Lipid-Entrapped GLP-1-RA Ionic Complexes in Mucoadhesive Bilayer Films: Ex-Vivo Porcine Buccal Mucosal Permeation

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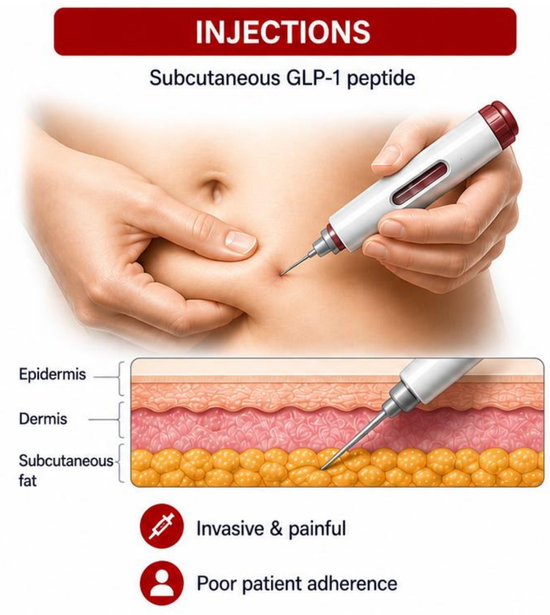
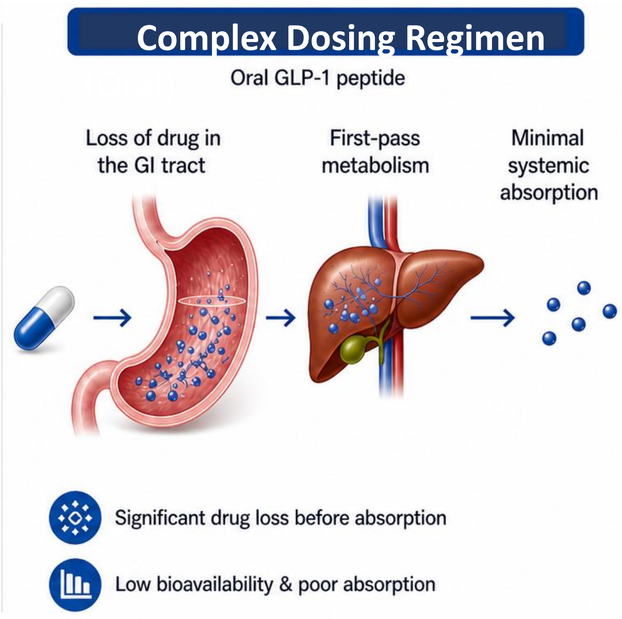
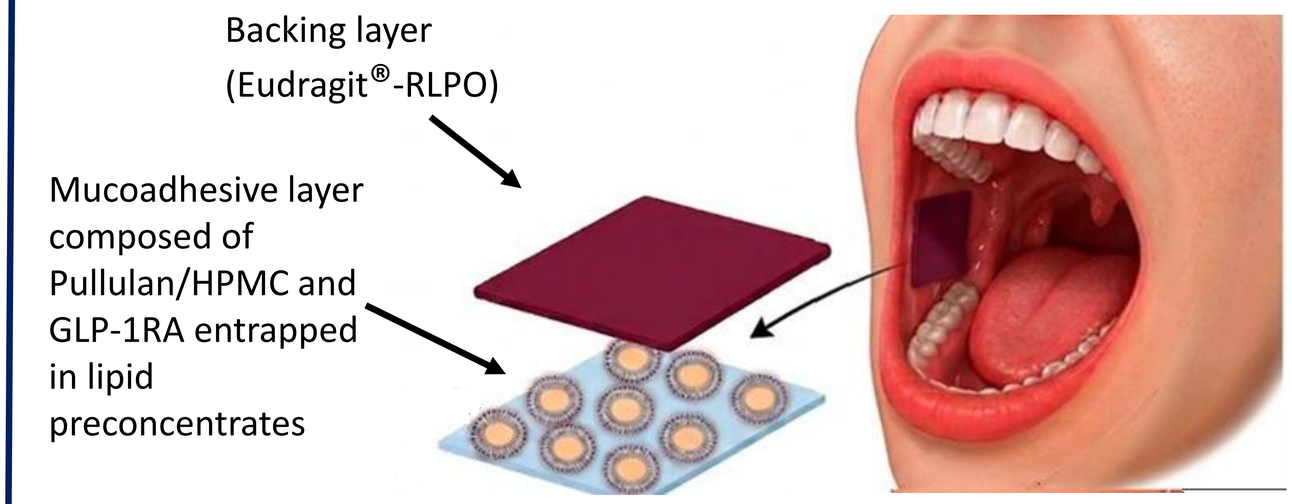
Introduction







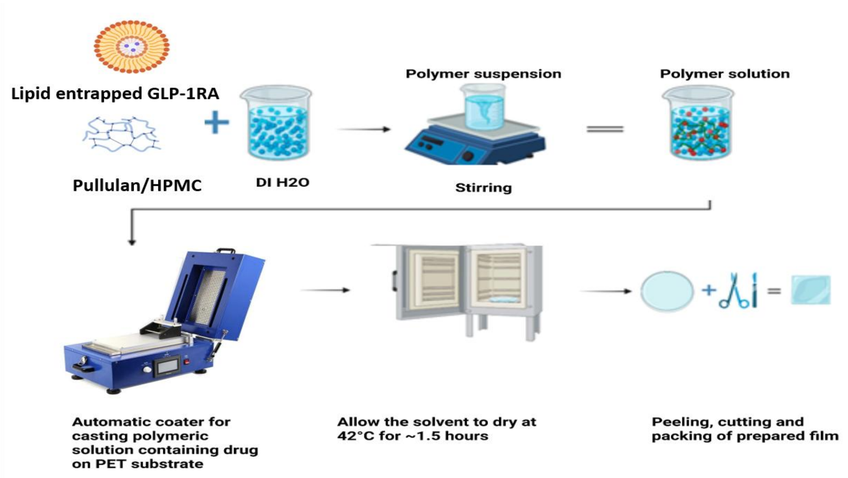
Methods/Results

1. Composition of lipid preconcentrates for entrapping GLP-1RA ionic complexes

Table 1. Droplet size characterization and compositions of lipid particulates, based on combination of different oils, surfactants and co-surfactants.

Lipid pre-conc	Oil (%)	Surfactant (%)	Co-Surfactant (%)	Solubilizer (%)	Droplet size (nm)	PDI
preconc-1	15	65	15	5	46	0.16
preconc-2	17	60	18	5	65	0.14
preconc-3	20	55	20	5	36	0.14
preconc-4	25	55	15	5	69	1.23
preconc-5	27	50	18	5	134	1.54
preconc-6	30	45	20	5	187	1.33

2. Formulation of mucoadhesive bilayer film using automatic coater



3. Uptake of fluorescently labelled GLP-1RA loaded in lipid preconcentrates

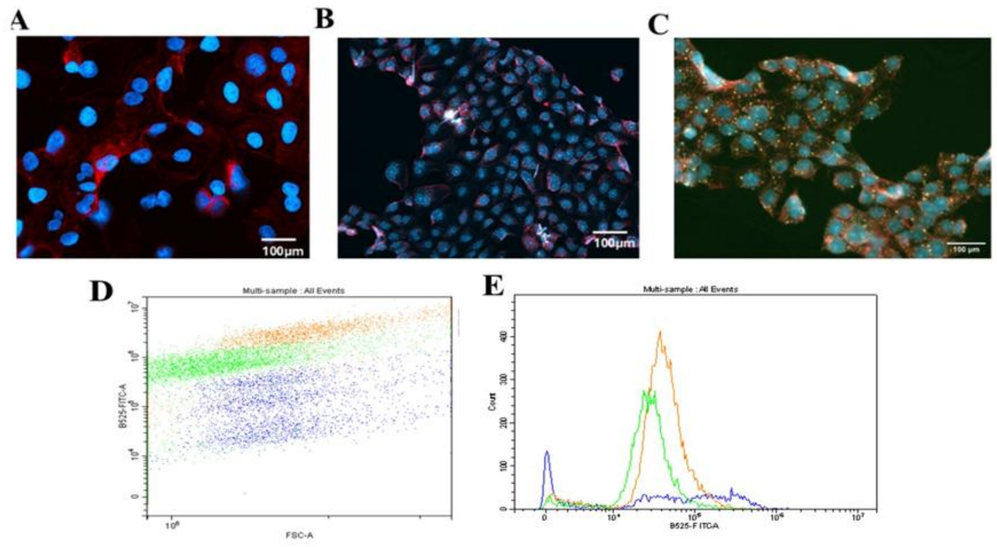


Fig. 1. Fluorescent microscopic images of (A) Blank TR146 cells treated with Alexa Fluor 647 phalloidin + DAPI, (B) TR146 cells treated with Rh-NN in PBS and stained with Alexa Fluor 647 phalloidin + DAPI, (C) TR146 cells treated with Rh-NN in Preconc-2 and stained with Alexa Fluor 647 phalloidin + DAPI, (D) Scatter plot of FITC-A fluorescence versus forward scatter area (FSC-A) for TR146 cells treated with (Blue) PBS, (Green) Rh-NN loaded in Preconc-2 and (Orange) Preconc-3. (E) Overlayed histograms showing the distribution of fluorescence intensity for TR146 cells treated with, (Blue) PBS, (Green) Rh-NN loaded in preconc-2 and (Orange) preconc-2.

4. Ex-vivo permeation of lipid entrapped GLP-1RA ionic complexes loaded into mucoadhesive bilayer film

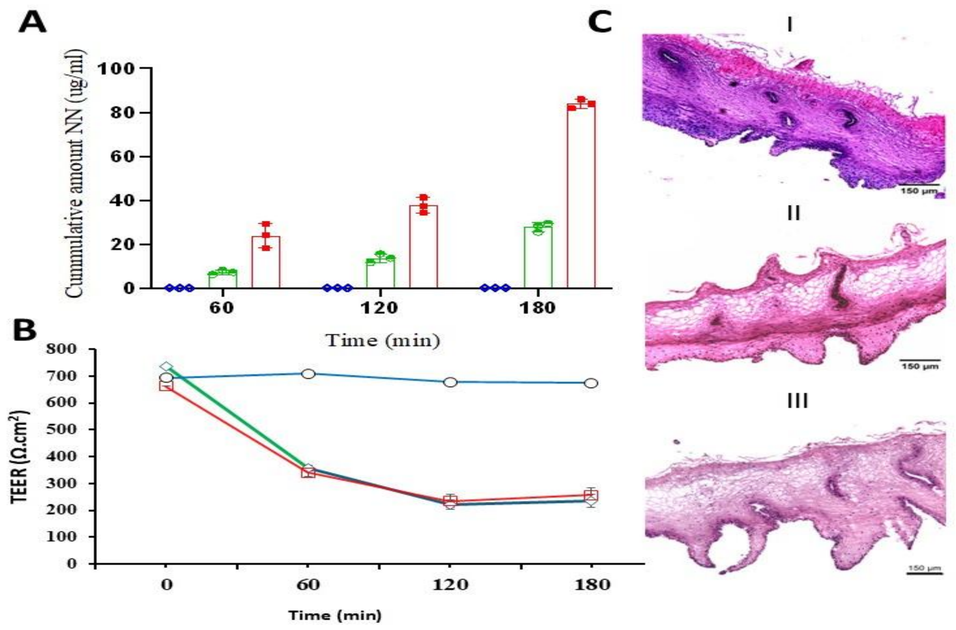


Fig. 2. (A) Ex-vivo permeation of the GLP-1 RA through porcine buccal epithelial mucosa fixed in 3D Transwell® inserts after application of GLP-1RA in PBS (Blue), HIPs loaded Preconc-2 in buccal Film F1(Green), and HIPs loaded Preconc-2 in buccal Film F2 (Red), (B) TEER value of porcine buccal tissues. (C) Histological characteristics of buccal tissue I) GLP-1RA in PBS, II) HIPs loaded Preconc-2 buccal Film F1, III) HIPs loaded Preconc-2 buccal Film F2.

Conclusion

This work supports the potential of non-covalent lipidation in the form of lipid pre-concentrate/particulate-entrapped GLP-1RA ionic complexes loaded in dissolvable mucoadhesive buccal films. This is a promising solution to enhance GLP-1RA peptide permeability across the buccal epithelium.

Reference

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2. Malhotra, S., Lijnse, T., O'Cearbhaill, E., & Brayden, D. J. (2025). Devices to overcome the buccal mucosal barrier to administer therapeutic peptides. Advanced Drug Delivery Reviews, 115572.2.

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Acknowledgements

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