Formulation of GLP-1 Polymer-Nanoparticle (PNP) Hydrogels For Treatment of Type 2 Diabetes

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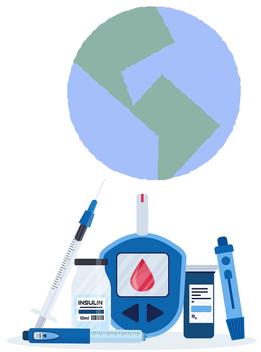
Introduction: Diabetes in a Global Context

There are over **463 million people** worldwide with diabetes.

90+% of cases are **Type 2 diabetes.**

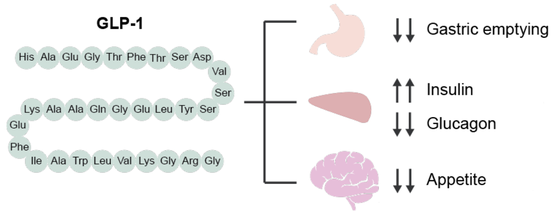
Current treatment of insulin, diet, and exercise are not successful in T2D management due to

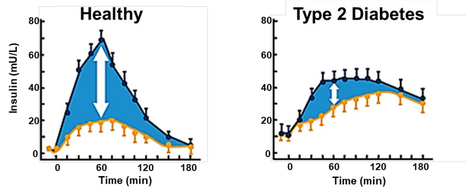
1) **risk for hypoglycemic events and**
2) **reliance on patient compliance**



Glucagon-like Peptide 1 (GLP-1) and the Incretin Effect

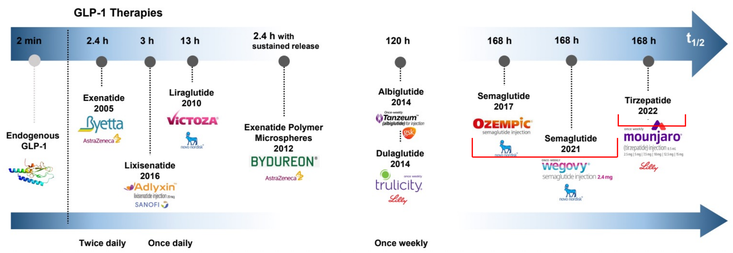
GLP-1 is an incretin hormone secreted from intestinal L-cells after large meals. GLP-1 is **inactive at low glucose levels, preventing hypoglycemia.**



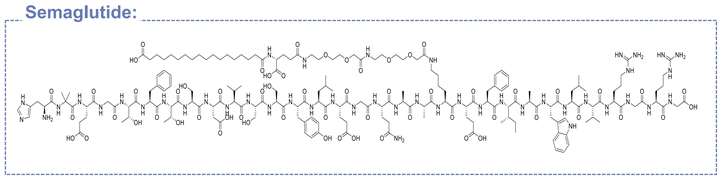


Current Promising T2D Therapies

Developing new treatment strategies which reduce patient burden and improve patient compliance, is important for effective diabetes treatment strategies.

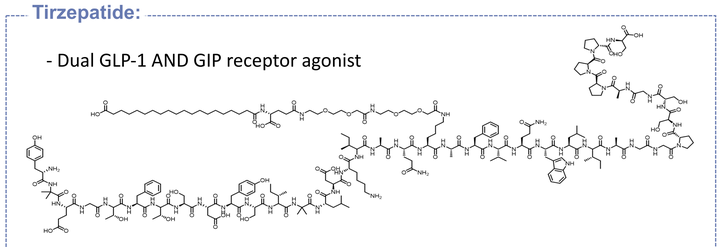


Semaglutide:



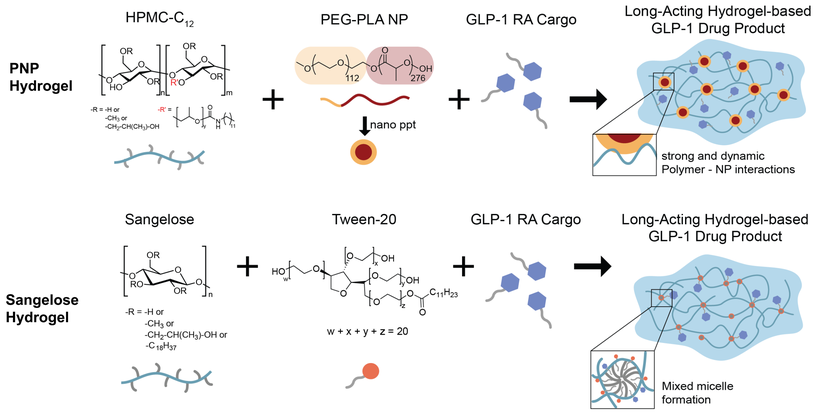
Tirzepatide:

- Dual GLP-1 AND GIP receptor agonist



Hydrogel Synthesis

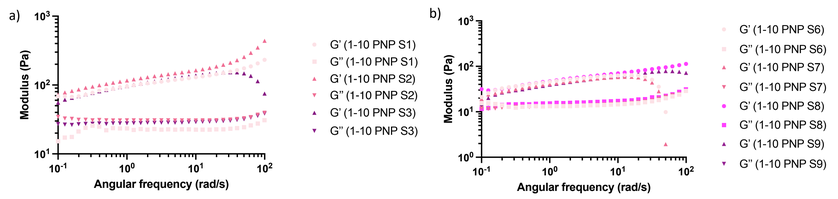
Long-acting hydrogels formed through dynamic polymer-nanoparticle interactions



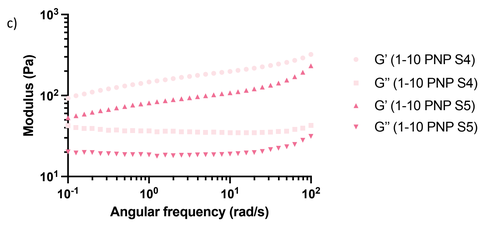
Nanoparticle and polymer solutions are mixed in syringes and injected as a **homogenous, bubble-free gel**.

Rheology Plots, G' > G''

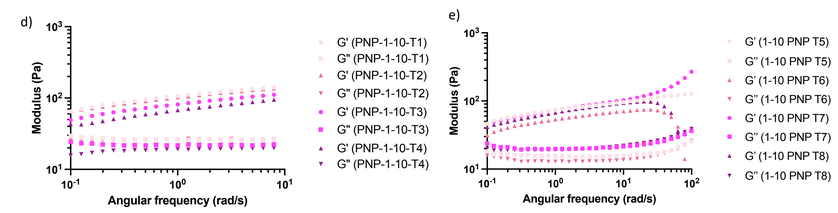
Changing Tween-20 levels in PBS- (a) and in water- (b) based semaglutide gels



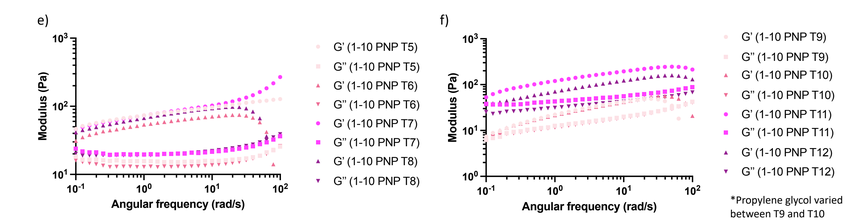
Changing aCD (excipient) levels in PBS (c)



Changing Tween-20 levels in PBS- (d) and in water- (e) based tirzepatide gels



Changing Tween-20 levels in low tirzepatide (e) and high tirzepatide (f) water-based gels*

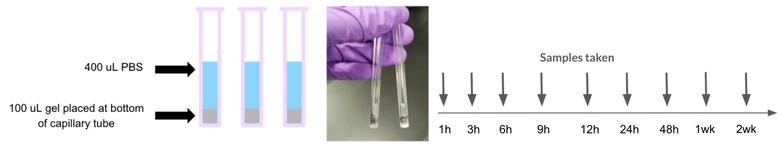


*Propylene glycol varied between T9 and T10

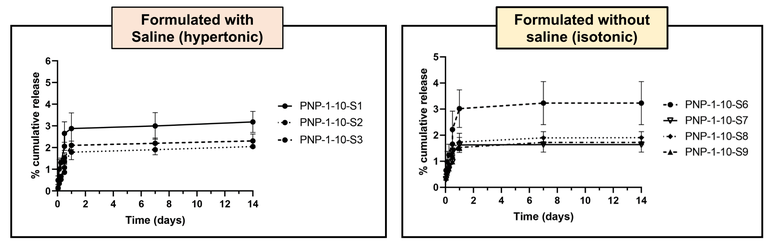
Hydrogels made in PBS are stiffer than those in water, and different excipients have different effects on hydrogel stiffness in both semaglutide and tirzepatide formulations.

In Vitro Release Assays

ELISA/In-Vitro Release and Burst Release

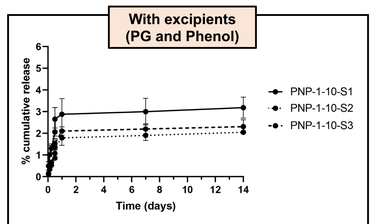


Semaglutide ELISA: Drug detection with a **colorimetric assay.**



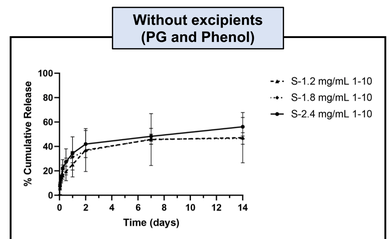
S1 = no tween20
S2 = low tween20
S3 = high tween20

S6 = no tween20, no saline
S7 = low tween20, no saline
S8 = medium tween20, no saline
S9 = high tween20, no saline



More than 10X reduction in drug release

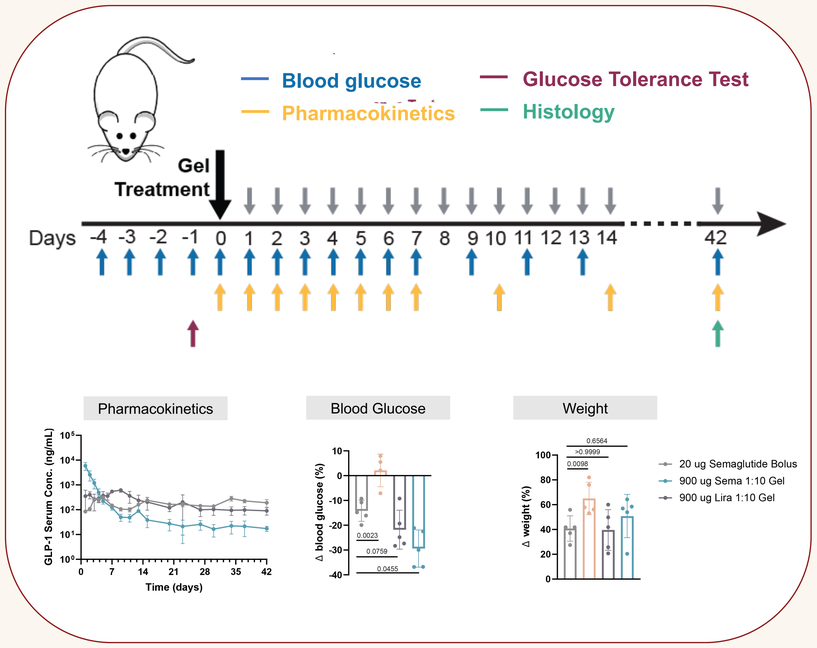
S1 = no tween20
S2 = low tween20
S3 = high tween20



S-1.2 = low concentration of drug
S-1.8 = medium concentration of drug
S-2.4 = high concentration of drug

Drug release from PNP-hydrogel formulations, *regardless of tonicity*, can be tuned changing the amount of tween-20 (surfactant).

In Vivo Design



Acknowledgements

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