

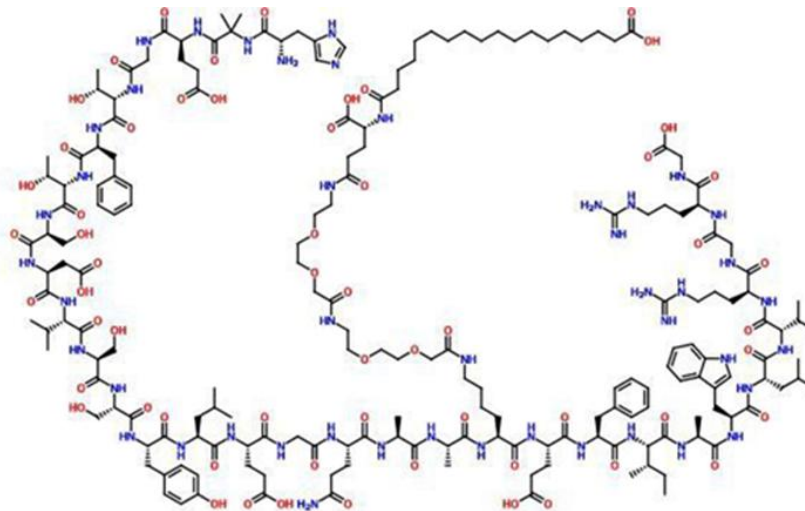
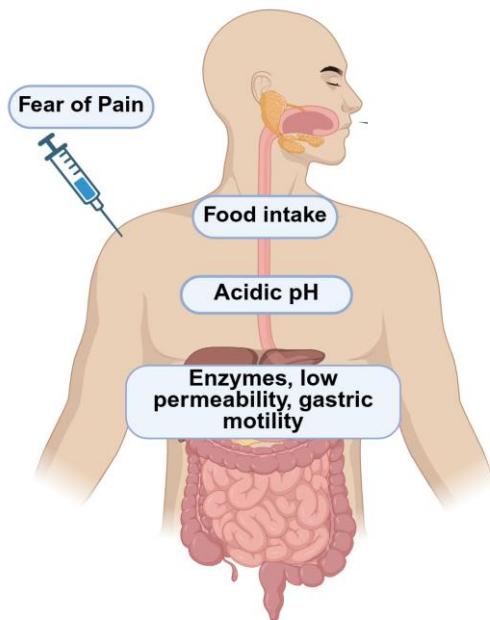


Non-covalent lipidation and self nano-emulsions: ex-vivo porcine buccal mucosal permeation of a GLP-1RA peptide

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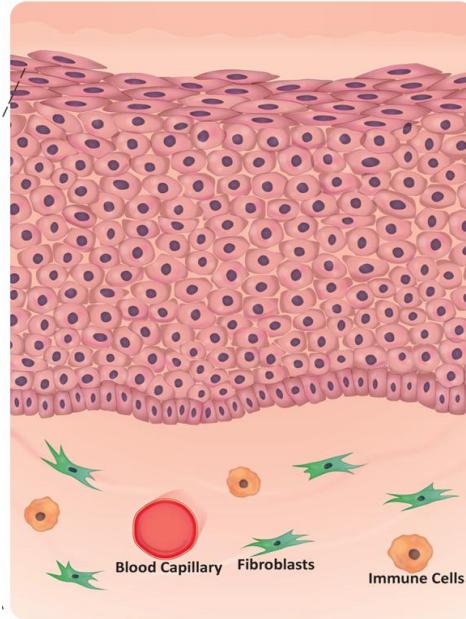
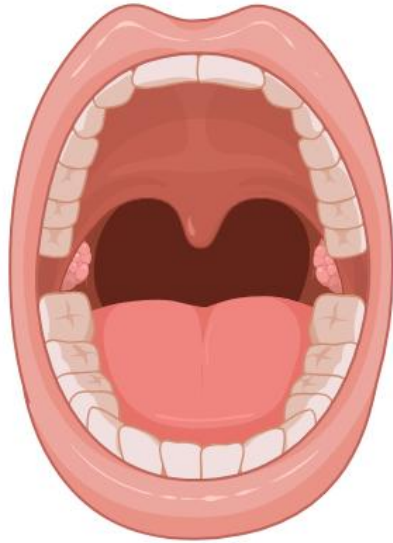
GLP-1 RA injection and oral delivery challenges



A low potency GLP-1 RA peptide

Niu, et al. J. Control Release 2025;378:92-102

Buccal administration: alternative to injected and oral

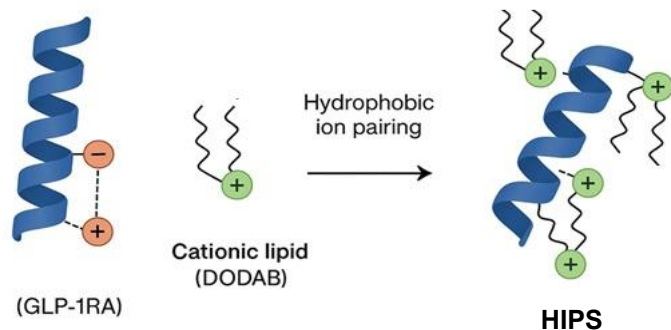


- Avoids liver first-pass metabolism
- Rapid onset
- Avoids food interaction
- High patient adherence
- Low side effect potential
- Compete with oral on bioavailability?

Malhotra, S., et al. Devices to overcome the buccal mucosal barrier to administer therapeutic peptides. *Advanced Drug Delivery Reviews* (2025): 115572.

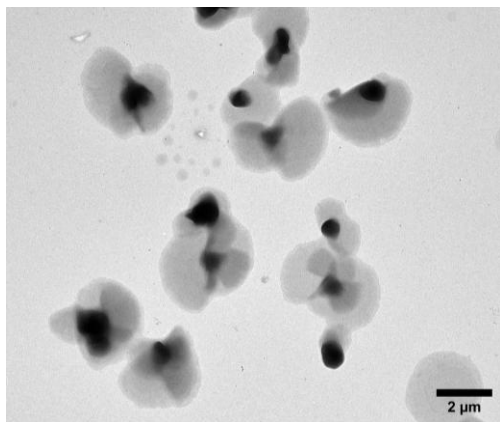
Hydrophobic ion pairs (HIP)

Hydrophobic ion pairing (HIP) is the process by which a charged hydrophilic molecule is electrostatically coupled with an oppositely charged hydrophobic counterion to produce a complex with greater hydrophobicity than the original molecule.



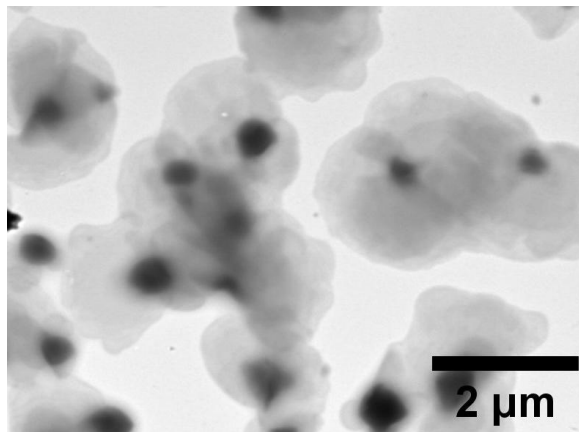
Bonengel S, et al. J Control Release. 2018;273:21-29. doi: 10.1016/j.jconrel.2018.01.012

TEM of HIPs entrapping complexes of GLP-1 RA : DODAB



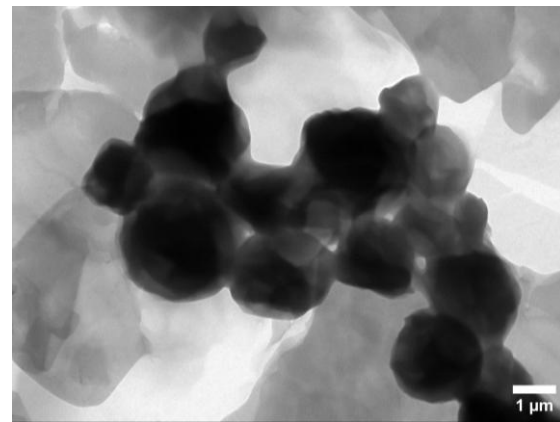
HIPs (1:4)

73% GLP-1 RA entrapped



HIPs (1:6)

89% GLP-1 entrapped

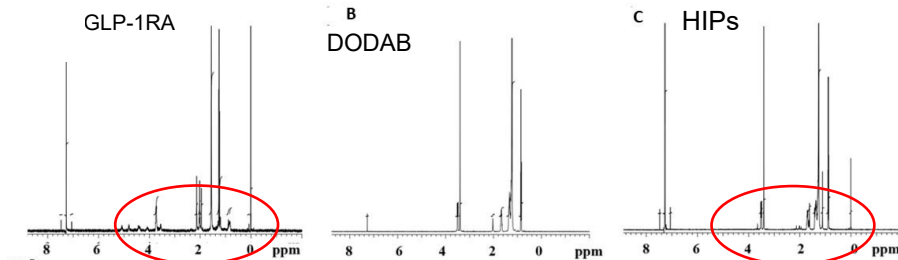


HIPs (1:8)

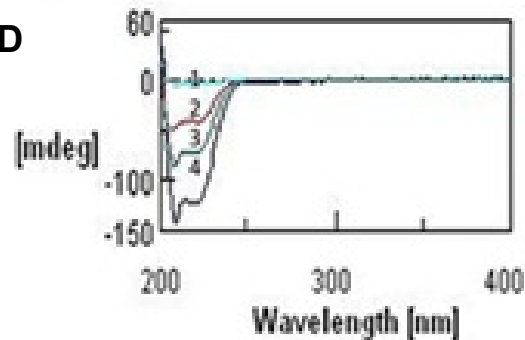
82% GLP-1 RA entrapped

Characterization of HIPs

¹H NMR

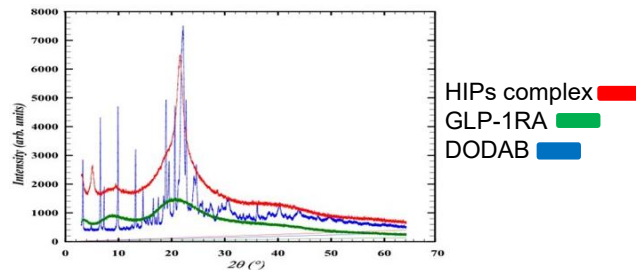


CD



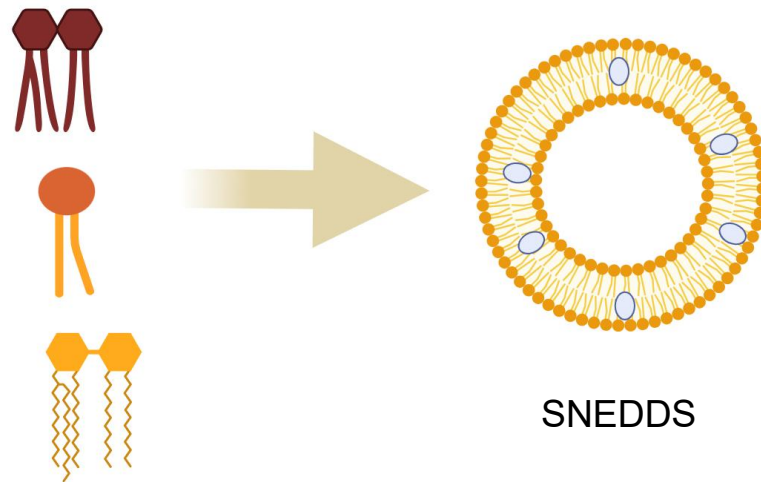
1. DODAB
2. GLP-1RA
3. HIP-1(1:6)
4. HIP-2(1:8)

PXRD



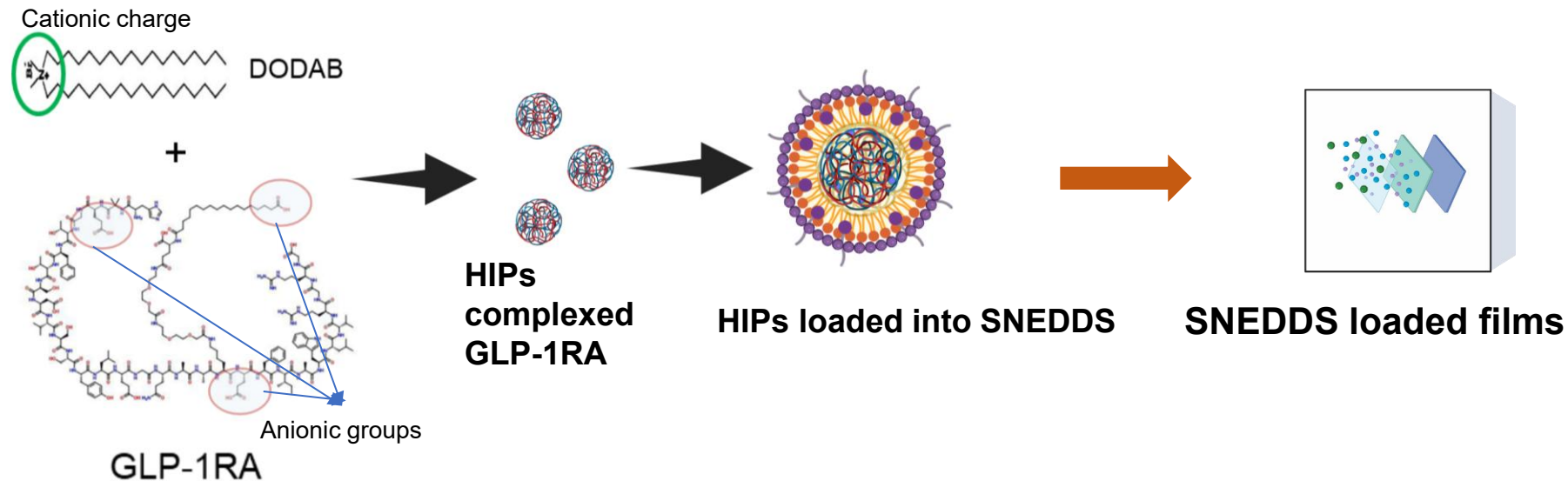
SNEDDS

A self-nanoemulsifying drug delivery system (SNEDDS) is a lipid-based formulation. It is a mixture of oil, surfactant, and co-surfactant, that spontaneously forms a nano-emulsion (tiny droplets, typically less than 200 nm) when mixed with water under gentle agitation.



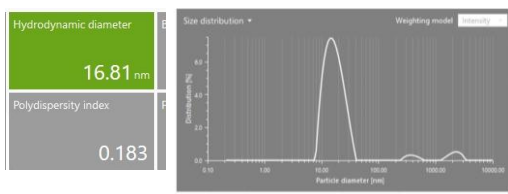
Venkatasubramanian R, et al. J Control Release ;379:440-451. doi: 10.1016/j.jconrel.2025.01.013

GLP-1 RA-HIP loaded SNEDDS for buccal films?

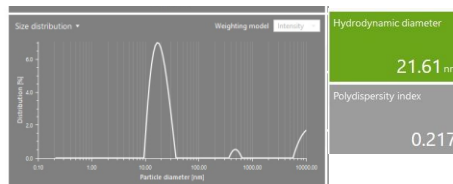


SNEDDS composition and droplet size

	Oil (%)	Surfactant (%)	Co-Surfactant (%)	Solubilizer (%)	Droplet size (nm)	PDI
	Labrafac®	Labrasol®	Transcutol®-HP	Benzyl alcohol		
SN-4	20	65	10	5	16.8	0.18
HIPs-SN4	20	65	10	5	21.6	0.21

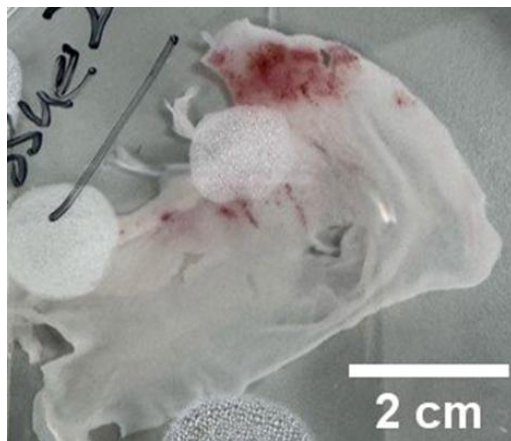
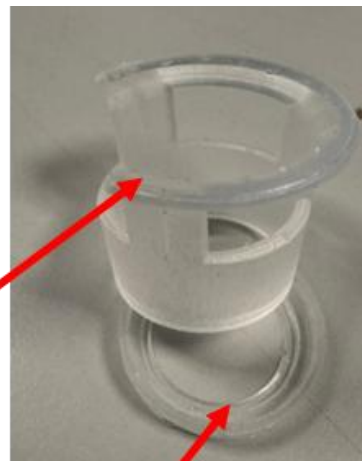


SN-4

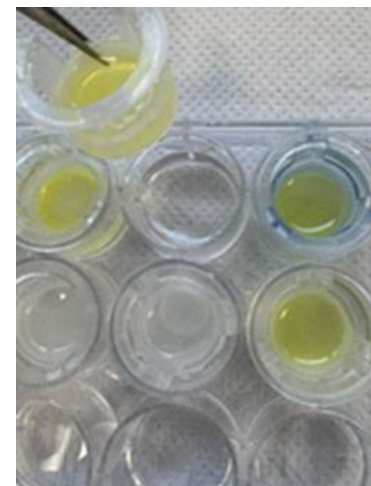


HIPs-SN4

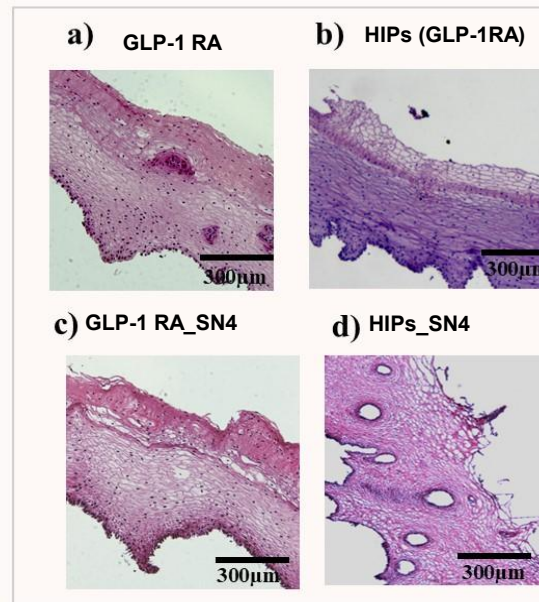
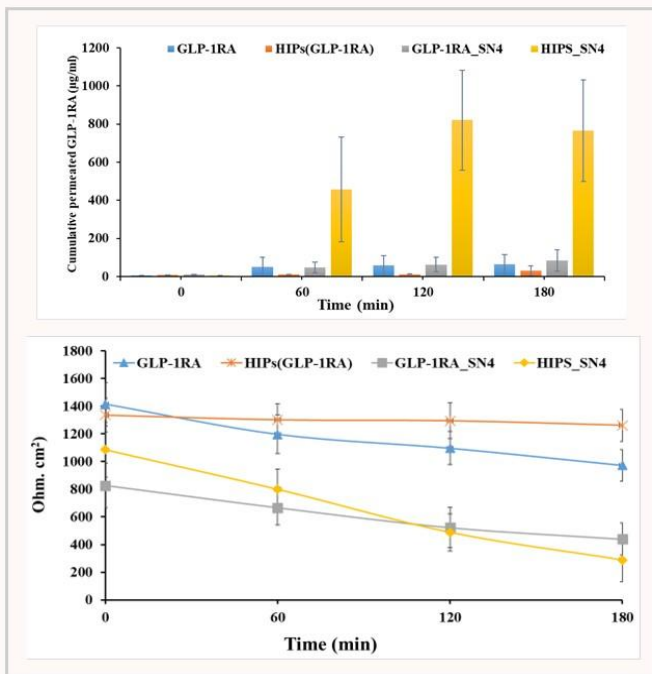
3D-Transwells for ex-vivo porcine buccal permeation



Porcine buccal tissue with holding ring



Porcine buccal permeation of GLP-1RA formulations



Conclusions

Combining SNEDDS and non-covalent lipidation (HIPs), is a promising solution to enhance GLP-1RA peptide permeability across the buccal epithelium



Uniform SNEDDS formulations have been synthesised



Designed 3D-printed Transwell inserts for testing expensive peptides



We are now formulating the SNEDDS and complexes into dissolvable buccal films for testing in pigs in vivo



Grant No: 101071054



ADHEX**PHARMA**

DTU

