Buccal delivery: Feasibility and Stability Using Isothermal Dry Particle Coating (iDPC)

Anthony Rajabi
PhD student
Aston University, Birmingham, UK

CRS 2025 ANNUAL MEETING & EXPOSITION
PHILADELPHIA, PA
JULY 13-18, 2025
Aston University BIRMINGHAM UK
Pharmacy School
NEXT-GENERATION DELIVERY INNOVATIONS

The Clinical Need: Biologics Delivery Challenges

- Biologics: highly specific macromolecules
  (e.g. monoclonal antibodies, therapeutic proteins, peptides, gene therapies, vaccines).
- Sensitive to heat, mechanical stress, solvents.
- Current delivery is predominantly given invasively:
  - Painful
  - Reduced patient compliance
  - Requires trained healthcare professionals
- Cold-chain logistics increase manufacturing and distribution costs.
- There is a clinical need for:
  - Non-invasive, patient-friendly delivery systems capable of systemic delivery.
  - Manufacturing approaches that preserve protein stability and simplify production.

Buccal route

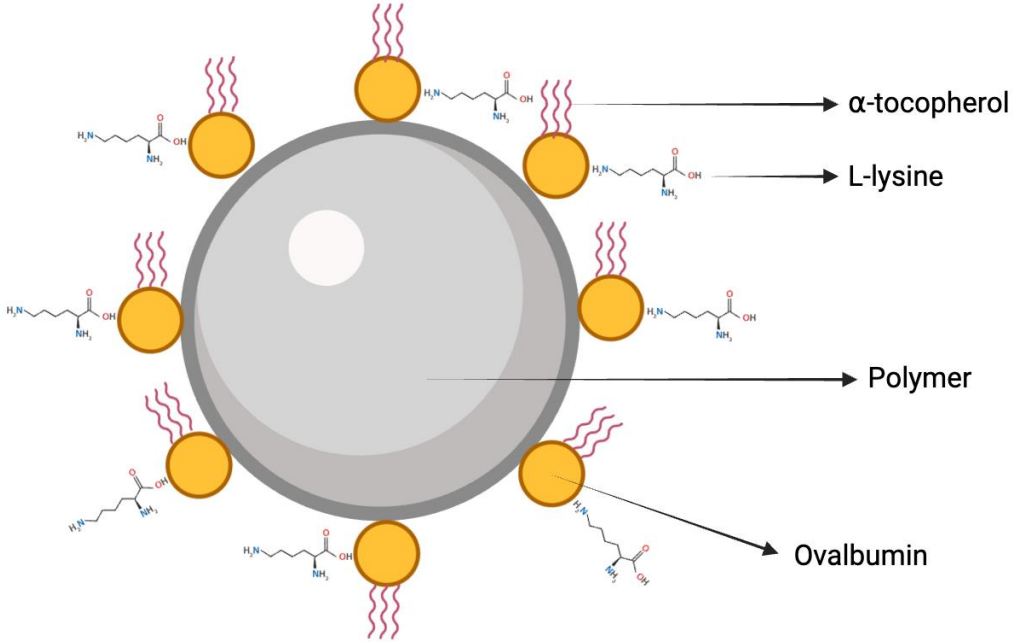
- **Buccal route:** the area of the gums and inner cheek
- **Avoids:**
  - First-pass hepatic metabolism
  - GI enzymatic degradation
  - Complex cold-chain logistics
- Potential for rapid systemic absorption
- **Key barriers:**
  - Limited permeability for large biologics
  - Salivary enzymatic degradation
  - Short mucosal residence time

Study Objective

- **Goal:** To assess buccal delivery feasibility by optimising co-localisation of a model biologic with permeation- and stability-enhancing excipients.
- **Model biologic:** Ovalbumin (OVA) (~45 kDa)
- **Technologies applied:**
  - Isothermal Dry Particle Coating (iDPC): iDPC enables dry-state particle coating via thin-layer fluidisation using nitrogen gas and rotation, without heat or solvents.
- **Evaluation:**
  - Coating efficiency, protein stability, and *in vitro* permeation (TR146 cell line)
  - FTIR, DSC, HPLC, SEM, Confocal Microscopy, Confocal Raman Mapping

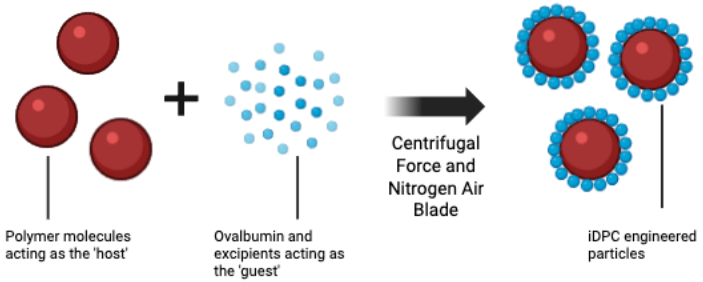
The Formulation Strategy

- **Process:**
  - Utilise an isothermal Dry Particle Coater (iDPC) to coat biologic and excipients onto carrier polymer
- **Model Biologic:**
  - Ovalbumin (~45 kDa)
- **Carrier polymer:**
  - Polyvinyl alcohol (PVA)
- **Functional excipients:**
  - L-lysine
  - α-tocopherol

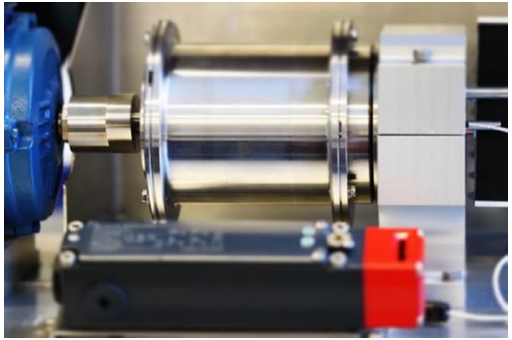


Isothermal Dry Particle Coater (iDPC)

- The iDPC processes powders in the dry state and coats small particles onto large particles without the use of heat, solvents or any physical mixing aid

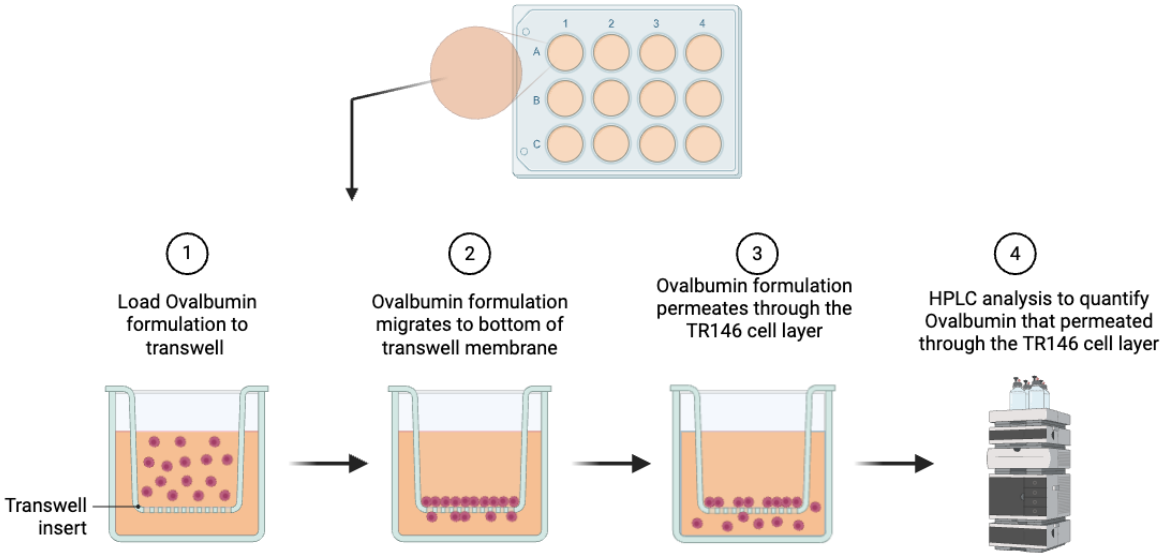


- The process parameters associated with the iDPC:
  - Time (minutes)
  - Speed (RPM)
  - Flow rate (l/min)



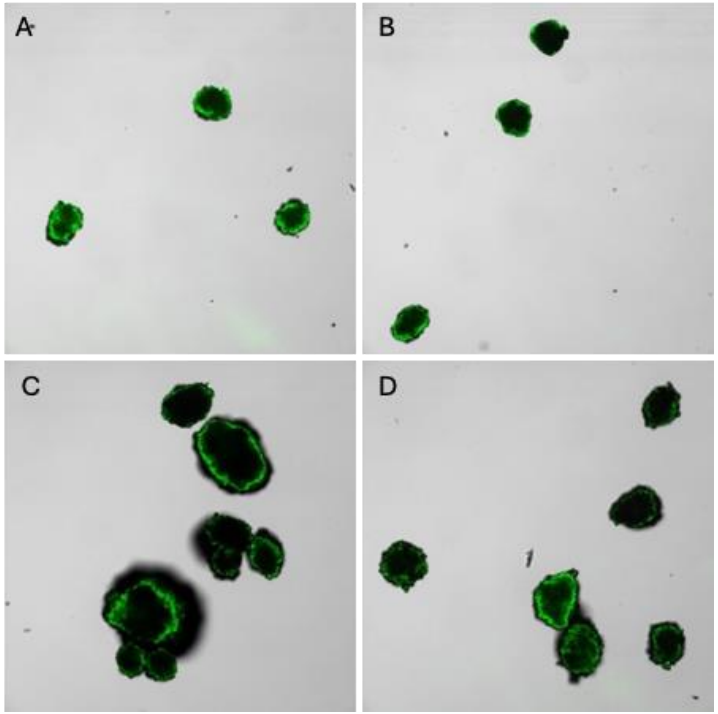
TR146 Buccal Permeation Studies

- TR146 cell line
  - TR146 is a continued cell line of human buccal epithelial origin, derived from the neck node of a 67-year-old female (primary tumour was sited in buccal mucosa)



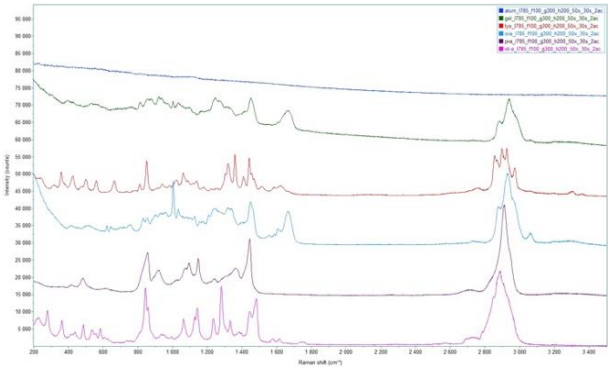
Coating Visualisation – Confocal microscopy

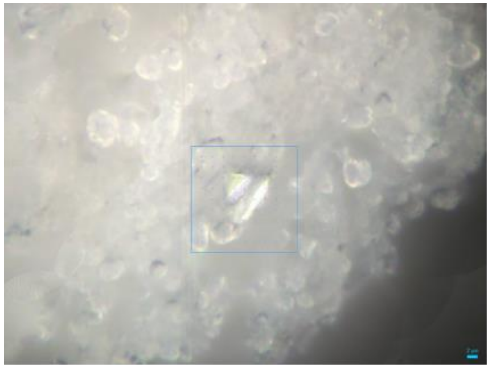
- **Objective:** Evaluate surface coating of OVA after coating with the iDPC.
- **Method:** Confocal laser scanning microscopy (FITC-labelled OVA).
- **Key observation:**
  - Uniform distribution of fluorescence across PVA particles.
  - Confirms successful surface deposition of OVA.
  - No visible aggregation or uneven coating.
- **Interpretation:**
  - iDPC allows homogenous coating of biologics onto carrier polymers.



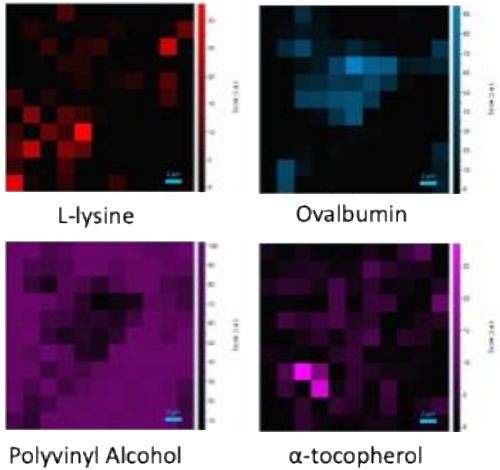
Coating Characterisation – Raman Microscopy

- **Objective:** Confirm simultaneous co-localisation of OVA and excipients on particle surface.
- **Method:** Confocal Raman mapping (CLS regression analysis).
- **Key observation:**
  - OVA, L-lysine, and α-tocopherol detected on same particle surface, confirming co-localisation.
  - Multicomponent uniform coating achieved.
  - Supports efficient multi-excipient deposition via iDPC.





100x optical, ViewSharp™ (wide)



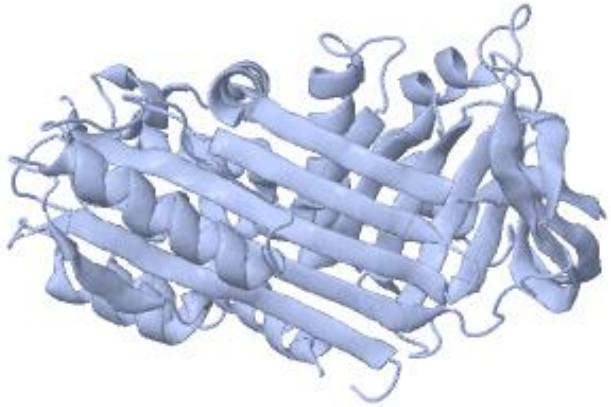
Ovalbumin Structural Stability Preserved

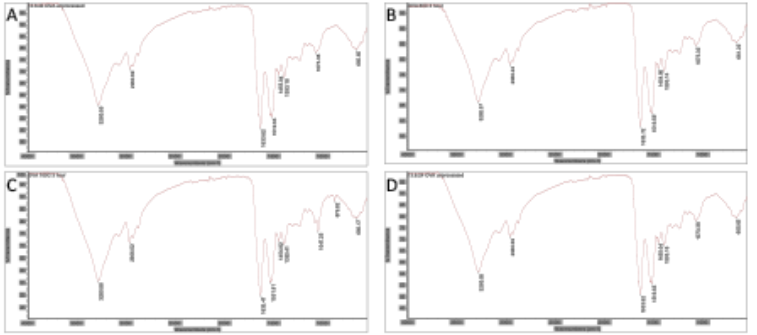
FTIR Analysis:

- Characteristic amide I (~1650 cm^{-1}) and amide II (~1540 cm^{-1}) bands associated with OVA showed no significant shifts.
- Confirms preservation of secondary protein structure post-iDPC processing.

HPLC Analysis:

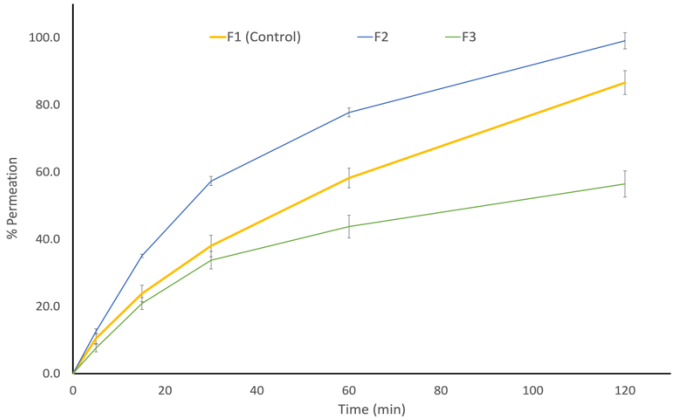
- No significant change in retention time or concentration post-iDPC processing.
- Confirms absence of significant degradation, aggregation, or loss of material.





Permeation Results

- **F1 (Control – OVA only):**
  - 86% permeation
- **F2 (iDPC + PVA):**
  - Highest permeation (~99%); significantly higher than control (F1) (P = 0.0058)
  - iDPC improved coating uniformity and excipient distribution
  - L-lysine likely formed ion-pairs with OVA → increased lipophilicity
  - α-tocopherol may have enhanced membrane fluidity via lipid domain disruption
- **F3 (Physical Mix PVA):**
  - Significantly lower permeation (~56%) than the control (P < 0.0001)
  - Highlights necessity of iDPC for functional delivery



Formulation Identifier	Composition	Cumulative Permeation %
F1	Ovalbumin (Control)	86.6 ± 3.5 %
F2	iDPC – PVA, 2% OVA, 1% L-lysine, 1% α-tocopherol	99.0 ± 2.4%
F3	Physical Mix – PVA, 2% OVA, 1% L-lysine, 1% α-tocopherol	56.4 ± 3.9%

Conclusion

- **iDPC platform:**
  - Enables ambient, solvent-free, low-shear coating of biologics
  - Preserves protein structure
  - Enables co-localisation of excipients / adjuvants and the model biologic

- ***In vitro* buccal permeation:**
  - PVA-based formulation achieved ~99% OVA permeation
  - Demonstrates feasibility for non-invasive systemic delivery of biologics

- **These findings support the feasibility of buccal delivery as a non-invasive platform for biologic administration.**

Acknowledgements & Contact

- Supervisors: Professor Afzal Mohammed, Dr. Affiong Iyire
- Collaborators: Aston Particle Technologies LTD, Birmingham, UK
  www.astonparticletechnologies.com
- Funding: Midlands Integrative Biosciences Training Partnership (MIBTP), Biotechnology and Biological Sciences Research Council (BBSRC)

- Contact: AnthonyRajabi95@gmail.com, 139166705@aston.ac.uk