Orally available formulation for peptide therapeutics

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Te Whare Wānanga o Tāmaki Makaurau
NEW ZEALAND

Oral available formulation for peptide therapeutics

Current Problem: Peptide therapeutics are currently not orally bioavailable due to instability in the gut.

Technology: A microemulsion which can encapsulate peptide drugs making them orally available. The nanoparticles can be further modified to increase the bioavailability of the bioactive.

Solution: This encapsulation technology can be used for any peptide drug to enable oral delivery of previously SC or IV drugs.

Features:

- Lipid encased, non-aqueous nano emulsion which can dissolve peptide therapies

Advantages:

- Makes oral administration possible for therapies that were previously only injectable.
- The drug's non-aqueous environment prevents it from degrading. Although it has water-like properties that allow it to dissolve the drug, it isn't water, which helps preserve the drug instead of causing hydrolysis.

Benefits:

- Makes any peptide drug treatment more accessible and less invasive.

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Additional advantages over conventional dosage forms:

1. **Improved Stability:** Non-aqueous emulsions reduce exposure to water, preventing protein denaturation, aggregation, and hydrolysis. This enhances the stability of sensitive protein drugs and prolongs shelf life.
2. **Controlled Release:** The non-aqueous phase can act as a barrier, enabling controlled and sustained release of the protein drug, potentially reducing dosing frequency and improving therapeutic efficacy.
3. **Reduced Immunogenicity:** By preventing protein aggregation, non-aqueous emulsions can reduce the risk of triggering immune responses, making them safer for patients.
4. **Enhanced Solubility**: Proteins that are poorly soluble in water may dissolve better in non-aqueous solvents (DMSO), improving their bioavailability.
5. **Protection from Enzymatic Degradation:** The non-aqueous environment can protect the protein from enzymatic degradation, particularly in gastrointestinal or extracellular conditions, enhancing delivery and effectiveness.
6. **Flexibility in Formulation:** Non-aqueous emulsions allow for the inclusion of excipients that stabilize proteins or enhance delivery, providing flexibility in optimizing the formulation for specific therapeutic needs.
7. **Easy to scale up and with low cost.**

Overall, non-aqueous emulsions can improve the stability, safety, and efficacy of protein drugs compared to conventional aqueous-based dosage forms. This technology represents a significant advancement in the field of oral drug delivery, offering a novel and effective platform.

Initial target market - Insulin

World and International Diabetes statistics

- Diabetes affects 537 million adults aged 20–79 years which represents 10.5% of the world's population in this age group.
- The total number is predicted to rise to 643 million (11.3%) by 2030 and to 783 million (12.2%) by 2045
- Over 1.2 million children and adolescents have type 1 diabetes. Over half (54%) are under 15 years of age

- In America 38.4 million Americans, or 11.6% of the population, had diabetes.
  - 1.2 million new cases every year.

Initial target market - Insulin

Standard of care

- Current standard of care for diabetics is still injectables.
- The two major drugs used by diabetics are insulin and extendin 4 (E4).
  - The oral bioavailability of these drugs is approximately 0.11% for insulin and 0.23% for E4 due to the nature of the compounds

- The insulin market is currently worth anything between $19 - 50 billion USD depending on which market report you look at.

- Eli Lilly, Novo Nordisk and Sanofi hold the majority of the insulin/diabetes therapeutic market share between them.

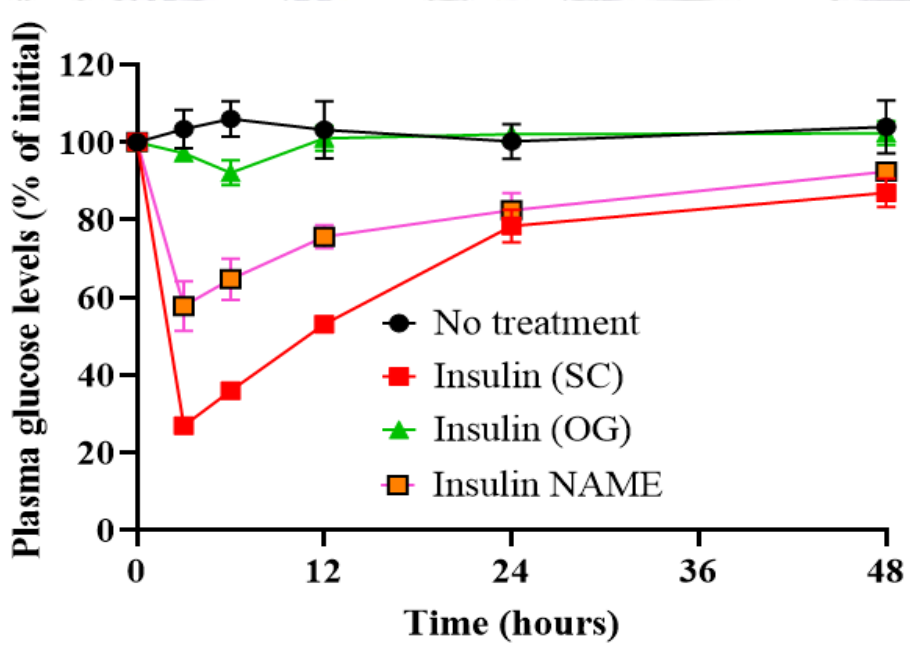
Non-aqueous Microemulsion

- The team have developed a formulation which protects peptide drugs, like insulin, long enough for them to travel through the GI tract until they can be absorbed systemically.

- Similarly to when an oil/water mixture forms droplets when shaken, the current technology uses a hydrophilic carrier to dissolve the bioactive which is then encapsulated in droplets upon mixing with an oily solvent. These droplets can then be prevented from separating by the addition of stabilisers.

- In the right ratios, these microemulsions become a “liquid crystal”, an organised latice that can still flow like a liquid.

- When administered via oral gavage (OG), the microemulsion formulation showed a 42% reduction in blood glucose while the SC administration showed a 75% reduction at the same dose. (5 IU/kg).



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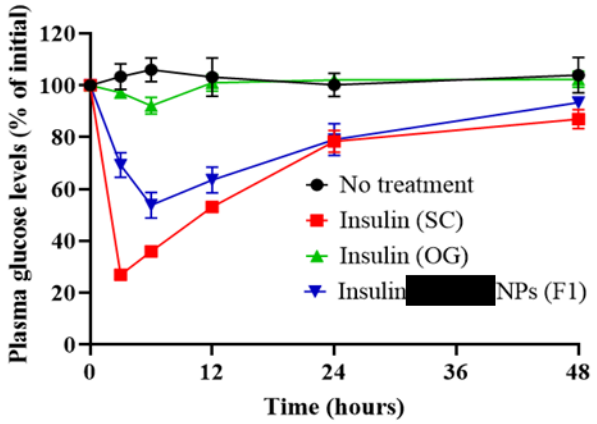
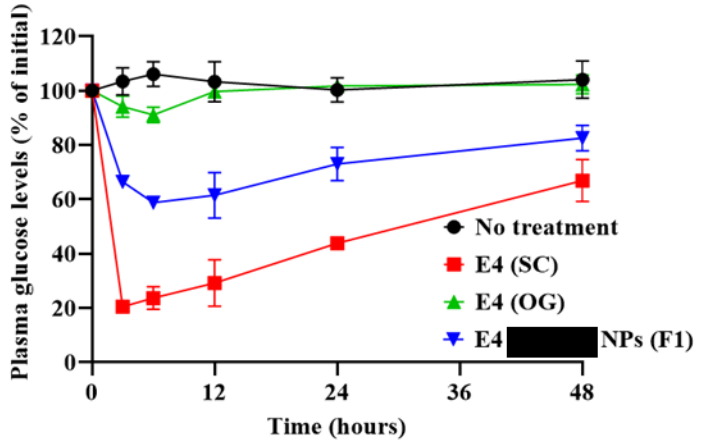
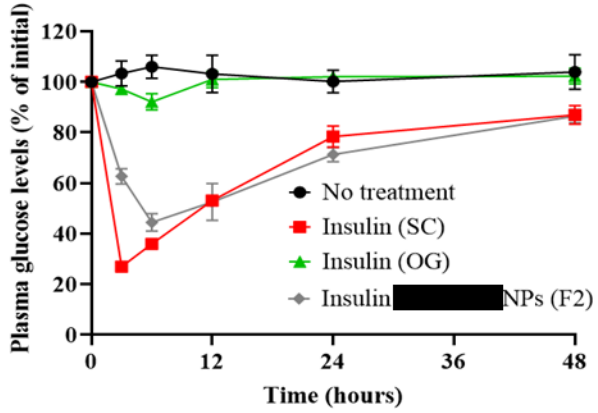
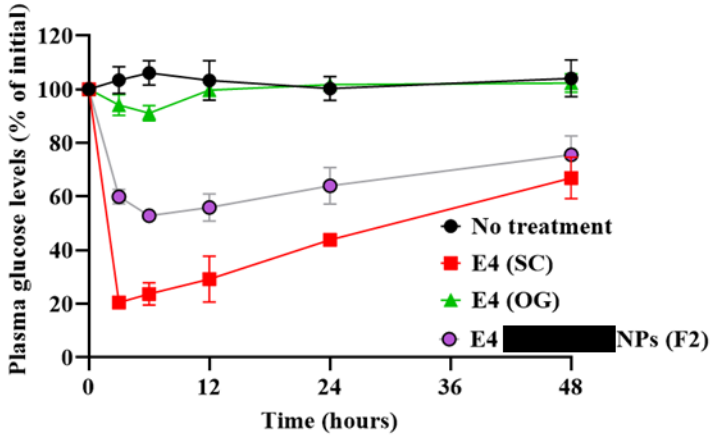
Functionalised Nano-particles

- Functionalised nanoparticle formulations are shown to be between 40-80% as efficacious as the SC injection.









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Platform technology for peptide therapeutics

- This technology could enable oral administration for any peptide therapeutics that are currently limited to SC or IV.
  - Been shown that Thymopentin, Glutathione, and Lactoferrin can be formulated in the microemulsion.

- Peptide therapeutics cover a broad range of drugs including monoclonal antibodies (mAbs), peptide hormones, vaccines, fusion proteins, blood factors and peptide antibiotics, cytokines, and therapeutic enzymes.
  - NOT ALL RELEVANT TO THIS TECHNOLOGY.
  - Subset would be smaller peptides such as peptide hormones, fusion proteins, blood factors, some peptide antibiotics, and maybe some vaccines.
    - Common peptide hormones include insulin, GLP1 agonists, hormone replacement therapy.

- Most of the major pharma companies have peptide drugs, thus this could be a widely sought after technology.