td>Insulin+Zn into 0.75 mg/ml Alginate</td>
<td>Insulin+Zn+Zein into 2 mg/ml Pectin</td>
<td>Insulin+Zn+Zein into 10 mg/ml Pectin</td>
<td>Insulin+Zn+Zein into 0.25 mg/ml Alginate</td>
<td>Insulin+Zn+Zein into 0.75 mg/ml Alginate</td>
<td>Insulin+Zn+Zein into Buffer</td>
<td>Defragmentation of Insulin antisolvent into Buffer</td>
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</tbody>
</table>

More intense bands indicating a low insulin encapsulation rate

Less intense bands indicating higher encapsulation efficiency rates

Multiple bands indicating defragmentation
ENCAPSULATION EFFICIENCY
Method 2 SANS Results
Model: Guinier Porod

<table>
<thead>
<tr>
<th>Coating Polysaccharide</th>
<th>Insulin:Zn 1:3</th>
<th>Insulin:Zn 1:9</th>
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</thead>
<tbody>
<tr>
<td>2 mg/mL Pectin</td>
<td>178.8</td>
<td>126.3</td>
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<td>10 mg/mL Pectin</td>
<td>130.9</td>
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<tr>
<td>0.25 Alginate</td>
<td>209.3</td>
<td>207.8</td>
</tr>
<tr>
<td>0.75 Alginate</td>
<td>174.5</td>
<td>161.7</td>
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</table>

SANS Analysis
- Particles with various Rg are formed
- Smaller particles are formed with increasing amount of polysaccharide as well as increasing Insulin to Zinc ratio
Method 2 release results

Conclusions: parameters need to be tuned so that targeted release can be achieved. Perhaps coat the nanoparticle with multiple layers of polysaccharide so that gel matrix is formed, which, from previous study to be beneficial in sustained release of insulin.
CONCLUSIONS & FUTURE STUDIES

- CaCl2 aided in the formation of insulin hexomers (M1)
- A lower concentration of CaCl2 provided a better insulin release system (M1)
- A higher concentration of polysaccharide provided better nanoparticle formation (M2)
- Zinc is important to avoid insulin degradation as well as nanoparticle formation (M2)
- Zein caused insulin degradation in the digestive system release

- Further optimization of method 2 nanoparticle formation to improve polysaccharide concentrations/insulin release in digestive system
- In-vitro nanoparticle release
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- Dr. Yimin
- Shark Tank & all of NCNR SURFERS