Enhancing transmucosal uptake of GLP-1RA: Ionic lipidation and Self Nanoemulsifying Delivery system

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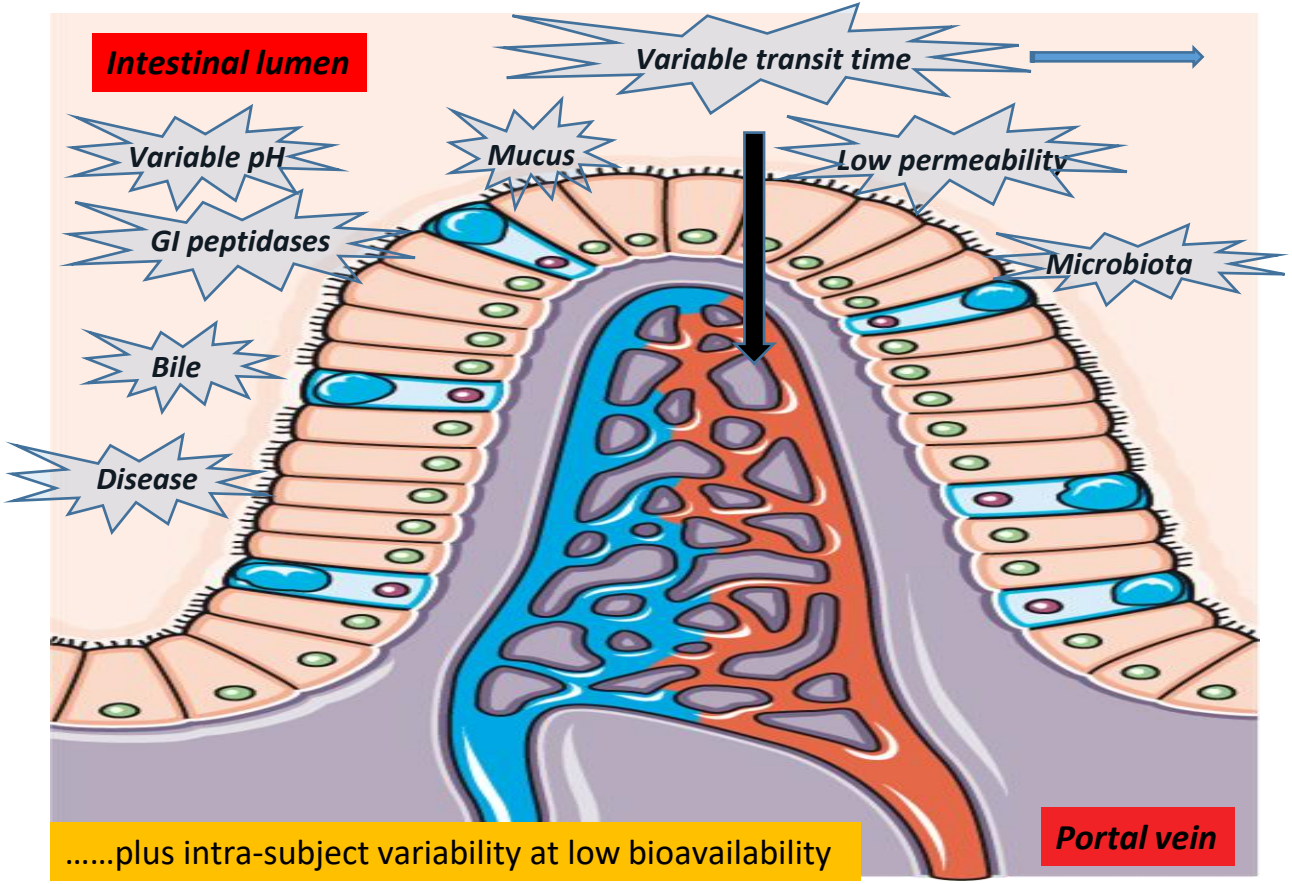
NEXT-GENERATION DELIVERY INNOVATIONS

The problems for oral peptide administration

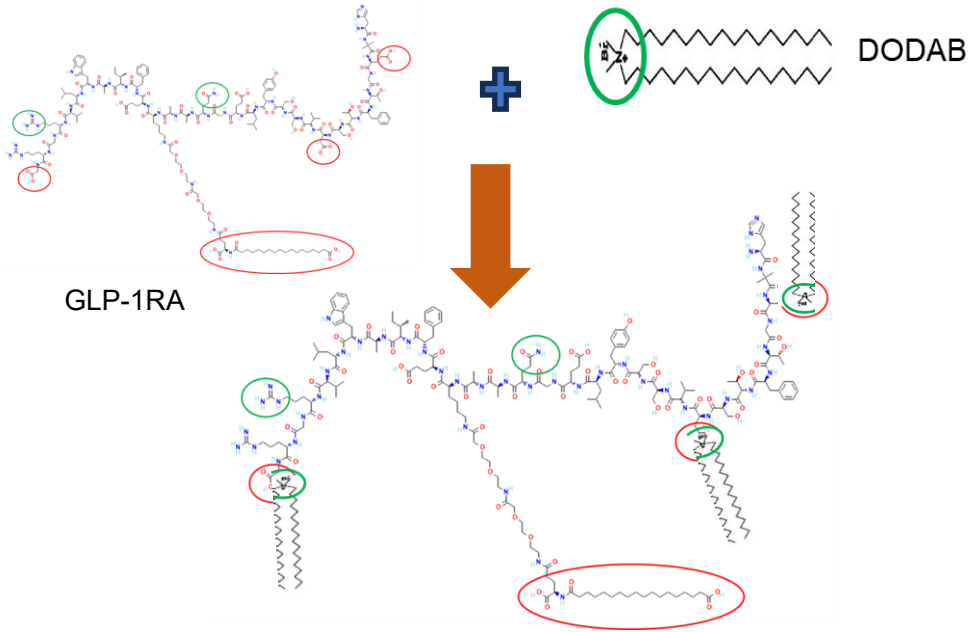


Brayden DJ, et al. (2020). Adv Drug Deliv. Rev. 157:2-36.

Hydrophobic ion pairs with a GLP-1 RA

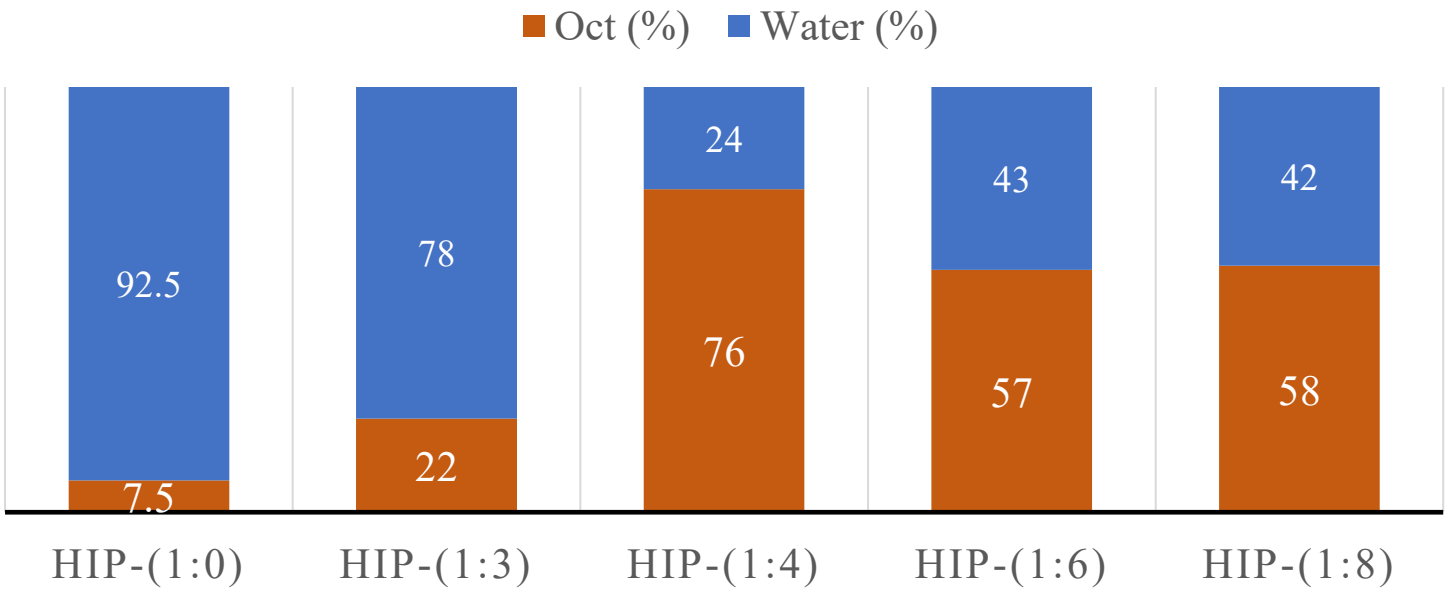
➢Hydrophobic ion pairing (HIP) is a non-covalent lipidation technique that enhances lipophilicity

➢The HIP technique does not cause loss in peptide bioactivity because complexation is reversible and secondary structure is not affected

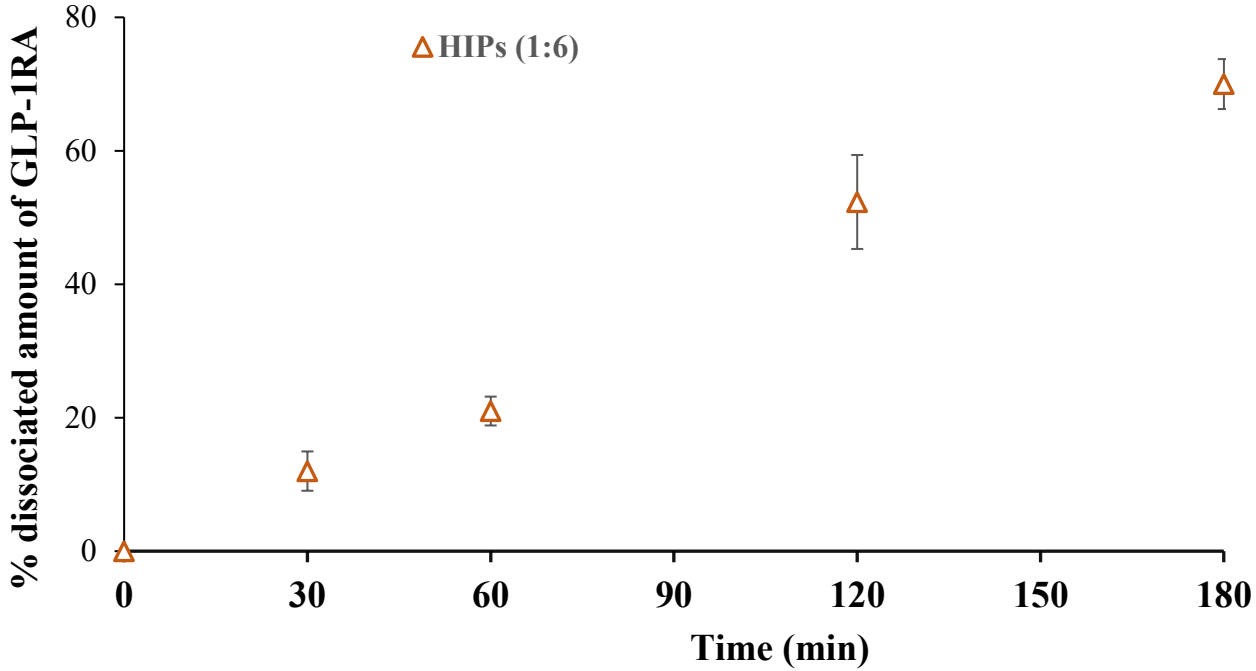


Niu, et al. J. Control Release 2025;378:92-102)

Water/Octanol Coefficients for HIPs of GLP-1 RA: DODAB



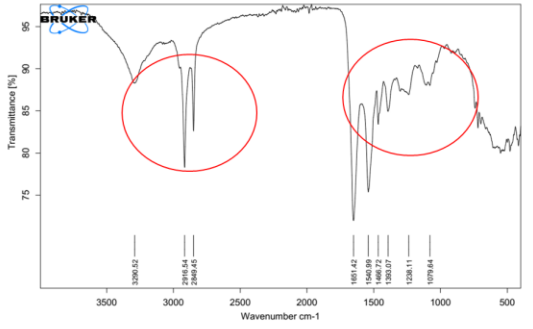
Dissociation of GLP-1RA from HIPs



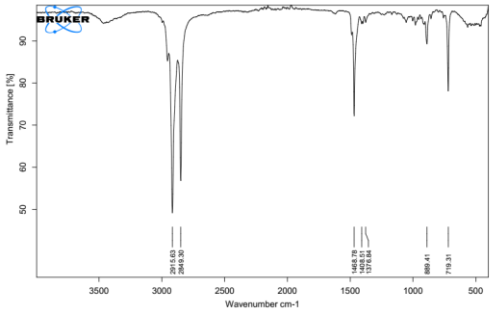
5mg HIPs were stirred in

PBS 7.4 at 37^0C for 3h

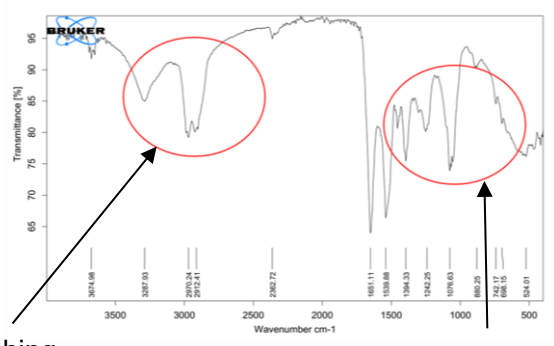
FTIR spectra of HIPs



FTIR Spectrum of GLP1-RA



DODAB



-C-H stretching

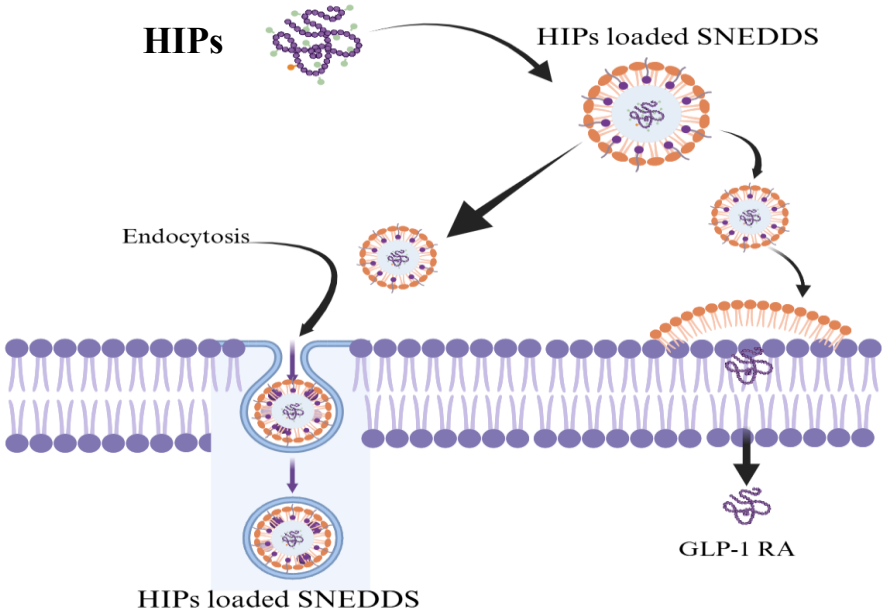
Alkyl amine
Carbonyl stretching

FTIR Spectrum of HIP complex

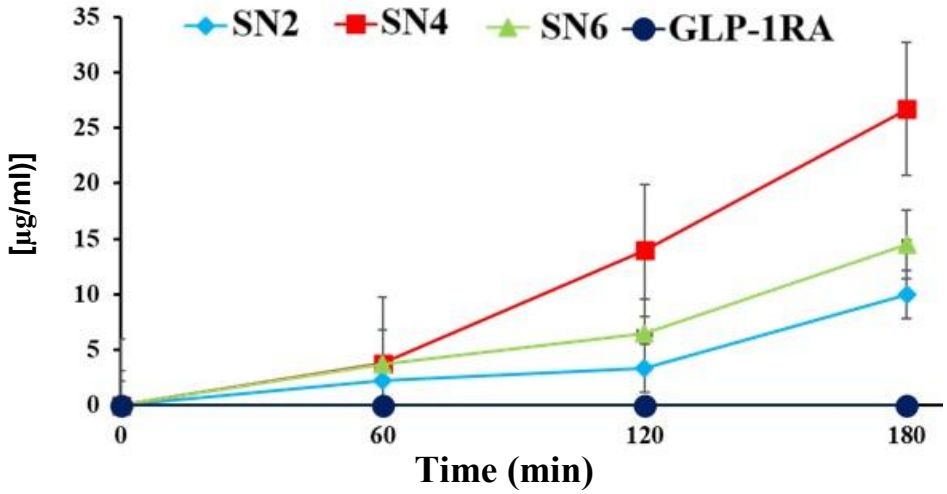
SNEDDS composition and droplet size

Formulation	Oils (%)	Surfactant (%)	Co-Surfactant (%)	Solubilizer (%)	Droplet size (nm)	PDI
	Labrafac®	Labrasol®	Transcutol®-HP	Benzyl alcohol		
SN-2	15	65	15	5	67.5	0.16
SN-4	20	65	10	5	16.8	0.18
SN-6	10	70	15	5	125.1	0.08

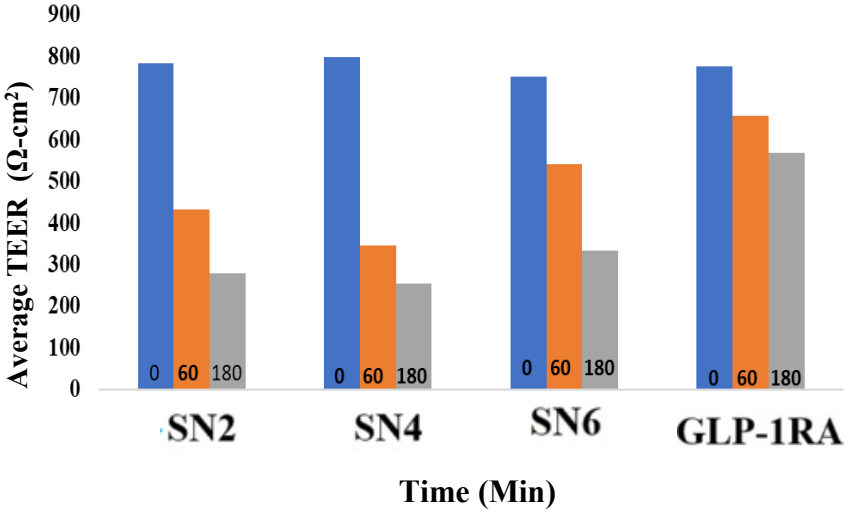
HIPs in Self Nano-Emulsifying Drug Delivery Systems (SNEDDS)



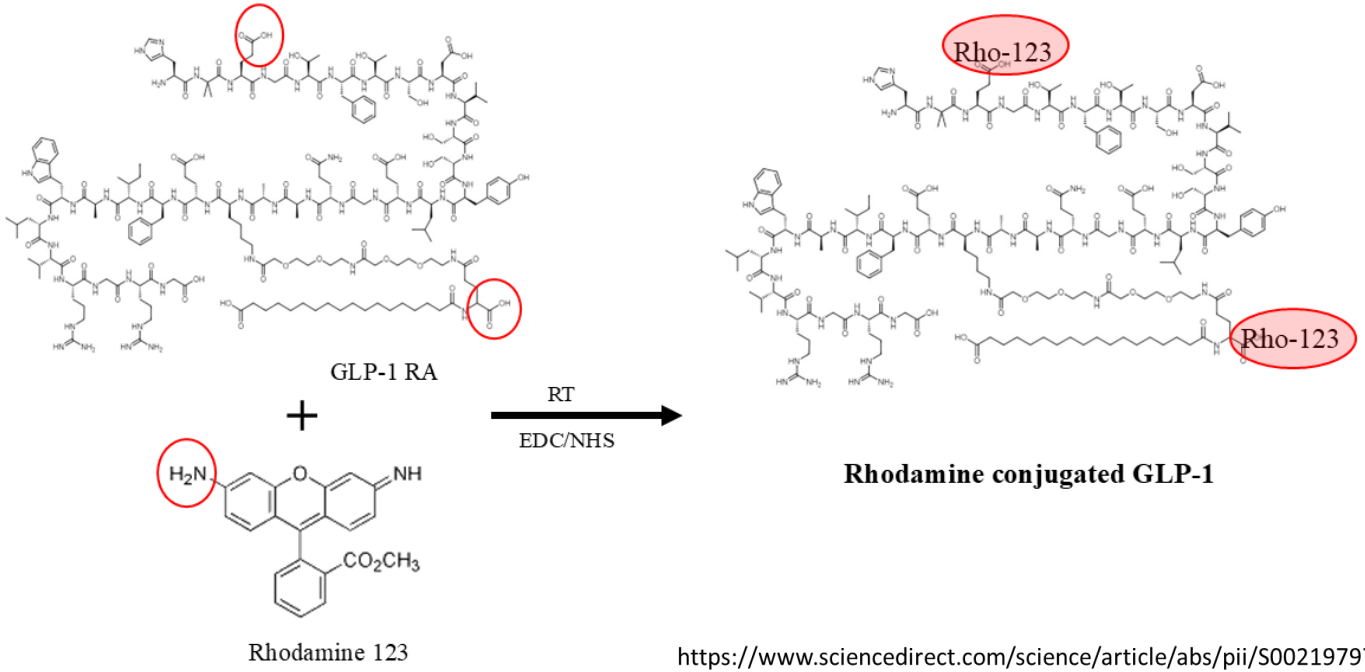
Cumulative flux of the GLP-1RA-HIPs-SNEDDS across Caco-2 monolayers



HIPs-loaded SNEDDS formulations

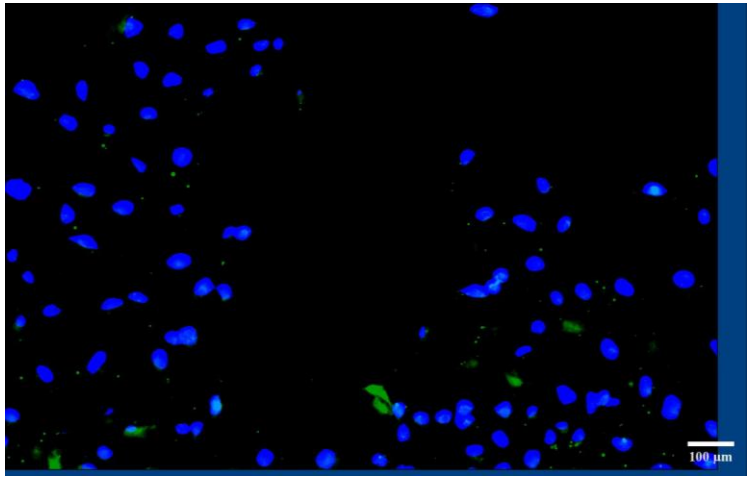


Conjugation of rhodamine with GLP-1RA

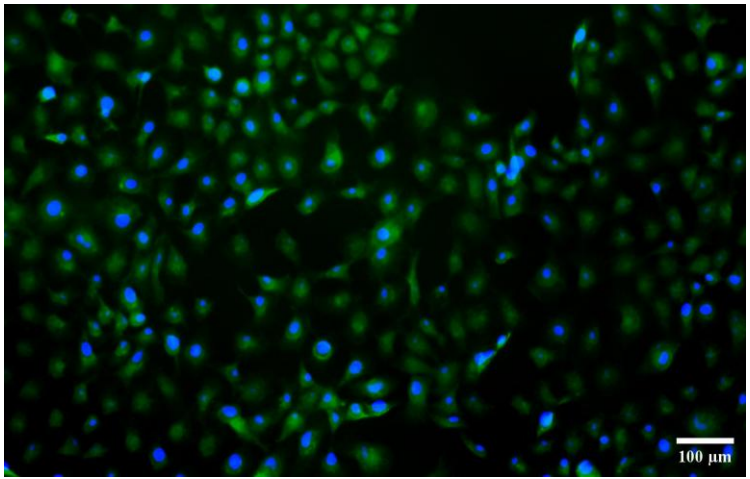


https://www.sciencedirect.com/science/article/abs/pii/S0021979721010894

Caco-2 cell uptake of GLP-1 RA-HIPs in SNEDDS



Rh-GLP-1RA (0.005mg/ml in HEPES



Rh-GLP-1RA (0.005mg/ml) loaded SN4

Conclusions

- Hydrophobic ion paired complexes with a GLP-1 RA peptide were synthesized using DODAB as the counter ion
- Rhodamine conjugated GLP-1RA incorporated within SNEDDS showed cell uptake in Caco-2 cells
- HIPS-SNEDDS formulations improved epithelial permeation of the GLP-1RA
- These formulations will be further evaluated in vivo in rat gut instillations

BUCCAL-PEP

Grant No: 101071054

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