National Science Challenges

HIGH-VALUE NUTRITION

Ko Ngā Kai Whai Painga

Right time, right place: bioactive delivery systems

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Plant & Food RESEARCH RANGAHAU AHUMĀRA KAI

Developing High-Value Foods

Food Systems & bioactive compounds

- Semi solid
- Solid
- Liquid

Stability of bioactive compounds

- Processing
- Storage

***In vitro* gastrointestinal behaviour**

- Food matrix change
- Bioaccessibility

Human trials

- To be done by the Health Platforms

Food Systems & Bioactive Compounds

Selection criteria of Food Systems

- Healthy
- ‘Fit for purpose’
- Ready-to-eat
- Shelf life

Bioactive compounds

- Rutin (Metabolic Health)
- Probiotics/kiwifruit fibre (Digestive Health)
- Short chain fatty acids (Immune Health)

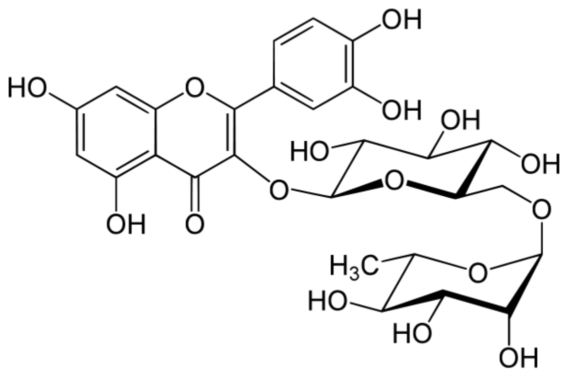
Rutin: a Case Study

Metabolic Health Platform identified a bioactive of interest (rutin) for formulating model food products for a human clinical trial in 2018

Evaluated the state of art with regards to the delivery of rutin *via* food using the decision support system database

Tested 5 types of delivery systems for compatibility with rutin and begun formulating model food products

Rutin



Flavonoid composed of a molecule of **quercetin** and a disaccharide **rutinose**

Formulation challenges:

- Poor solubility in both water (≈ 0.05 mg/mL, 70°C) and oil (≈ 1 mg/mL above 90°C)
- Low bioavailability due to its poor solubility

Encapsulation systems

Emulsions
Liposomes
Cyclodextrins
Whey protein complexes
Casein complexes

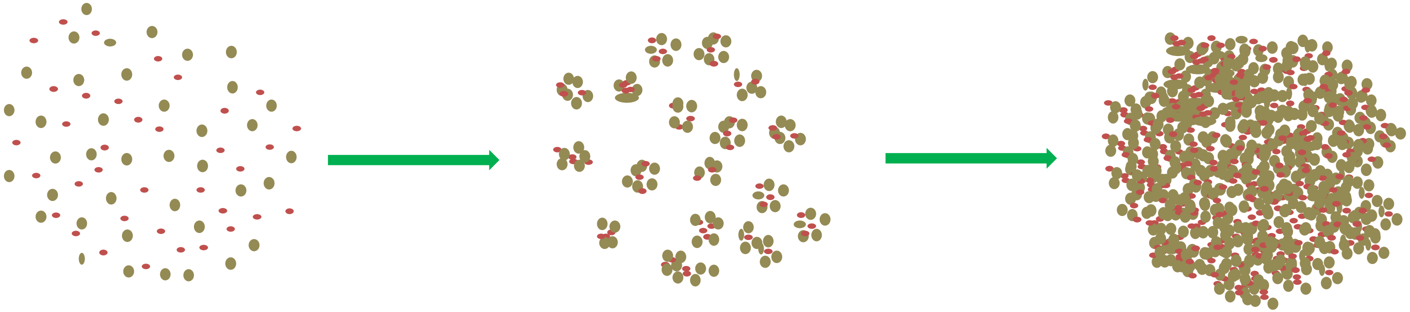
Novel Delivery System for Rutin Encapsulation

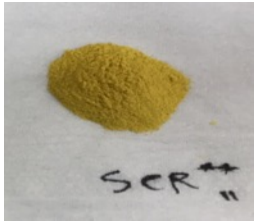
Co-assembly of casein and rutin molecules

Casein and Rutin

(Soluble Complexes)

(Co-precipitated complexes)





Rutin

Sodium caseinate

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Rational Formulation of Food Prototypes for Metabolic Health Platform

Formulation suitable for pre-diabetic participants

- Low sugar
- Low fat
- High protein

Bioactive dose

- 500 mg of rutin / serve

Main challenges in product development:
- Achieve palatable products under these conditions
- Overcome changes in the original food properties due to the presence of rutin

Available in the market

Rutin fortified juice

6 mg rutin / serve

Food Prototypes for Rutin Delivery

Low-fat Yoghurts | **Protein beverages** | **Protein bars**

Selected for Metabolic Platform

control | encapsulated rutin | free rutin

control | encapsulated rutin | free rutin

Target: 500mg Rutin/Serve

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Rutin-fortified Set-type Yoghurts

- **Informal sensorial test (10 panellists)**

Sample	Overall acceptability
Control	Acceptable
Free rutin 500 mg	**Not acceptable**
Encapsulated rutin 500 mg	Acceptable

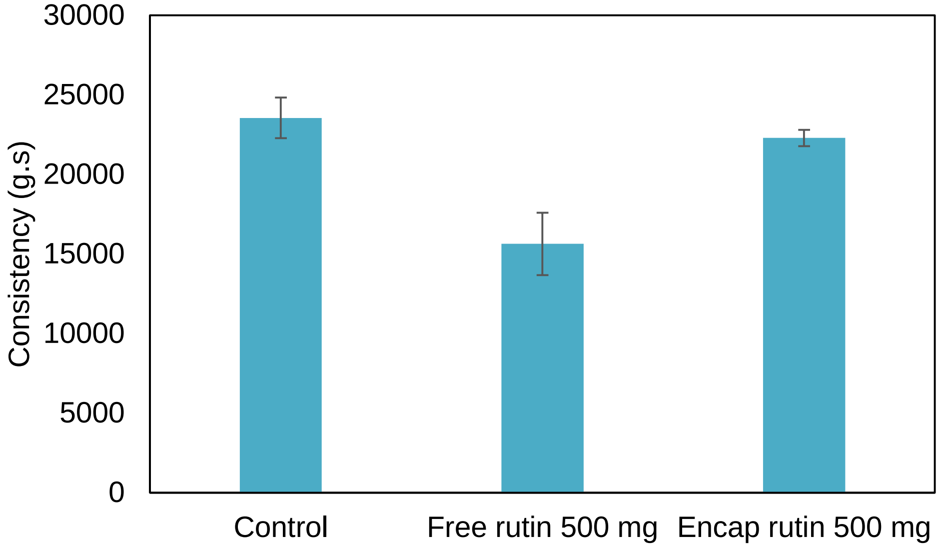
Undesired texture
Unpleasant taste

Changes in taste compared with control, but can improve with flavourings:

- Lemon
- Passion fruit
- Cappuccino

Rutin-fortified Set-type Yoghurts: Effect on the Quality Attributes

- **Changes in the texture properties**



- **Appearance**

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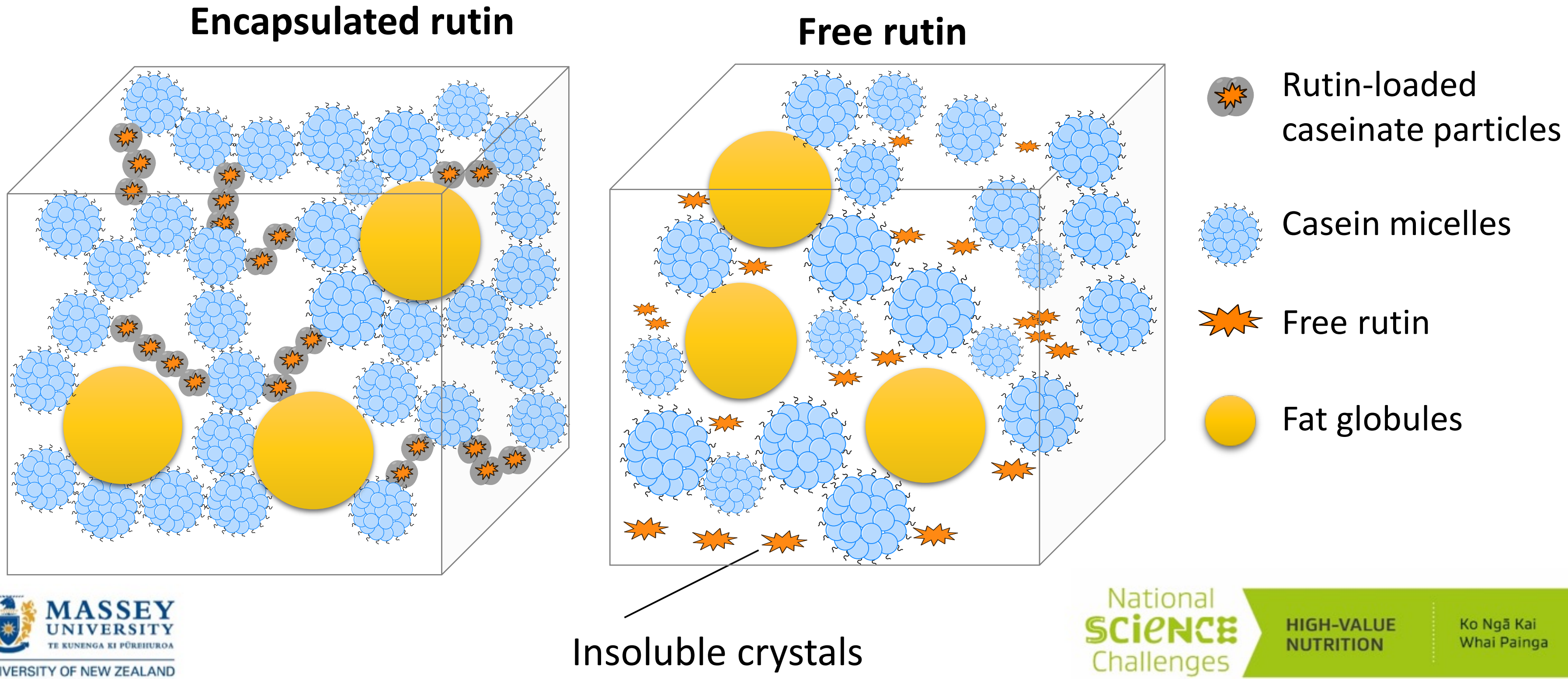
Schematic Representation of Rutin-fortified Yoghurt Network



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Summary

- A new technology was developed for improving the dispersibility of rutin
- Three food prototypes were developed and tested for delivering high levels of rutin in an acceptable form for human consumption
- In discussion with the Metabolic Platform, low-fat yoghurts were selected for human trials
- Free rutin compromises the quality and sensorial attributes of yoghurts. This could be avoided using a delivery system

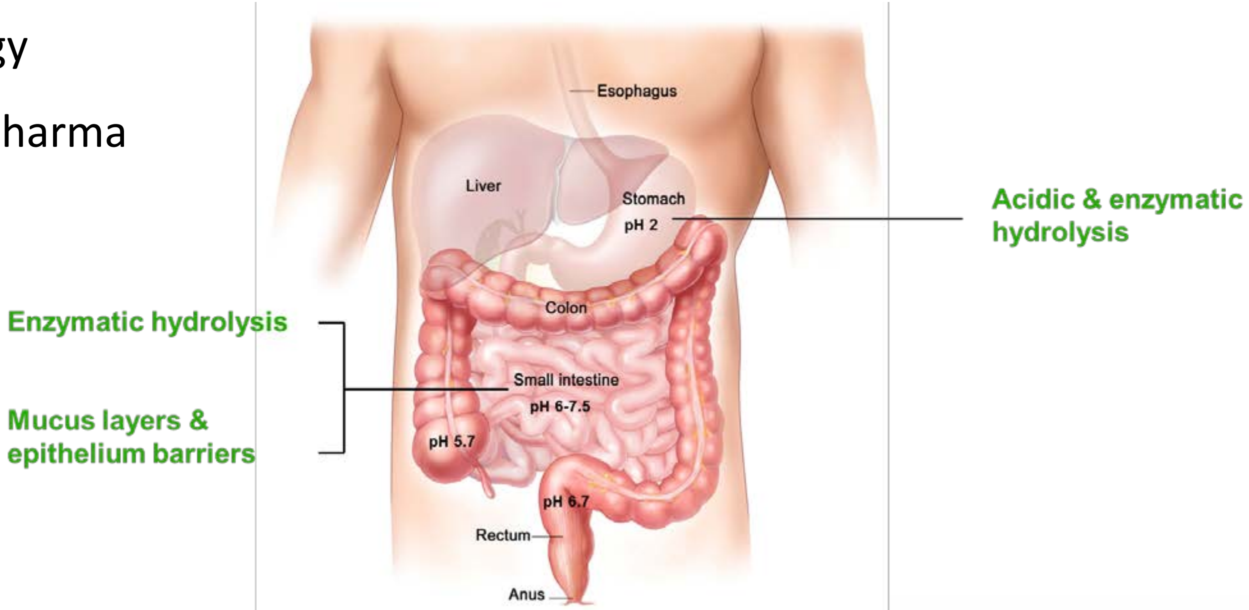
Future directions

- Investigate bioaccessibility and bioavailability of rutin in fortified foods
- Apply a similar approach with the other bioactive compounds

Gastric Protection & Targeted Delivery

- Growing demand for healthy foods
- Oral delivery technology
- Chance to learn from Pharma

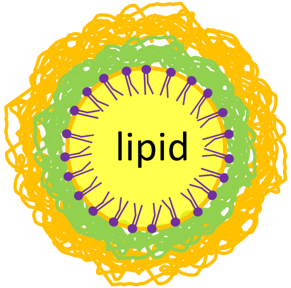
  - Solubility
  - Stability
  - Permeability



Strategies for Targeted Release: Delivery Systems

Bioactive Compounds

Hydrophobic

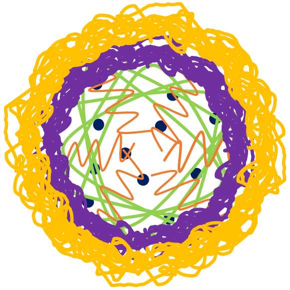


Emulsion

Some examples:

- Polyphenol
- Vitamin
- Coenzyme **(eg. CoQ10)**
- Therapeutic peptide
- Omega-3 fatty acid
- Short chain fatty acid

Hydrophilic



Polyelectrolyte complex

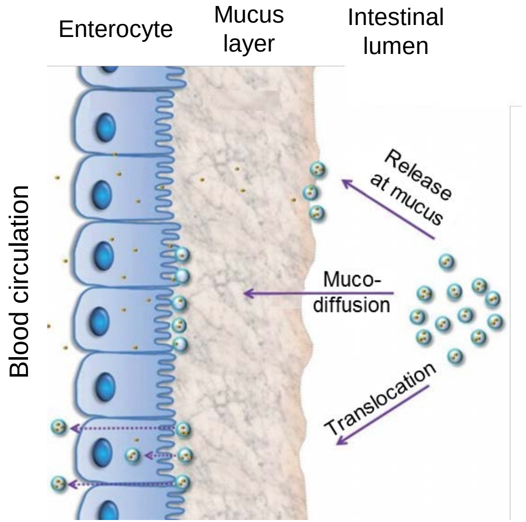
Strategies to Improve Bioavailability

Step 1 (accomplished):

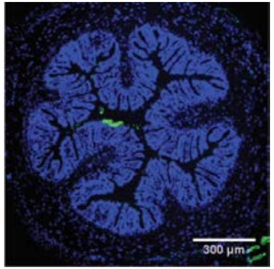
- Solubilisation
- Gastric protection
- Targeted release

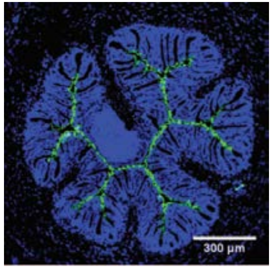
Step 2 (upcoming):

- Mucodiffusion
- Enhanced cell penetration



Non muco-diffusive particles





Muco-diffusive particles

K Maisel, et al., Nanomedicine, 2016

Mouse intestinal tissue cryosections

Blue: Cell nuclei Green: Drug delivery system

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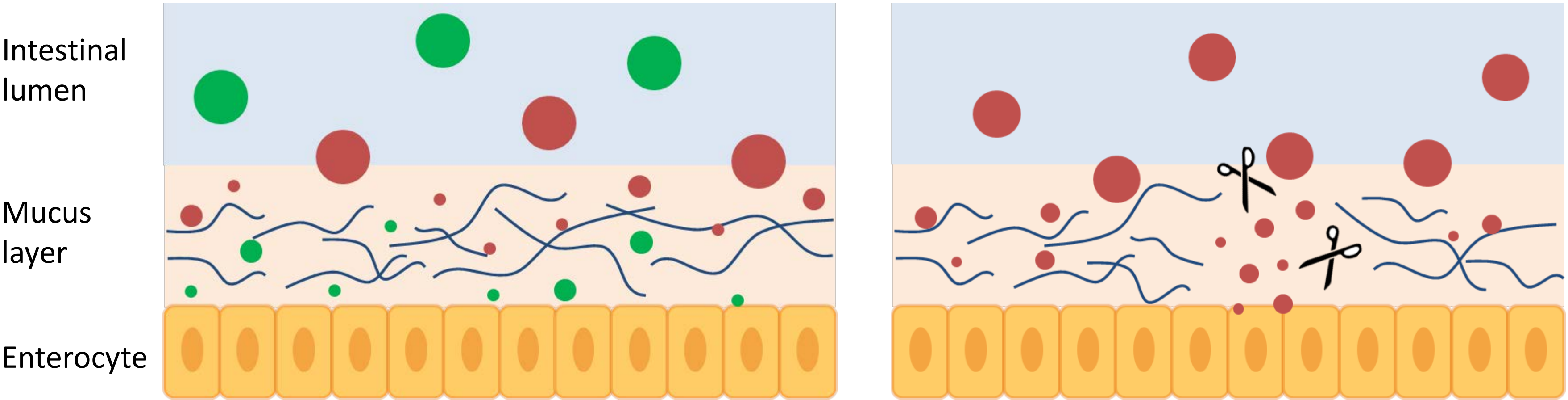
Crossing Mucus Barrier

Approach 1 (common in pharmaceutical area)

Surface PEGylation of nanoparticles

Approach 2 (new emerging)

Mucolysis by fruit-derived enzymes



Surface PEGylated

Non-modified

Mucolytic enzyme

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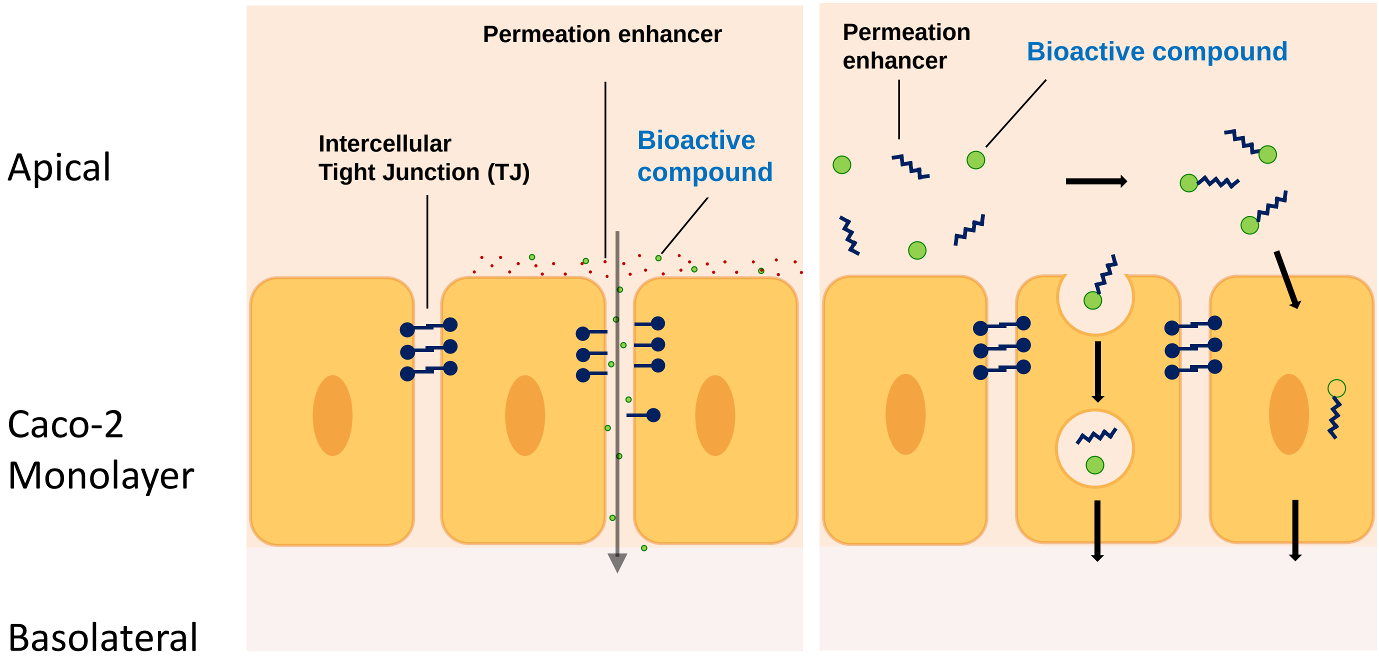
Cell Permeability Enhancement



Food derived permeation enhancers:

- Mid-chain fatty acids
- Arginine rich peptides
- Lysine rich peptides
- Chitosan

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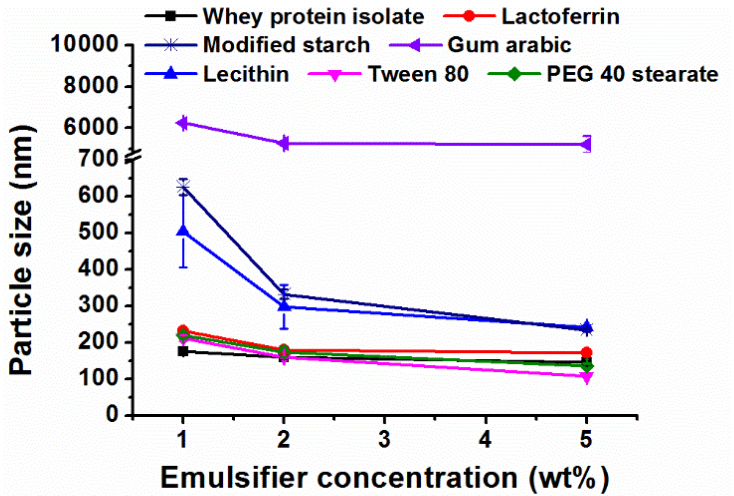
Emulsions: From Trial-and-error to Rational Design

Preliminary screening



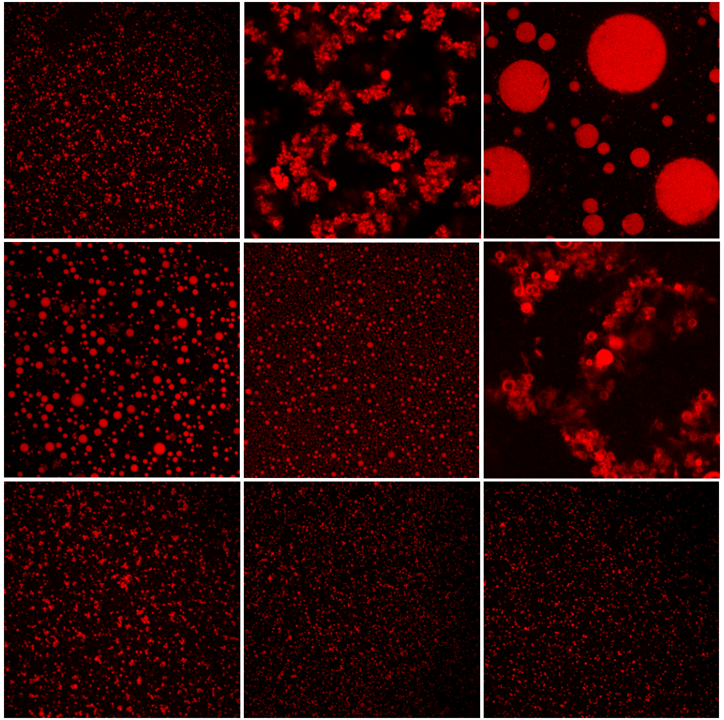
Rational design & optimization

Optimal systems identified for:

1. Targeted release (Gastric stable)
2. Improved interaction with intestinal membrane (Multilayer coating)

Microstructures in Gastric/intestinal Conditions

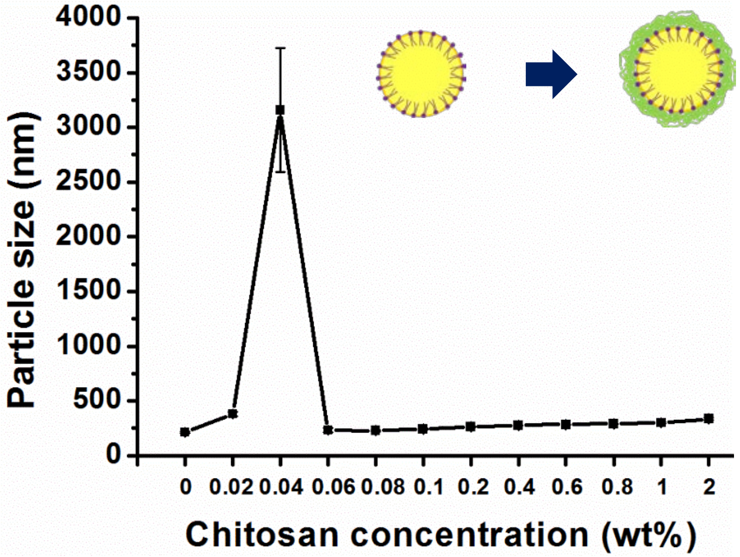
Emulsions based on

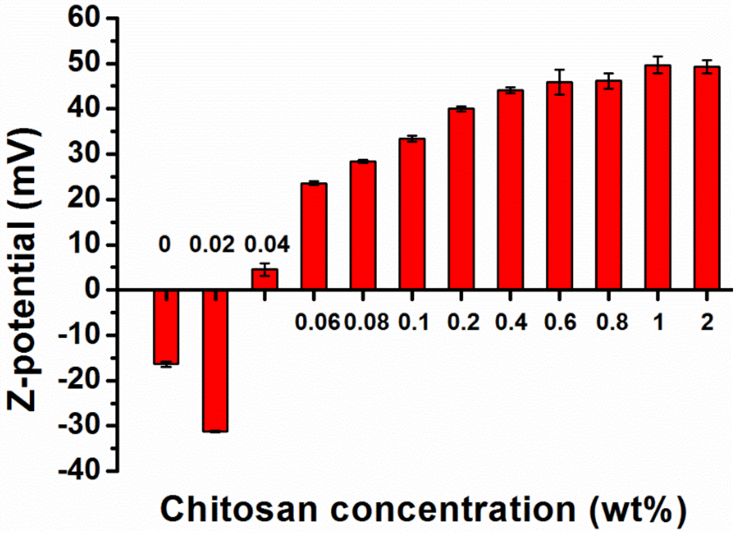


	Water	Gastric	Intestinal	
Whey protein				Unstable in gastric condition
Modified starch				Gastric protection Intestinal release
Tween 80				Colon targeted delivery

Emulsion Droplets Coated by Biopolymers

Chitosan-coated emulsion droplets (1% lecithin + 1% Tween 80)



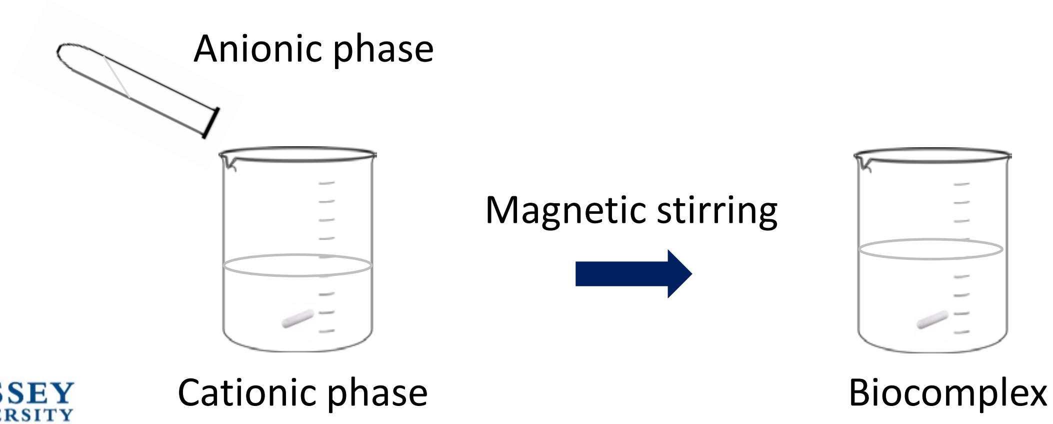


Polyelectrolyte Complexes: Preparation

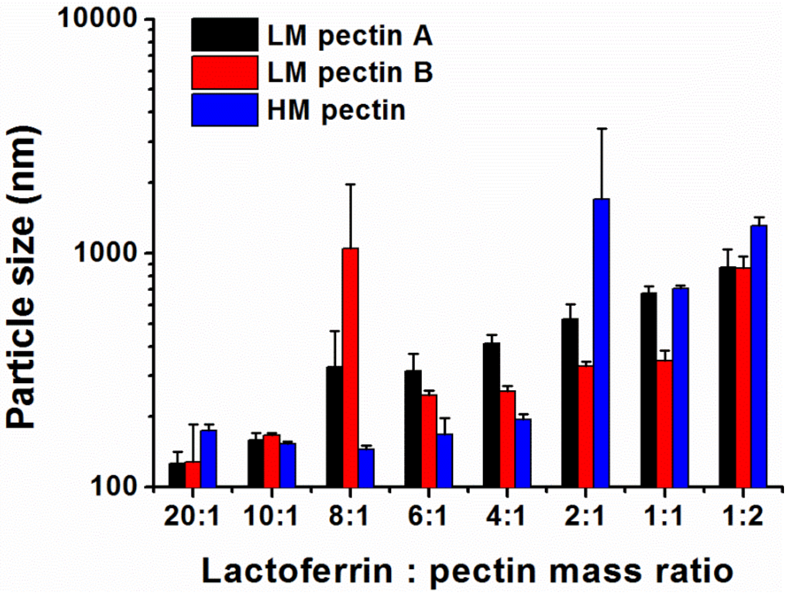
Materials

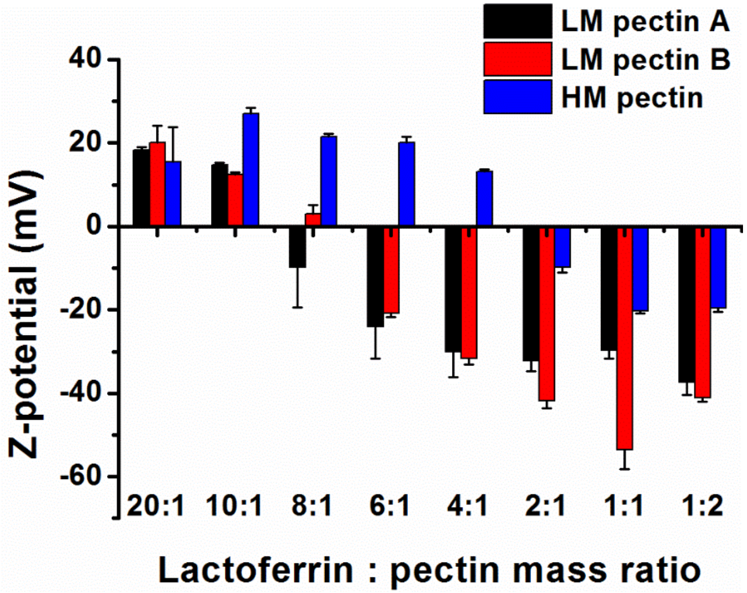
- Polysaccharides: Pectin (-), Gum Arabic (-), Chitosan (+), etc.
- Proteins/polypeptides: Whey protein (-), Lactoferrin (+), Polylysine (+), etc.
- Salts: Tripolyphosphate (-), cyclodextrin salts (-), etc.

* Charge: at neutral pH (in water)



Screening: Lactoferrin - Pectin Complexes





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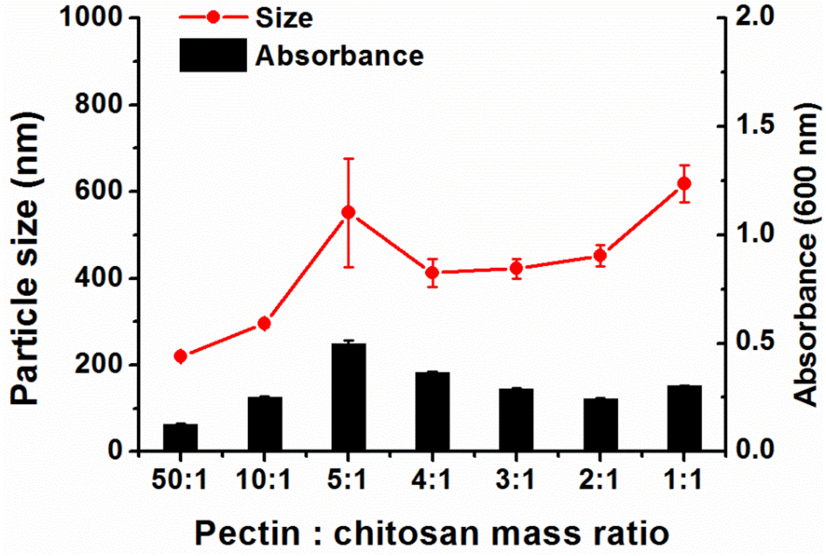
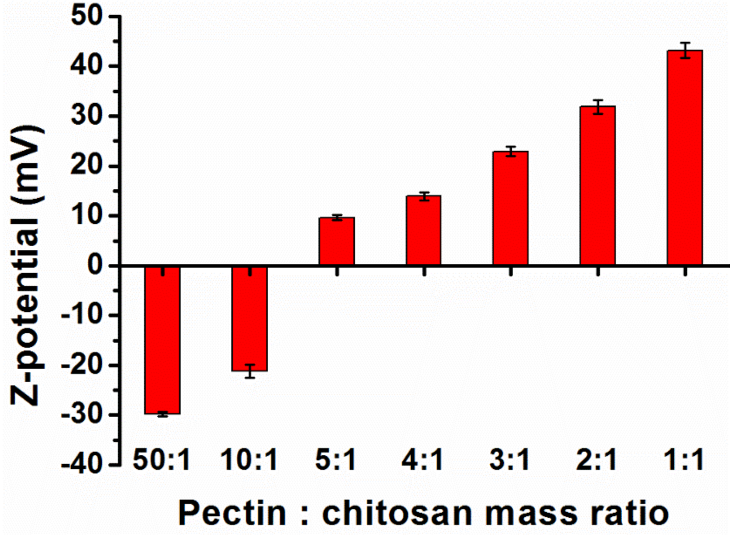
Multi-biopolymer Layer Stabilized Lactoferrin

Chitosan enveloped lactoferrin - pectin complexes (Lf: pectin mass ratio 4:1)





Summary

Accomplished work:

- A literature review on Pharma-inspired delivery systems & potential for food delivery
- Screening & rational design of delivery systems
- Gastric protection and intestinal targeted release

Upcoming work (Collaborating with Digestive Health):

- Interactions between delivery systems and intestinal mucus and enterocytes
- Bioavailability & biodistribution *in vivo*