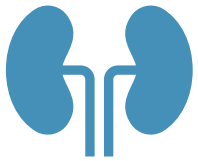
EXPLORING ORAL INSULIN DELIVERY VIA MICROENCAPSULATION

JULIANNA PRICE &

MENTOR DR. AMY XU

UNIVERSITY OF MARYLAND | NIST
INSTITUTE FOR BIOSCIENCE
& BIOTECHNOLOGY RESEARCH

NIST
National Institute of
Standards and Technology
U.S. Department of Commerce



What is Insulin?
What does it do?

Research Methods

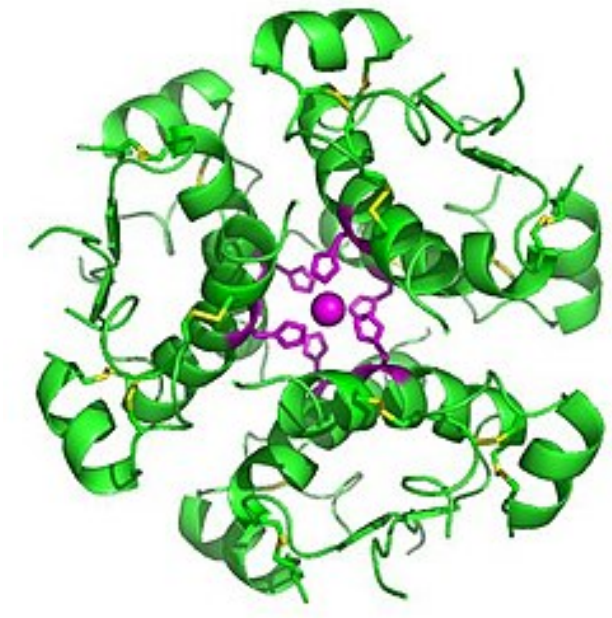
Results

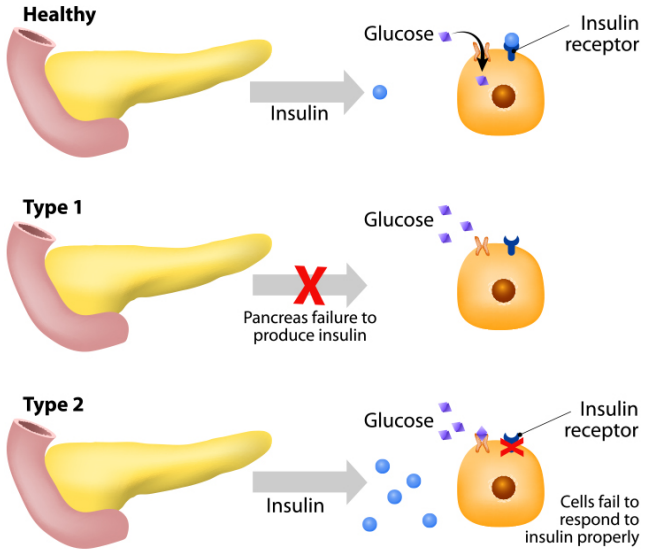
Future Research

OVERVIEW

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**

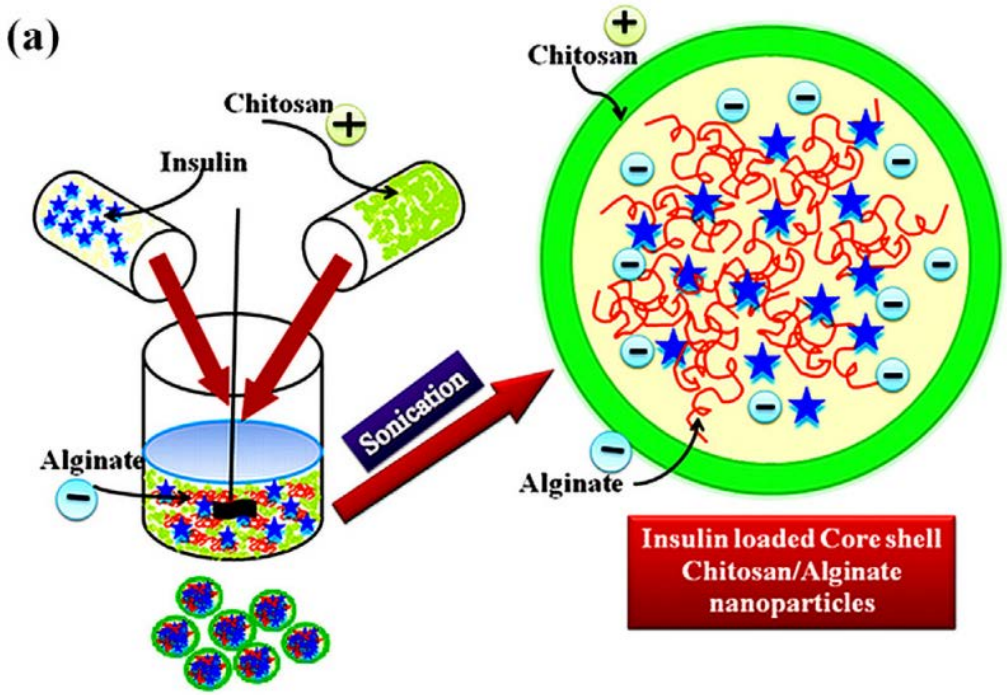
Zein Protein – pH(I) 6.8

Pectin Polysaccharide – pKa 3.5

Alginate Polysaccharide – Pka 3.4/4.4

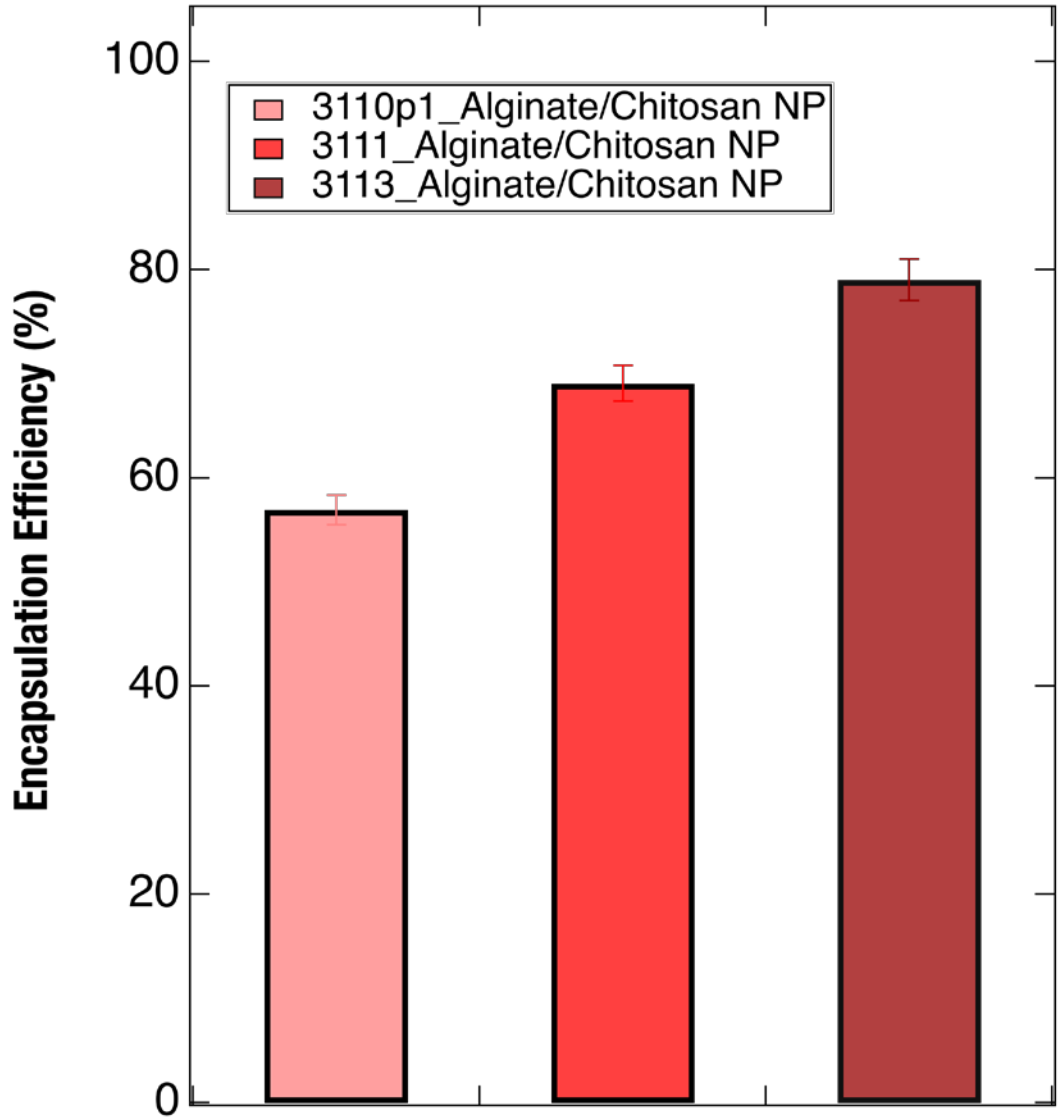
Chitosan Polysaccharide - 6.5

METHOD 1



Adapted from Chen et al. 2018

- 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



ENCAPSULATION EFFICIENCY METHOD 1

Beer's Law

$Absorbance = \varepsilon Lc$

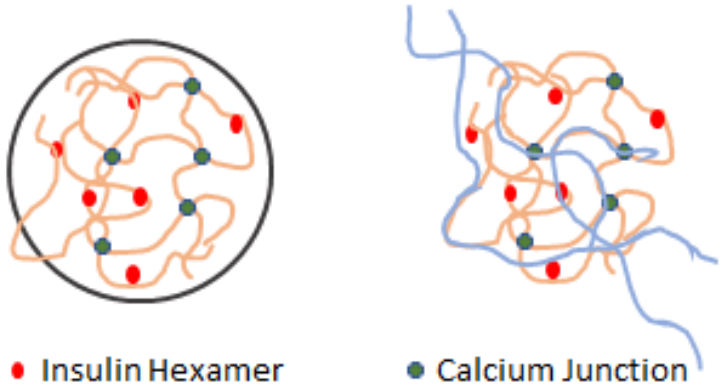
Extinction coefficient

Pathlength

Concentration

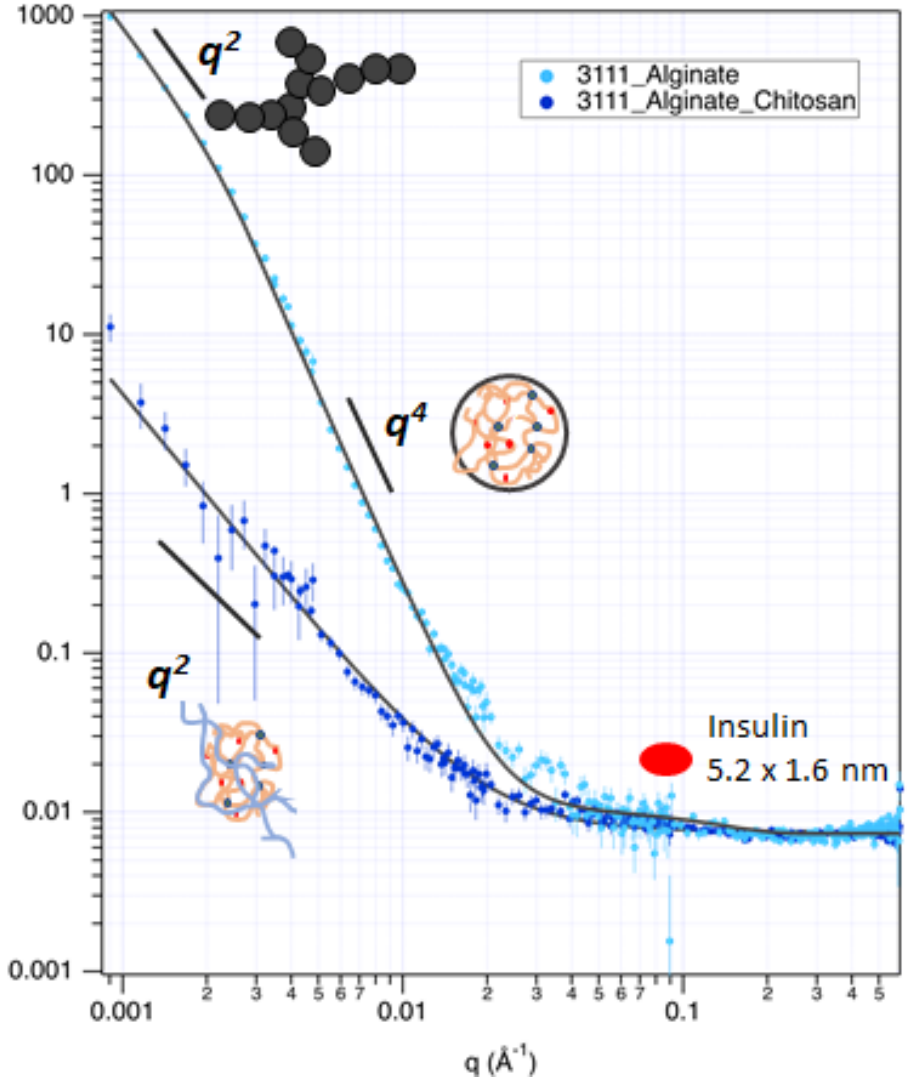
Method 2 SANS Measurements
3111_Alginate: Colloidal Aggregates
3111_Alginate_Chitosan: Polymer Networks

3111_Alginate **3111_Alginate_Chitosan**



Insulin Hexamer Calcium Junction

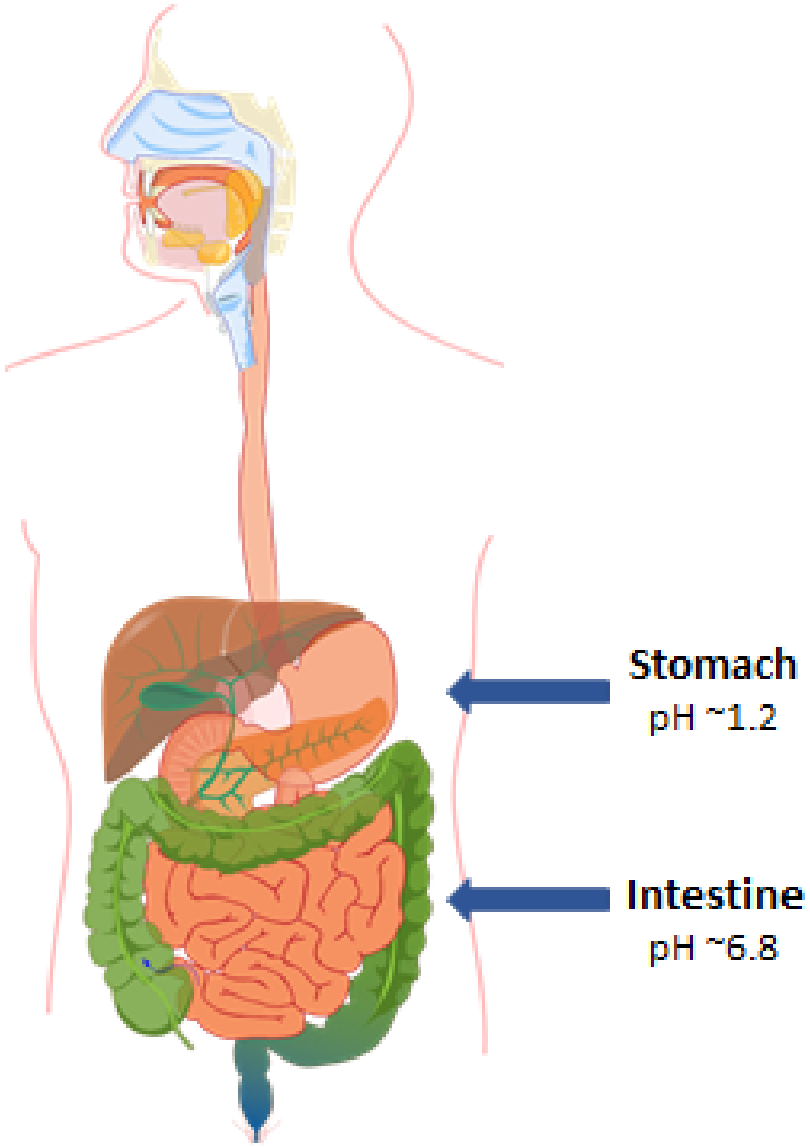
Alginate Chitosan



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

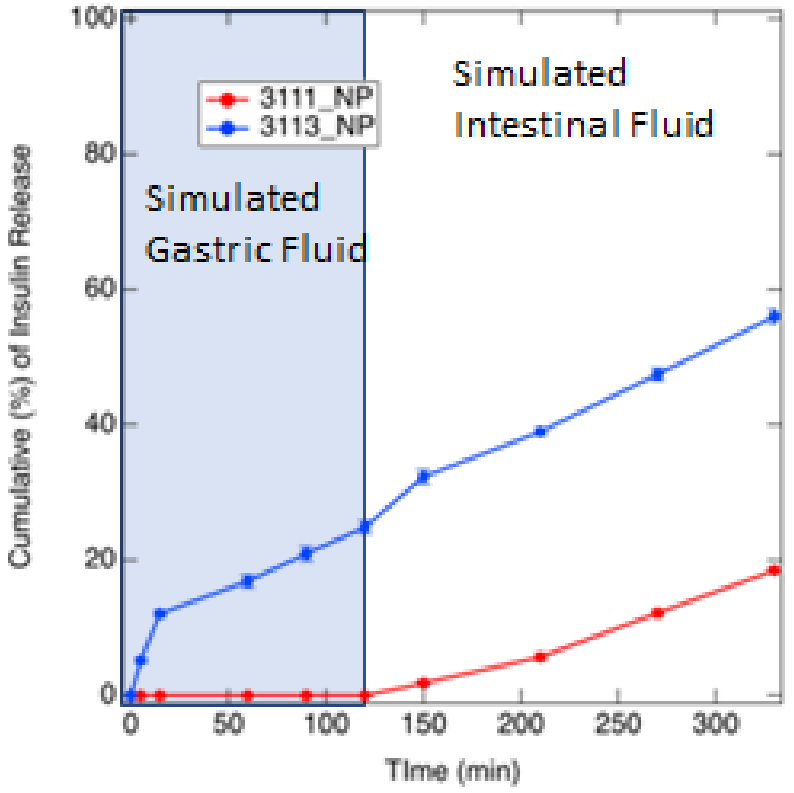
Gastrointestinal Tract



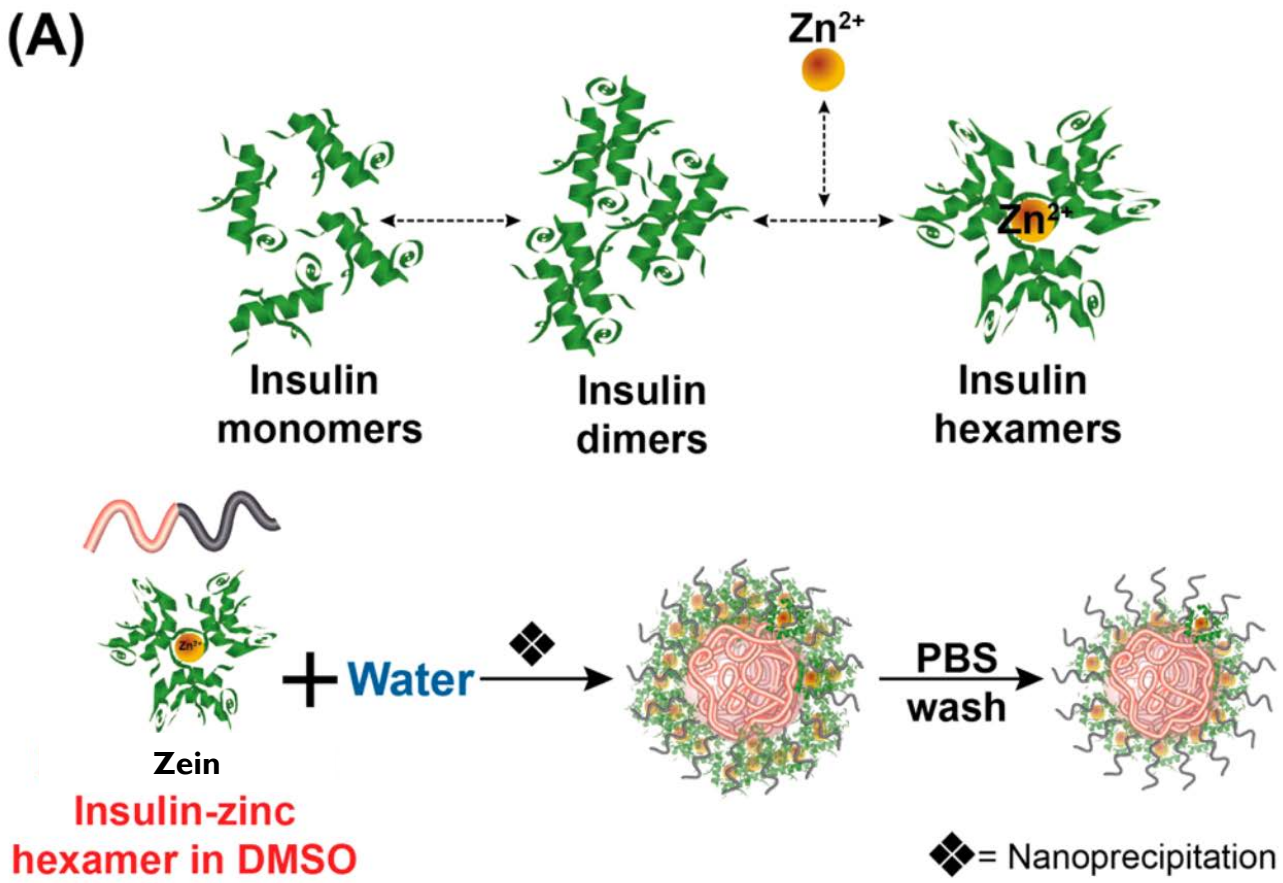
Targeted Delivery System:

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

Method 1 release results

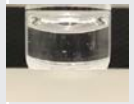
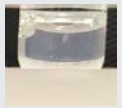


METHOD 2



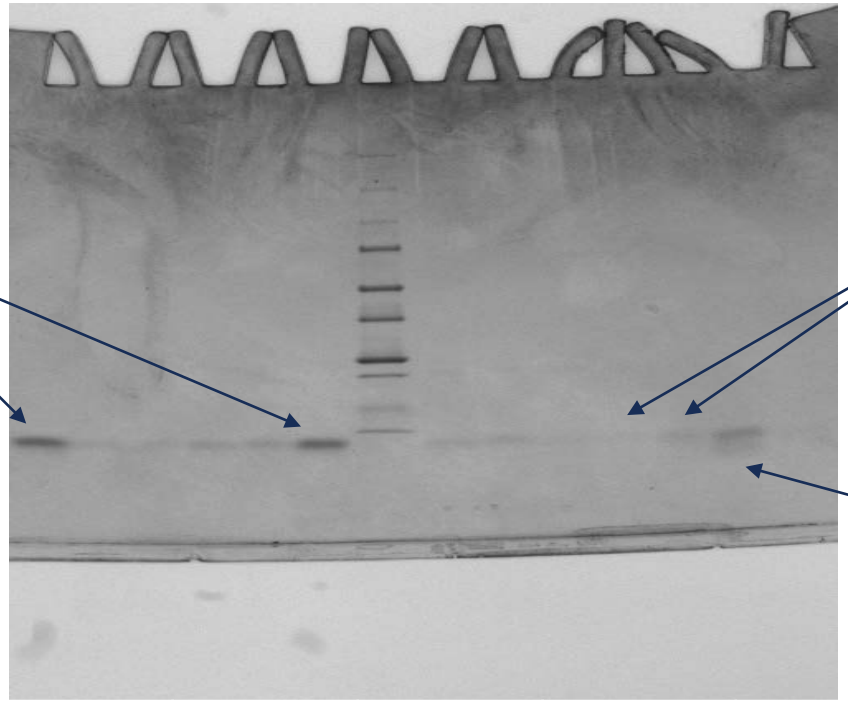
Adapted from Zhu et al 2019

PARAMETER OPTIMIZATION (METHOD 2)

Sample	1	2	3	4	5	6	7	8	9	10	11	12	13
Content (all inc. Ins)	Zn/ Buffer	Zn/2 Pectin	Zn/ 10 Pec.	Zn/ .25 Alg.	Zn/ .75 Alg	Zn/Ze Buffer	Zn/Ze/ 2 Pectin	Zn/Ze 10 pec	Zn/Ze/ .25 Alg	Zn/Ze/ .75 Alg	.75 Alg	Buff.	10 Pec.
Transmittance % (λ 630)	100	80.5	81.6	66.4	69.0	39.8	33.3	11.4	12.2	9.2	80.7	100	84.2
													

- 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

More intense bands indicating a low insulin encapsulation rate

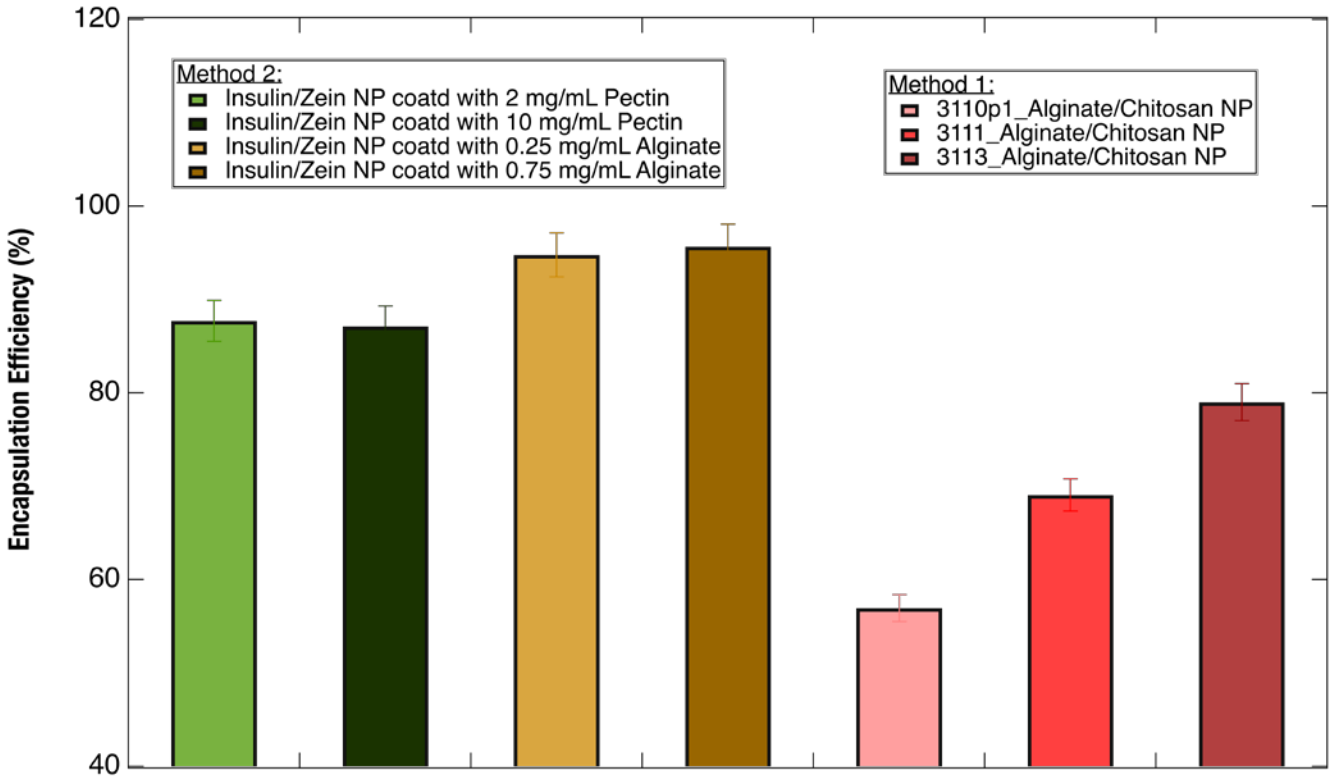


- A lack of Zinc leads to the defragmentation of Insulin

Less intense bands indicating higher encapsulation efficiency rates

Multiple bands indicating defragmentation

Lane	1	2	3	4	5	6	8	9	10	11	12
Encapsulation efficiency (%)	0	86.32	89.45	81.20	77.62	10.49	87.71	87.14	94.78	95.69	Defragmentation of Insulin
Sample	Insulin+Zn into Buffer as Control	Insulin+Zn into 2 mg/ml Pectin	Insulin+Zn into 10 mg/ml Pectin	Insulin+Zn into 0.25mg/ml Alginate	Insulin+Zn into 0.75mg/ml Alginate	Insulin+Zn+Zein into Buffer	Insulin+Zn+Zein into 2mg/ml Pectin	Insulin+Zn+Zein into 10mg/ml Pectin	Insulin+Zn+Zein into 0.25mg/ml Alginate	Insulin+Zn+Zein into 0.75 mg/ml Alginate	Defragmentation of Insulin antisolvent into Buffer



ENCAPSULATION EFFICIENCY

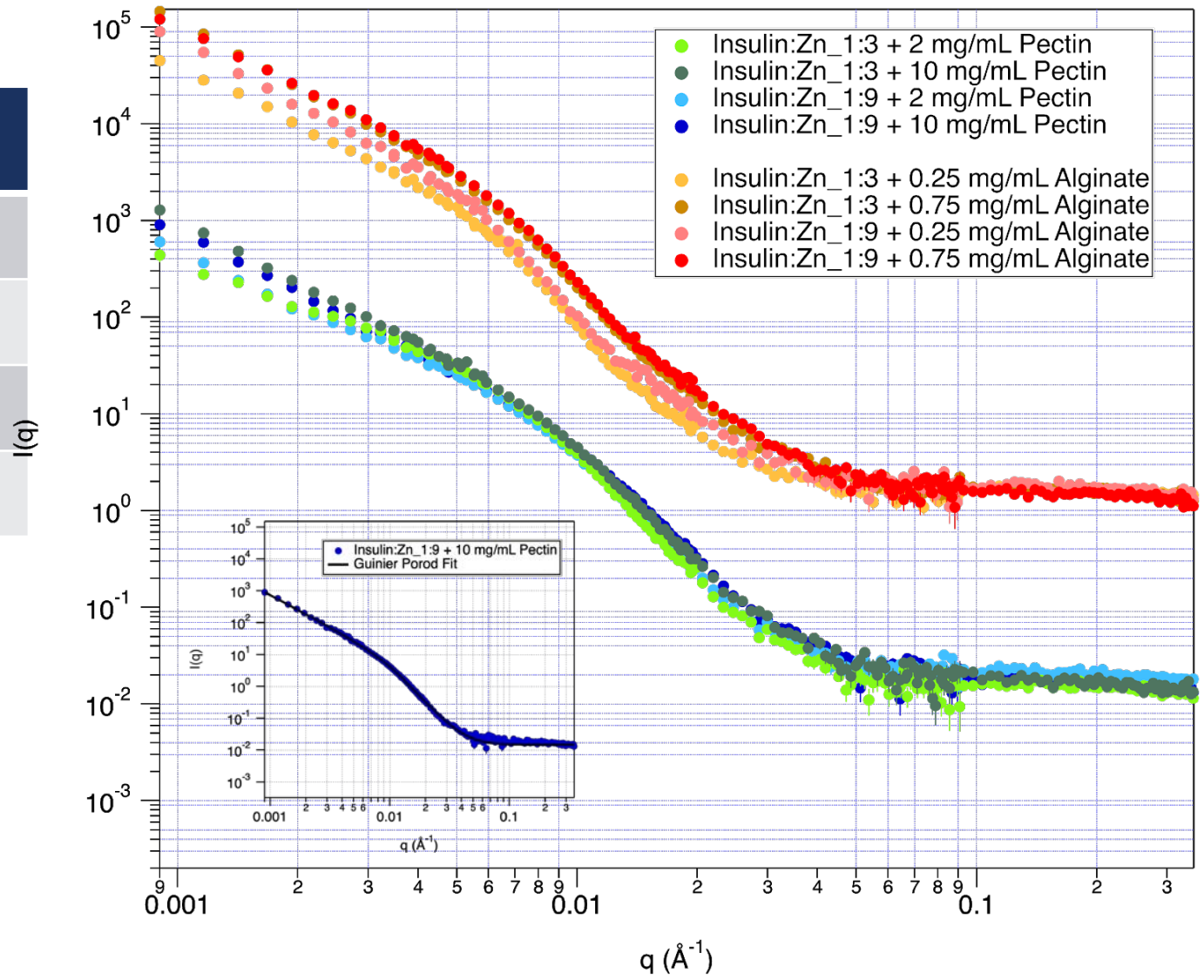
Method 2 SANS Results

Model: Guinier Porod

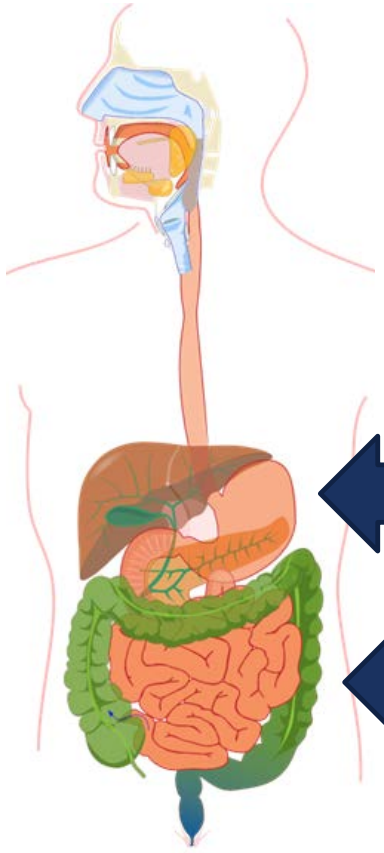
Coating Polysaccharide	Insulin:Zn 1:3	Insulin:Zn 1:9
2 mg/mL Pectin	178.8	126.3
10 mg/mL Pectin	130.9	73.5
0.25 Alginate	209.3	207.8
0.75 Alginate	174.5	161.7

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



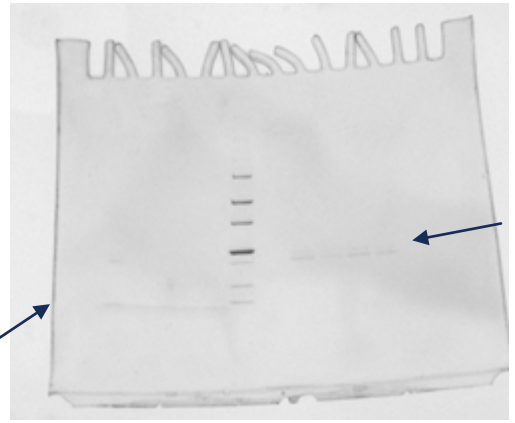
Method 2 release results



Stomach pH ~1.2

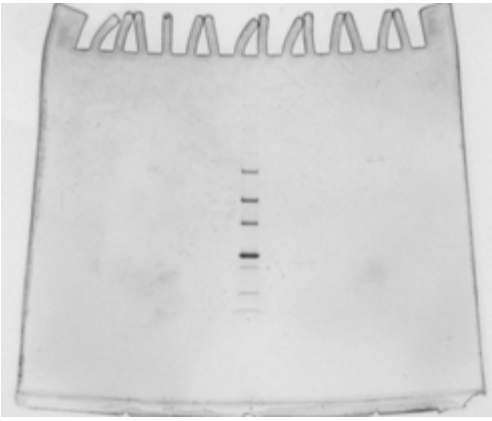
Intestine pH ~ 6.8

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.



Zein 20 kDa

Insulin
5.8 kDa



CONCLUSIONS & FUTURE STUDIES

- $CaCl_2$ aided in the formation of insulin hexomers (M1)
- A lower concentration of $CaCl_2$ provided a better insulin release system (M1)
- A higher concentration of polysaccaride 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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CHRNS
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