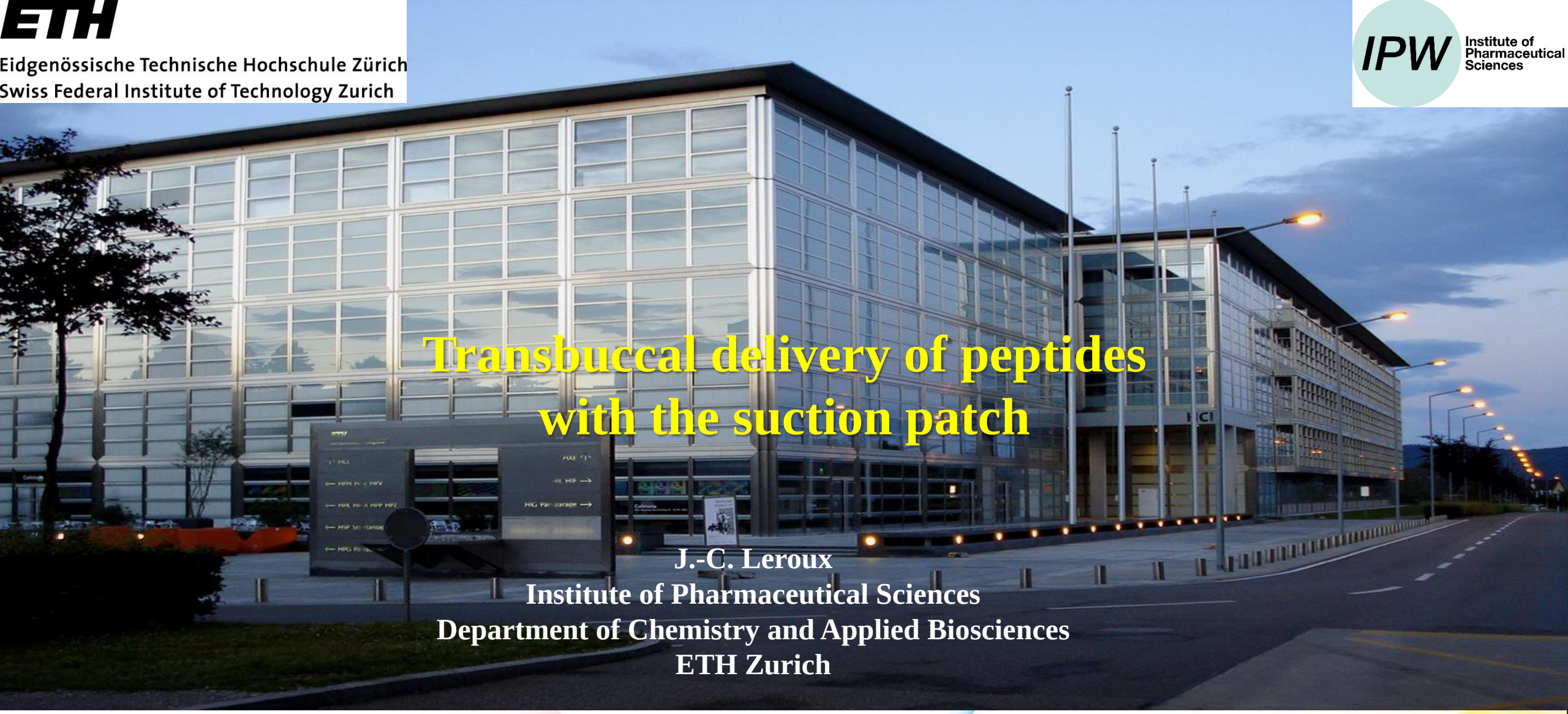


Transbuccal delivery of peptides with the suction patch

J.-C. Leroux
Institute of Pharmaceutical Sciences
Department of Chemistry and Applied Biosciences
ETH Zurich

Eidgenössische Technische Hochschule Zürich
Swiss Federal Institute of Technology Zurich

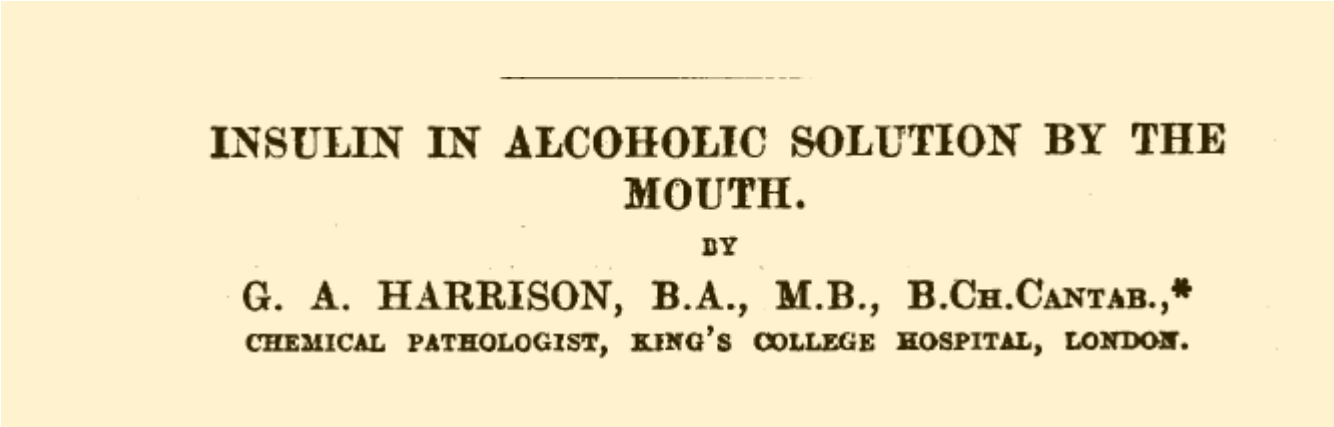
IPW Institute of Pharmaceutical Sciences

CRS 2025 ANNUAL MEETING & EXPOSITION
PHILADELPHIA, PA
JULY 13-18, 2025

NEXT-GENERATION DELIVERY INNOVATIONS

Oral delivery of proteins/peptides

Insulin was first extracted in 1921



INSULIN IN ALCOHOLIC SOLUTION BY THE MOUTH.

BY

G. A. HARRISON, B.A., M.B., B.CH.CANTAB.,*

CHEMICAL PATHOLOGIST, KING'S COLLEGE HOSPITAL, LONDON.

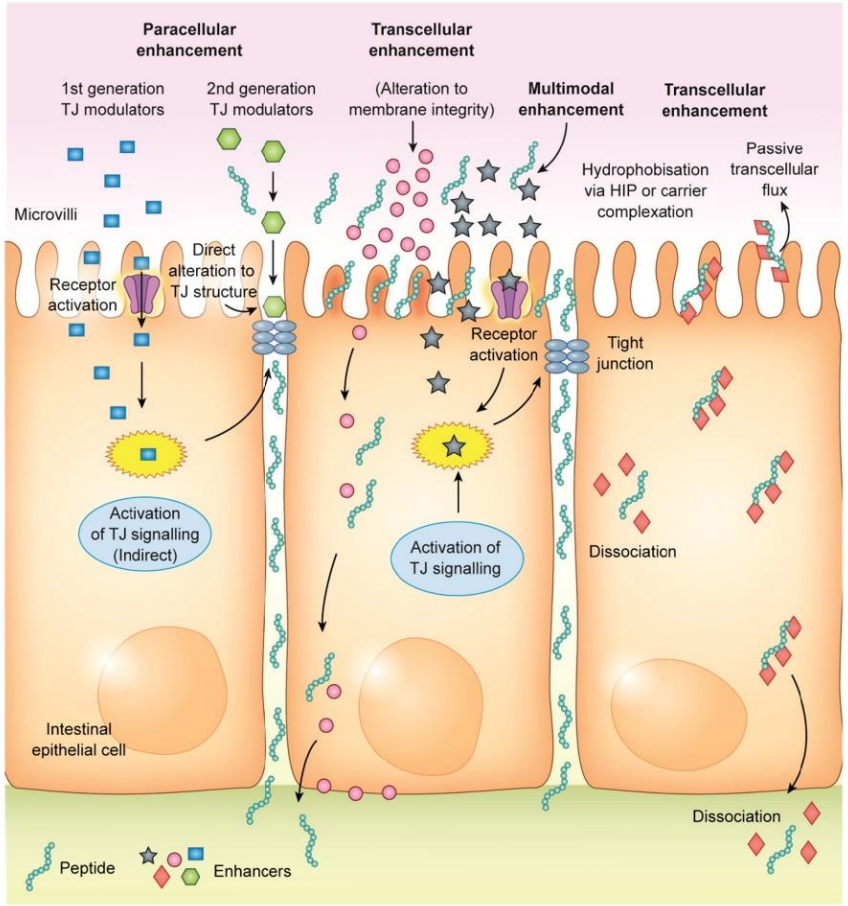
Brit Med J, **1923**

One patient, responded once

Oral delivery of peptides

Chemical means

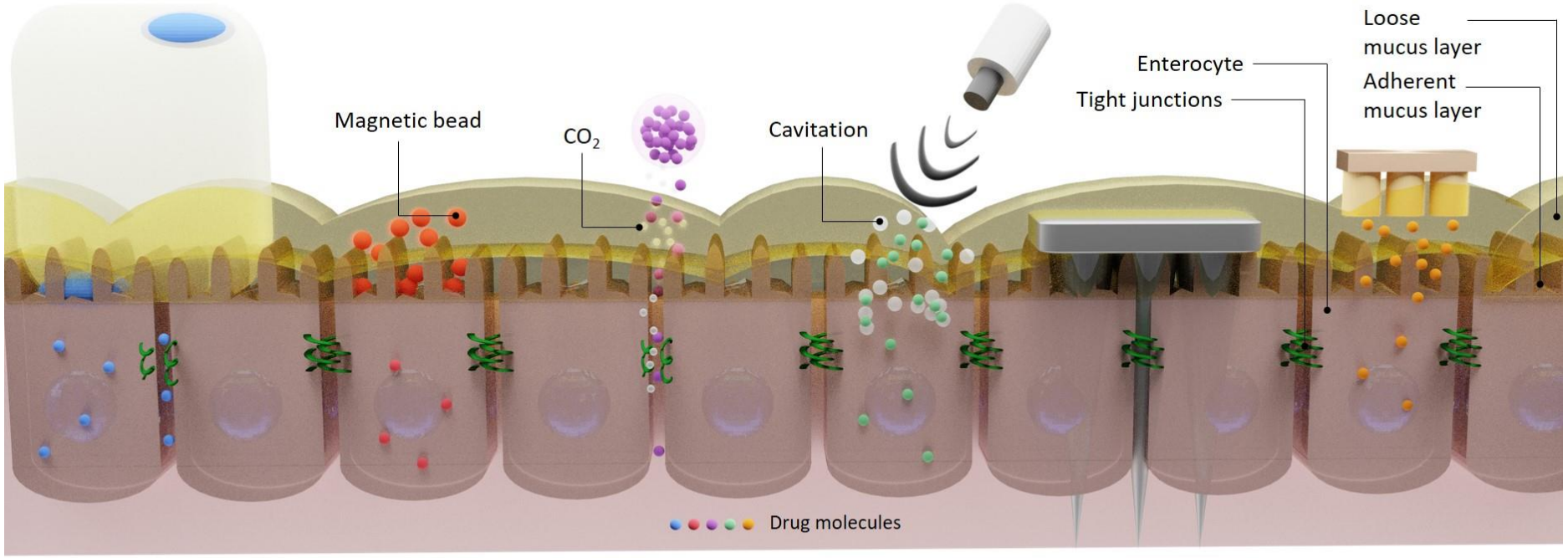
- Enteric coating
- Protease inhibitors
- Permeation enhancers



Maher S *et al. Adv Drug Deliv Rev* **106** (2016) 277-319.

Oral delivery of peptides

Physical means

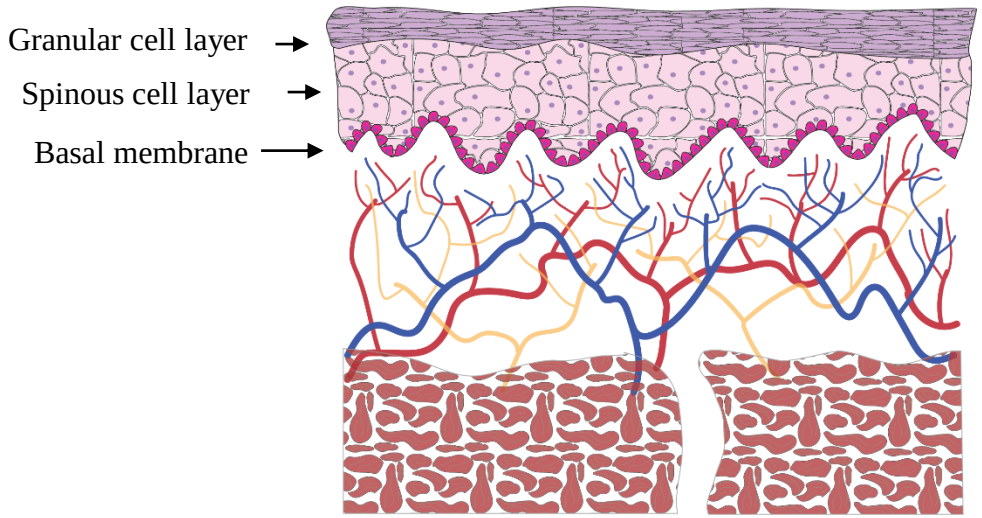


Luo Z *et al. Adv Drug Deliv Rev* **175** (2021) 113814.

Transbuccal delivery of peptides

- ☑ Easily accessible
- ☑ Low chemical & enzymatic degradation
- ☑ Thin epithelium (500 – 800 µm)
- ☑ Nonkeratinized epithelium
- ☑ No first-pass metabolism
- ☑ High epithelial turnover rate

- ⊘ Low penetration of large molecules
- ⊘ Washout
- ⊘ Low adhesion



High potential but limited success

Transbuccal delivery of peptides

Journal of Controlled Release, 21 (1992) 155–164
 0168-3659/92/$05.00

Buccal delivery for peptide drugs*

Hans P. Merkle and Gregor Wolany

Department of Pharmacy, Swiss Federal Institute of Technology Zurich (ETH), ETH-Zentrum, Zürich, Switzerland

(Received 7 July 1991; accepted in revised form 18 February 1992)

Author(s)	Year	Peptide (in vivo model)
Wieriks [34]	1964	α-Amylase (guinea pig, rat)
Earle [35]	1972	Insulin[a] (human)
Laczi et al. [36]	1980	Vasopressin-analogues[a] (human)
Ishida et al. [13]	1981	Insulin (dog)
Anders et al. [11]	1983	Protirelin (human)
Anders [10]	1984	Protirelin, buserelin (rat)
Schurr et al. [33]	1985	Protirelin (human)
Veillard et al. [37]	1987	Model tripeptide (dog, hamster)
Aungst and Rogers [25]	1988	Insulin (rat)
Aungst et al. [38]	1988	Insulin (rat)
Nakada et al. [30]	1988	Calcitonin (rat)
Oh and Ritschel [27,28]	1988	Insulin (rabbit)
Paulesu et al. [32]	1988	Interferon-α_2 (rat)
Ritschel et al. [14]	1988	Insulin (dog)
Aungst and Rogers [26]	1989	Insulin (rat)
Burnside et al. [39]	1989	Gonadorelin-agonist (sheep)
Ho and Barsuhn [40]	1989	Protirelin, oxytocin (dog)
Wolany et al. [41]	1989	Octreotide (rat)
Dowty et al. [42]	1990	Protirelin (rabbit)
Vadnere et al. [43]	1990	Leuprolide[a] (dog)
Wolany et al. [15]	1990	Octreotide (dog)
Zhang et al. [29]	1990	Insulin (dog)

[a]Sublingual administration.

Transbuccal delivery of peptides

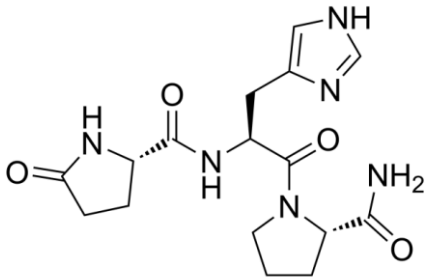
COMMUNICATIONS *J Pharm Sci* **1983**

Buccal Absorption of Protirelin: An Effective Way to Stimulate Thyrotropin and Prolactin

Keyphrases □ Protirelin—buccal absorption, stimulation of thyrotropin and prolactin, use as a diagnostic tool □ Buccal absorption—evaluation of protirelin, use as a diagnostic tool, measurement of thyrotropin and prolactin stimulation □ Thyrotropin and prolactin stimulation—buccal absorption of protirelin, use as a diagnostic tool

R. Anders
H. P. Merkle ˣ
Institute of Pharmaceutical Technology and Biopharmaceutics
W. Schurr
R. Ziegler
Department of Internal Medicine (Endocrinology)
University of Heidelberg
D-6900 Heidelberg
Federal Republic Germany

Received December 6, 1982.
Accepted for publication January 13, 1983.
Crystalline thyroliberin was generously supplied by Hoechst AG. Special gratitude is owed to Dr. M. von der Ohe.



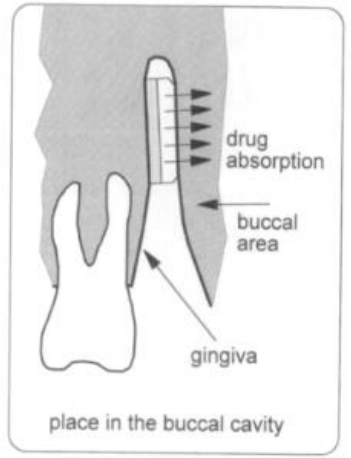
Human volunteers, 30 min application

Transbuccal delivery of peptides

Potential Therapeutic Levels of Glucagon-Like Peptide I Achieved in Humans by a Buccal Tablet

1996

Bioadhesive buccal tablet applied above the gingiva for **4.5 h**
Sodium taurocholate

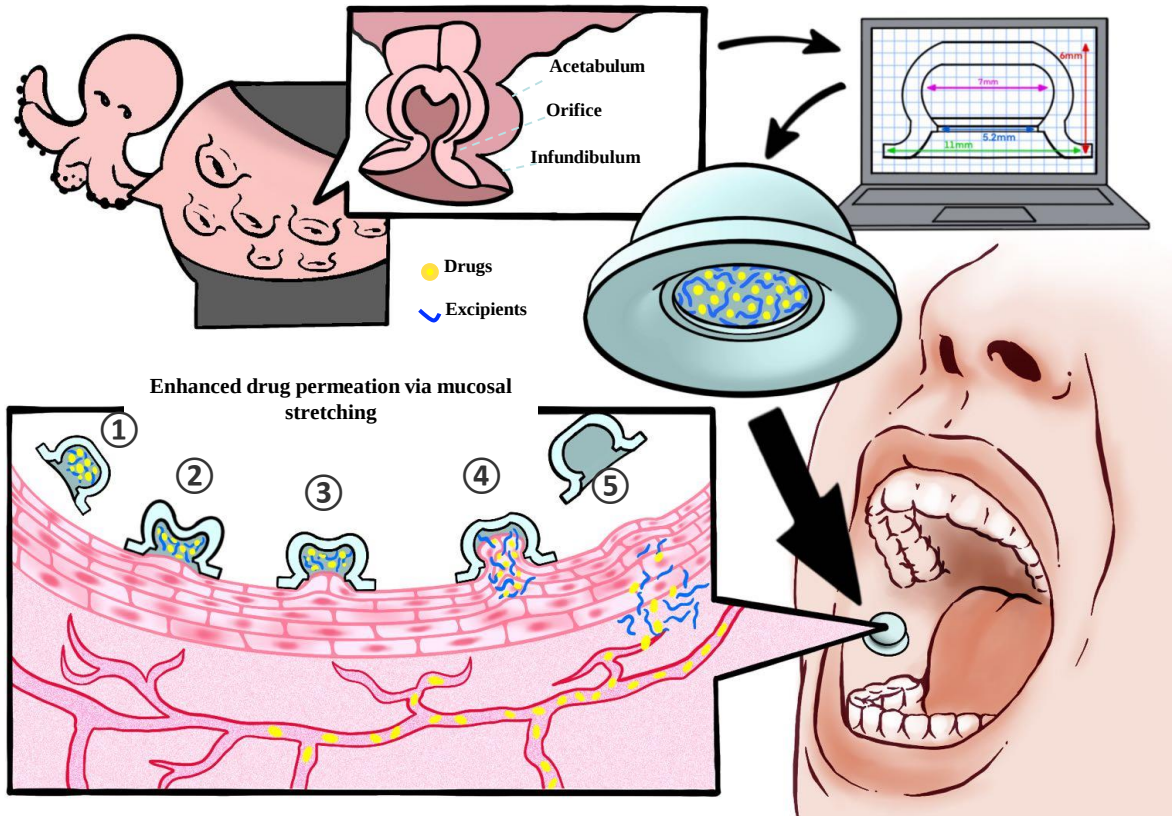


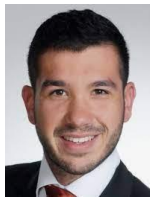
CONCLUSIONS — Therapeutic plasma levels of GLP-I in humans were achieved after a single buccal tablet. No increased degradation of GLP-I was found in the buccal mucosa compared to subcutaneous tissue. This alternative treatment form may be feasible in the future for NIDDM.

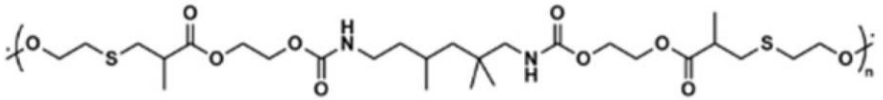
C_{max} 120 pmol/L

Gutniak MK *et al. Diabetes Care* **19** (1996) 843-848.

Transbuccal delivery of peptides

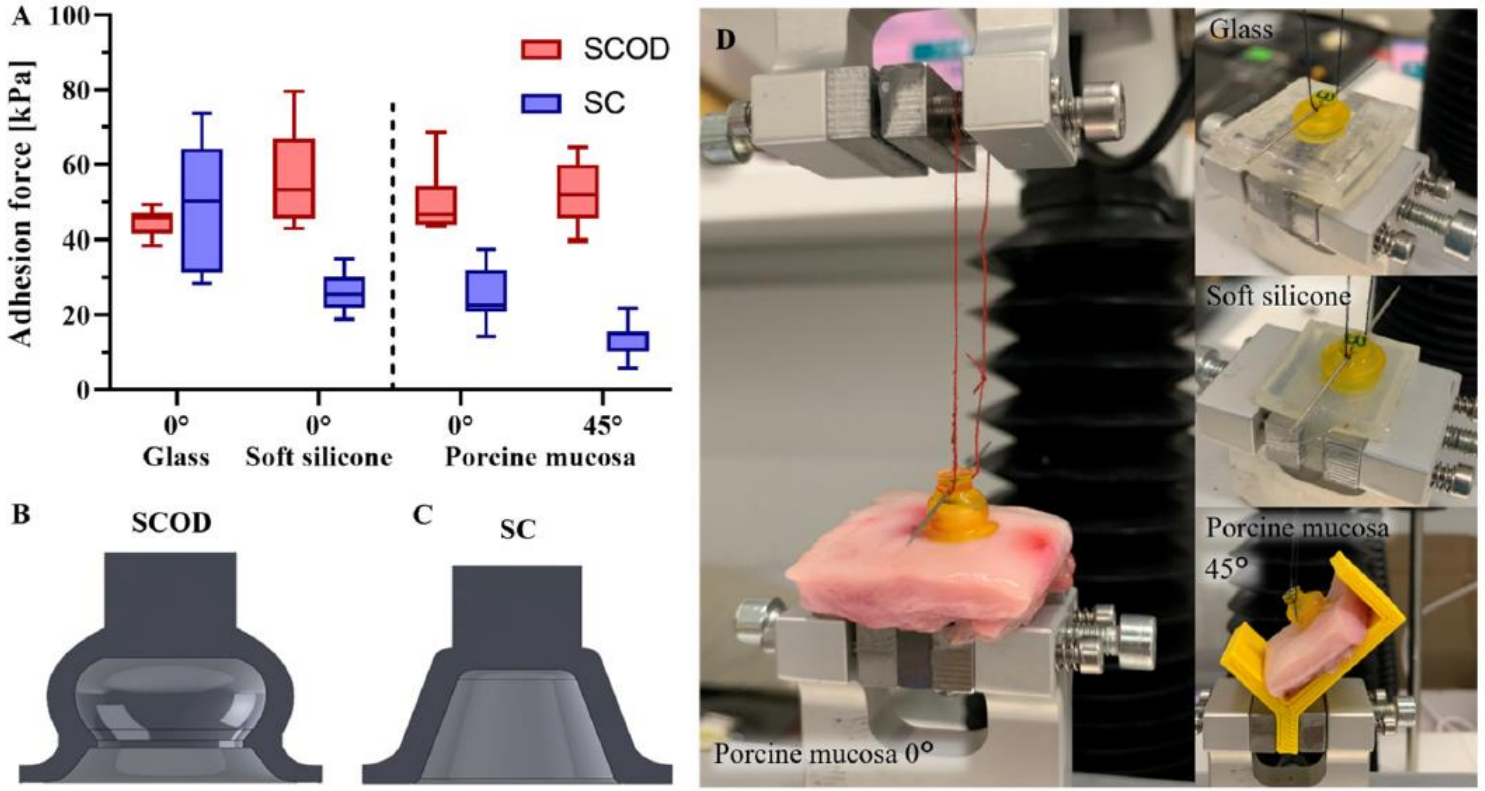






Luo Z *et al. Sci Transl Med* **15** (2023) eabq1887.

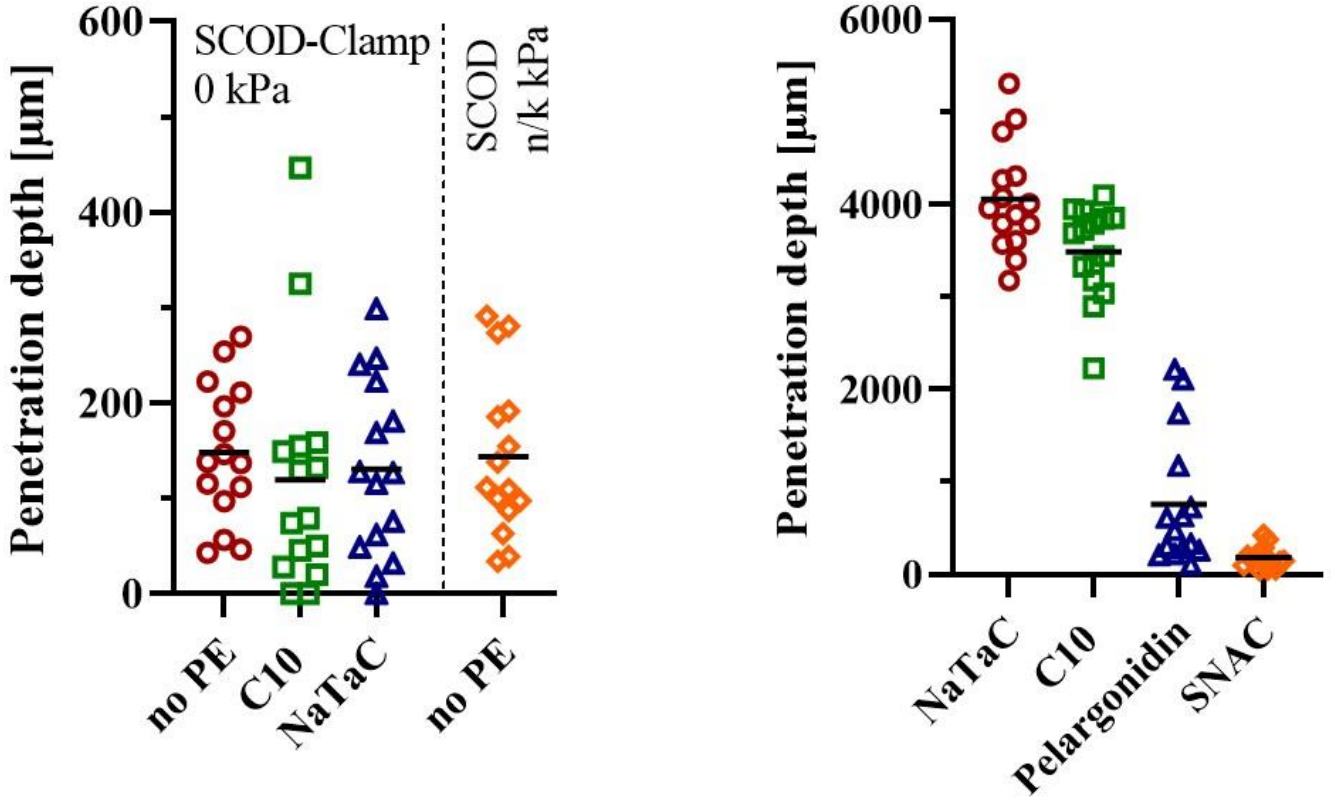
Buccal delivery of peptides



Luo Z *et al. Sci Transl Med* **15** (2023) eabq1887.

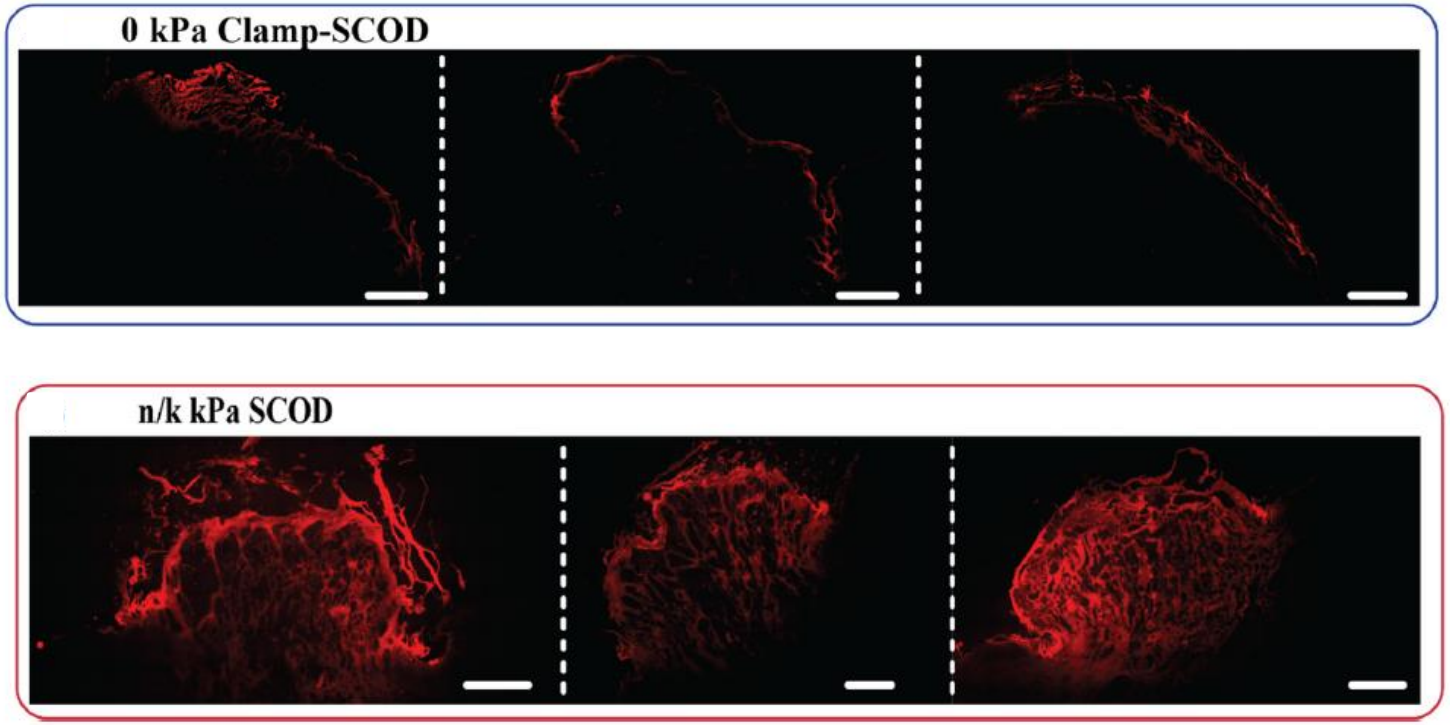
Transbuccal delivery of peptides

Permeation enhancers



Ex vivo – fresh porcine buccal mucosa – Cy5

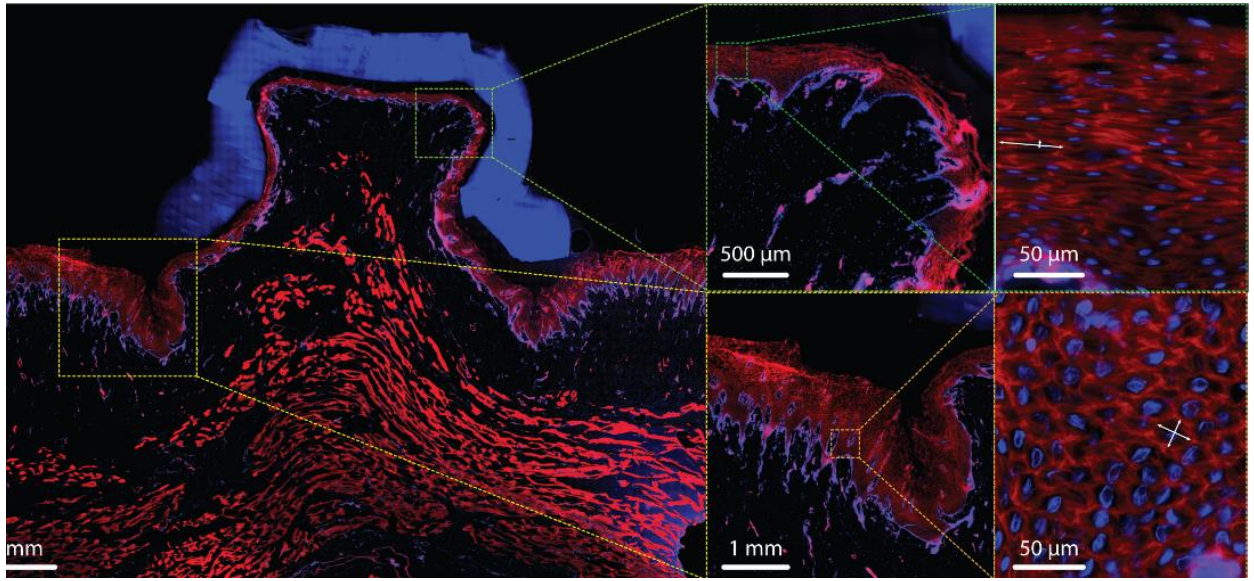
Transbuccal delivery of peptides

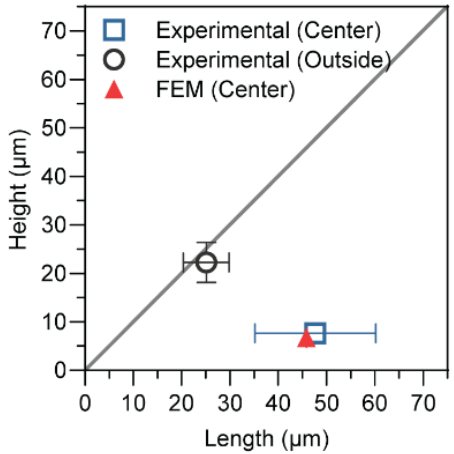


C10

Ex vivo – fresh porcine buccal mucosa – Cy5

Transbuccal delivery of peptides

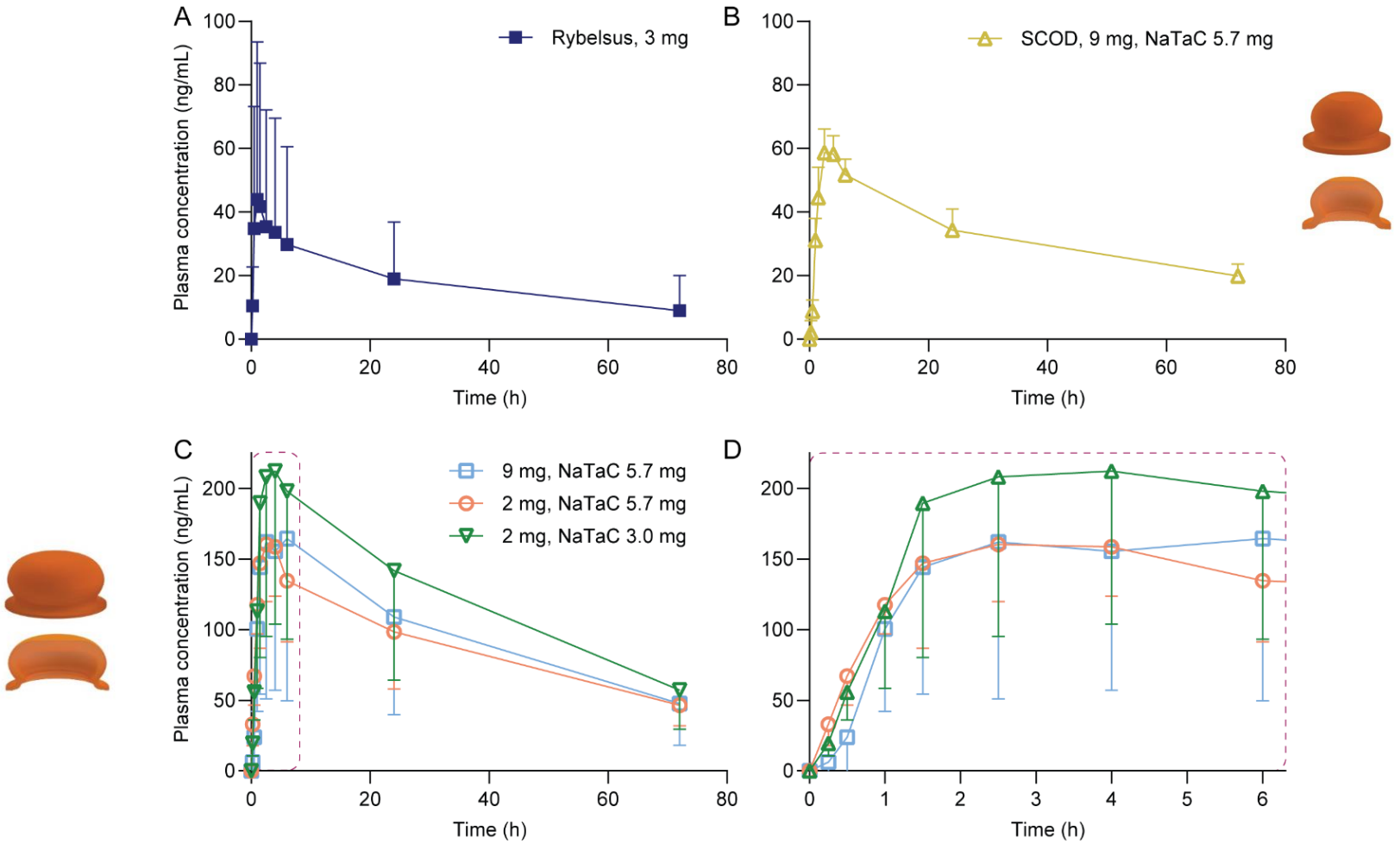




Klein D *et al*. *J Control Release* **377** (2025) 553-562.

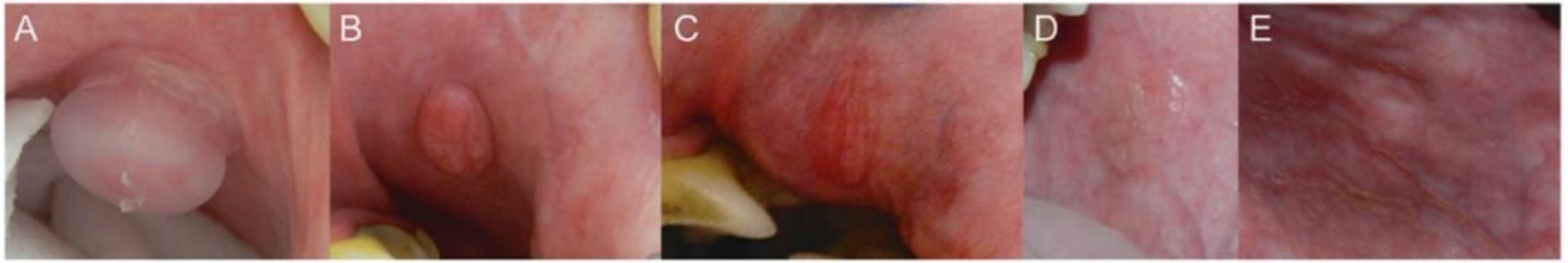
Transbuccal delivery of peptides

Beagle dogs, semaglutide (4113 g/mol), **30 min**



Klein D *et al*. *J Control Release* **377** (2025) 553-562.

Transbuccal delivery of peptides



After removal 30 min 6 h 24 h

Klein D *et al*. *J Control Release* **377** (2025) 553-562.

Transbuccal delivery of peptides

Towards more sustainable devices

t_0

Δt

Disintegrated
After max. 8 weeks in buffer

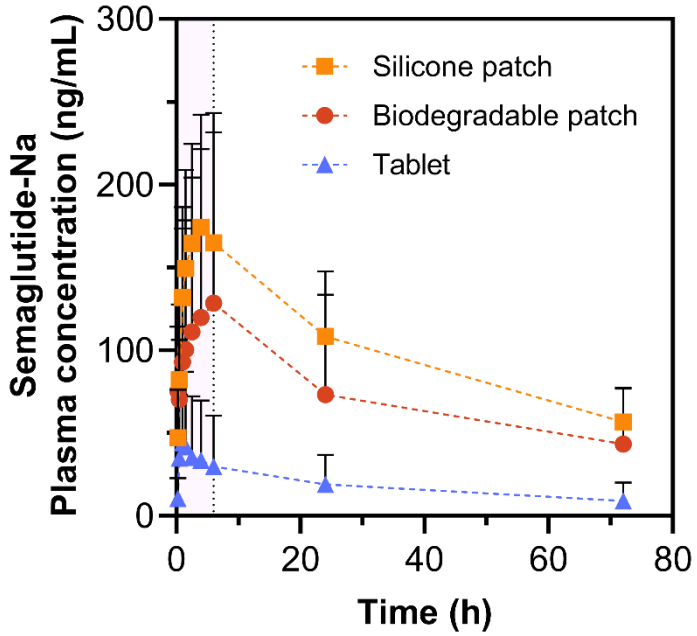
t_0

After 52 days in synthetic waste

Krupke H *et al. J Control Release* **384** (2025) 113947.

Transbuccal delivery of peptides

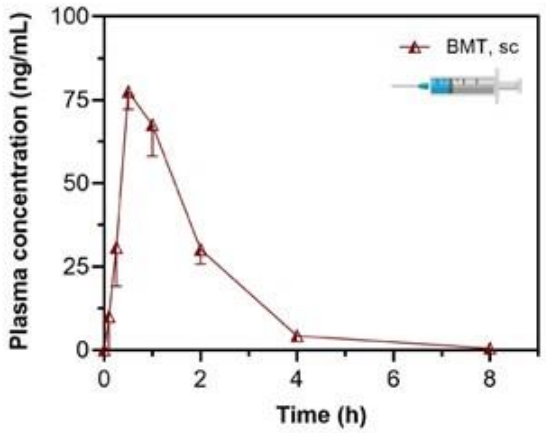
10 min

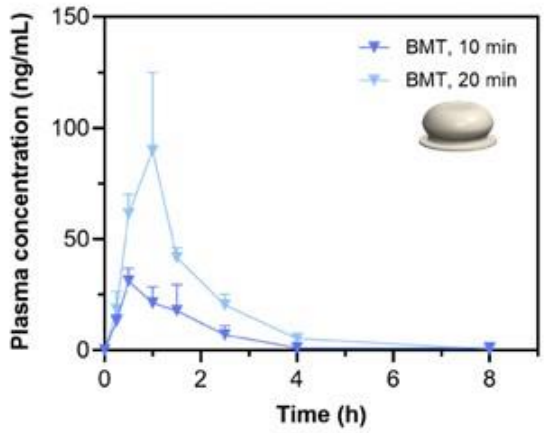


Semaglutide: 2 mg patch
3 mg tablet

Transbuccal delivery of peptides

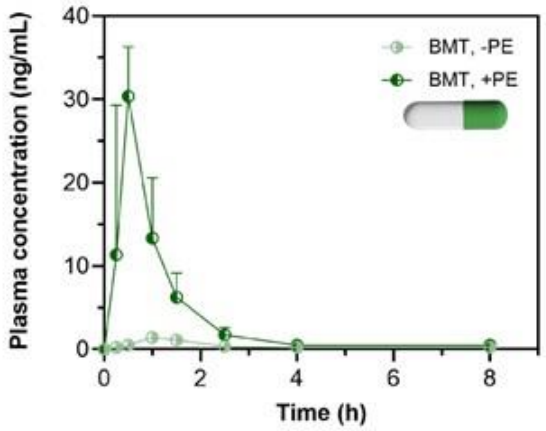
Bremelanotide (1025 g/mol)

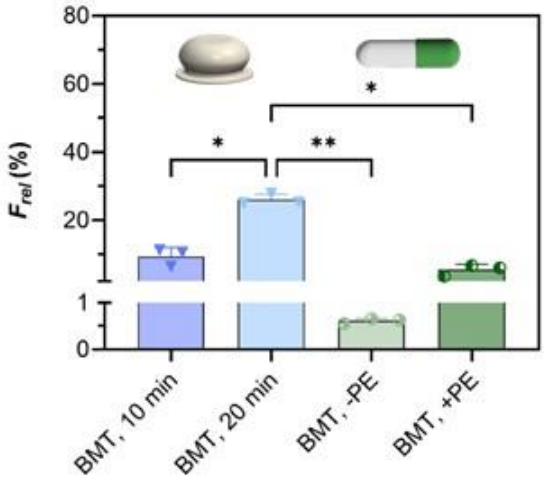




3 mg C10
No polymer

250 mg C10





Transbuccal delivery of peptides

REVIEW

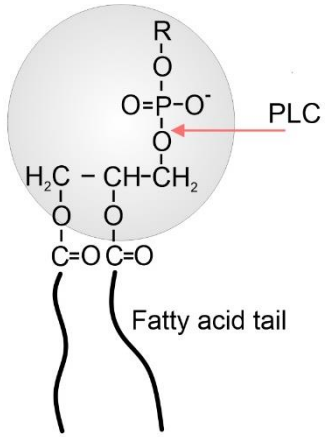
Adv Sci **11** (2024) 2400843

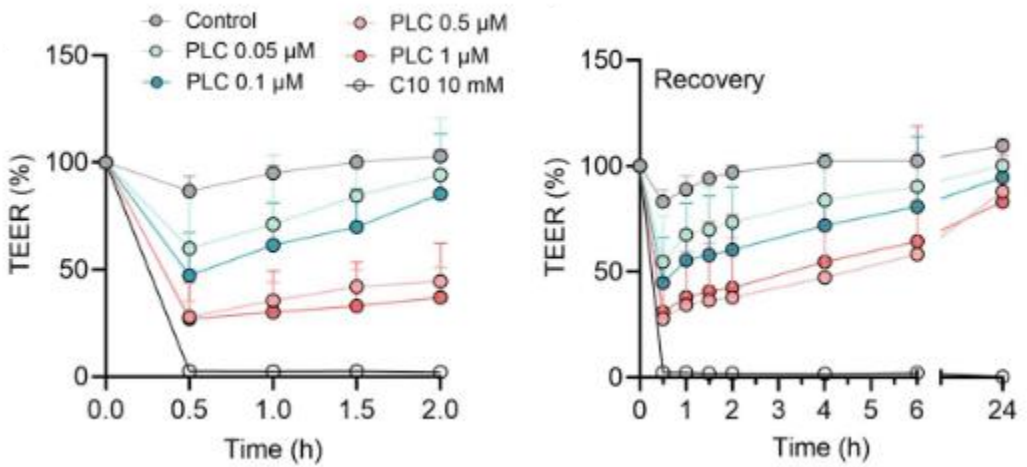
ADVANCED SCIENCE Open Access

www.advancedscience.com

Gastrointestinal Permeation Enhancers Beyond Sodium Caprate and SNAC - What is Coming Next?

*Marilena Bohley and Jean-Christophe Leroux**

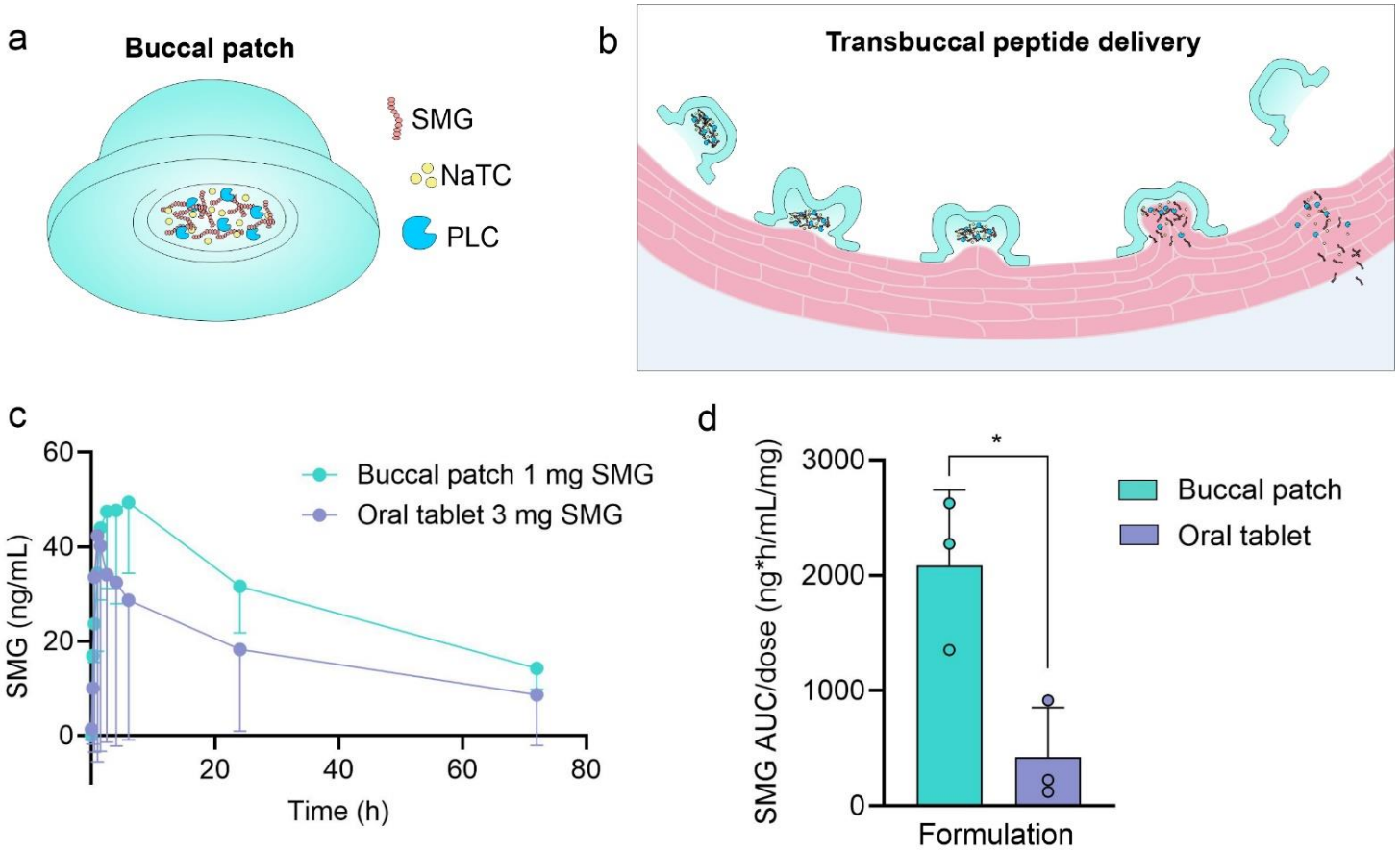




Bohley Steiger M *et al. J Control Release* **382** (2025) 113675.

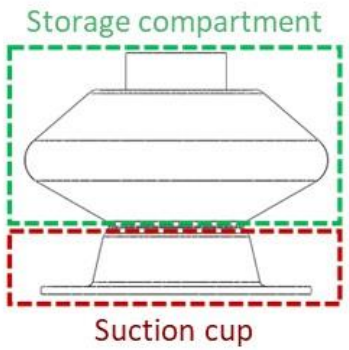
Transbuccal delivery of peptides

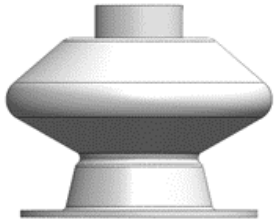
Beagle dogs, semaglutide (4113 g/mol), **10 min**

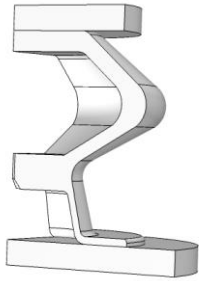


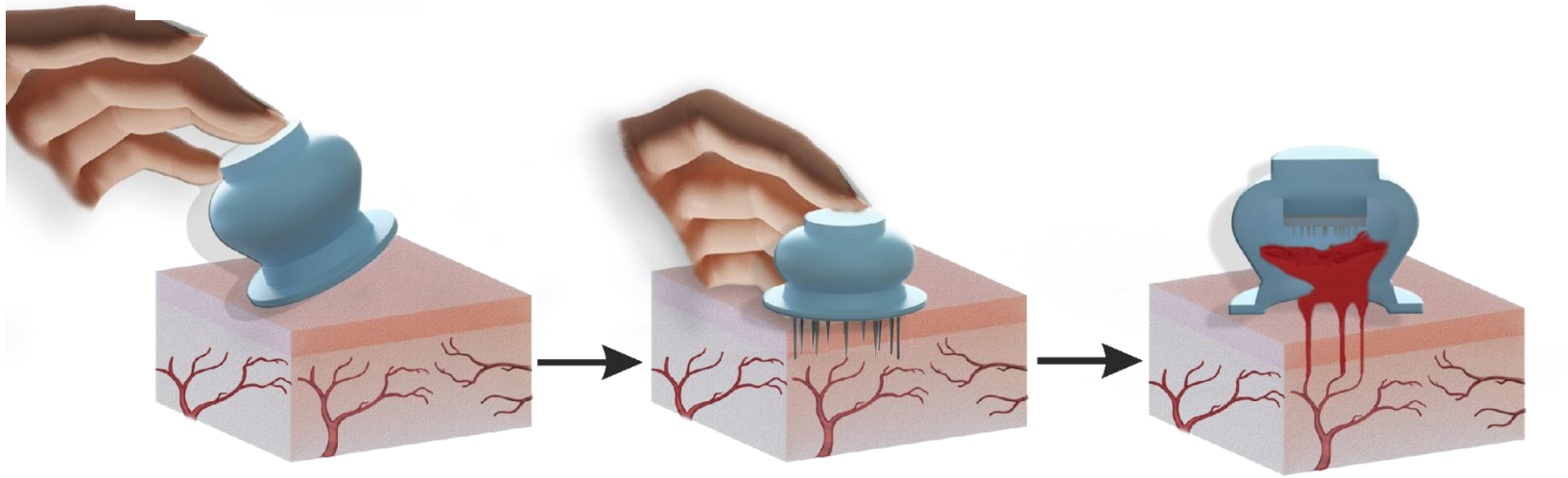
Bohley Steiger M *et al. J Control Release* **382** (2025) 113675.

Further development





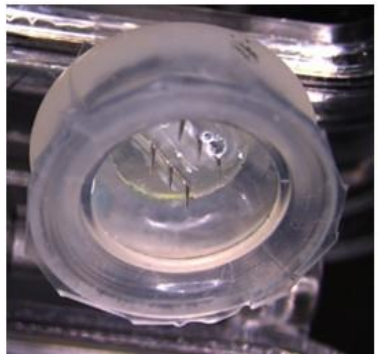


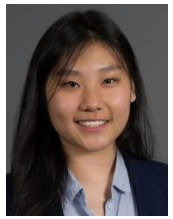


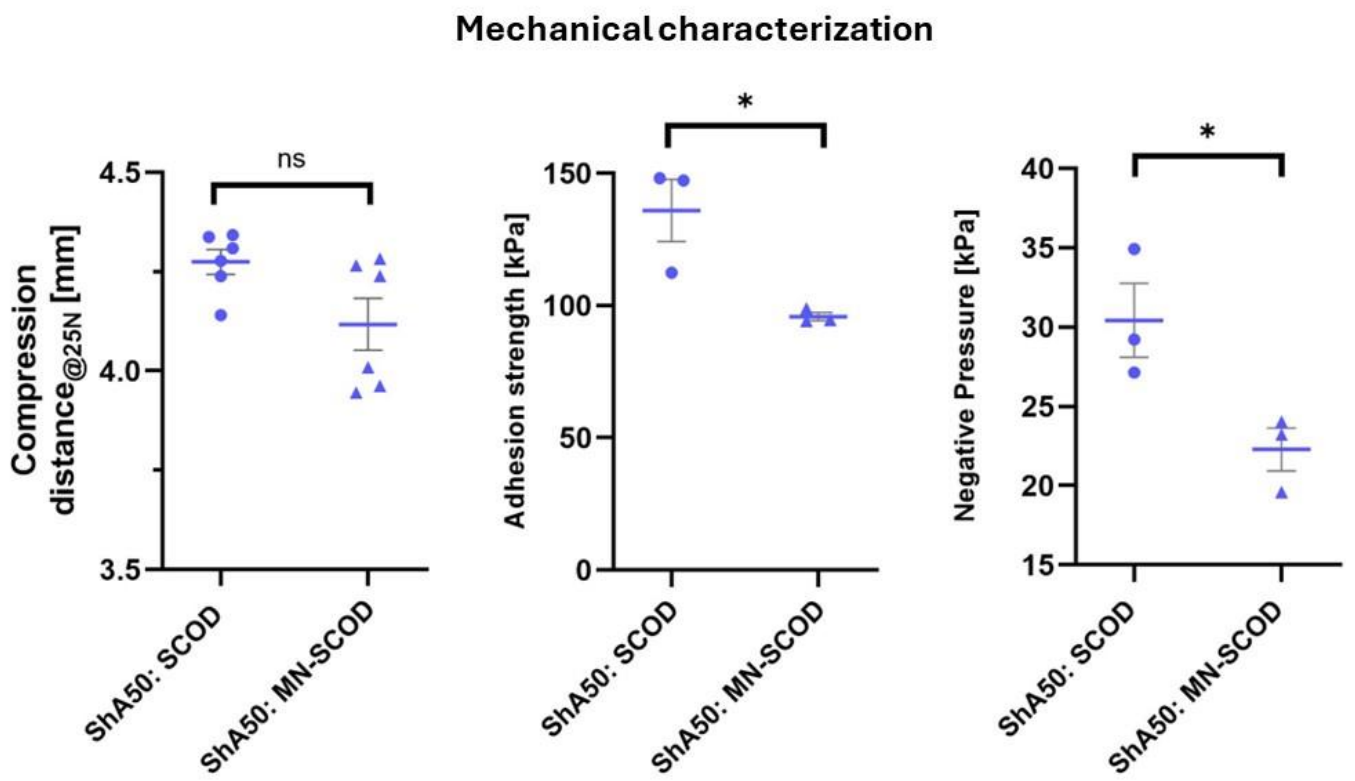
Blood sampling device

Zoratto N *et al. Adv Sci* **11** (2024) 2308809.

Further development







Unpublished data

Acknowledgements

Declaration of conflict of interest:
JCL is a shareholder and cofounder of Obaris AG

ETH
Eidgenössische Technische Hochschule Zürich
Swiss Federal Institute of Technology Zurich

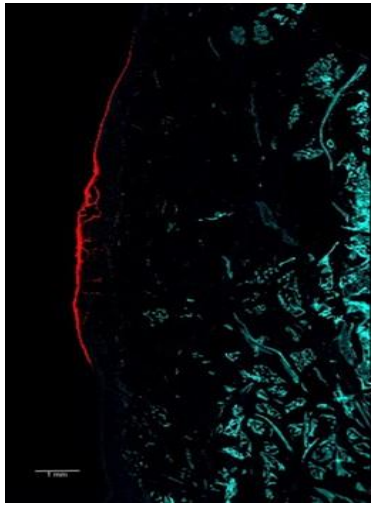
Innosuisse

Swiss National Science Foundation

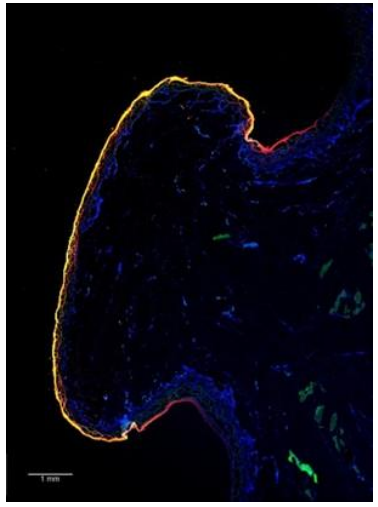
BRC CH Basel Research Centre for Child Health

Further development

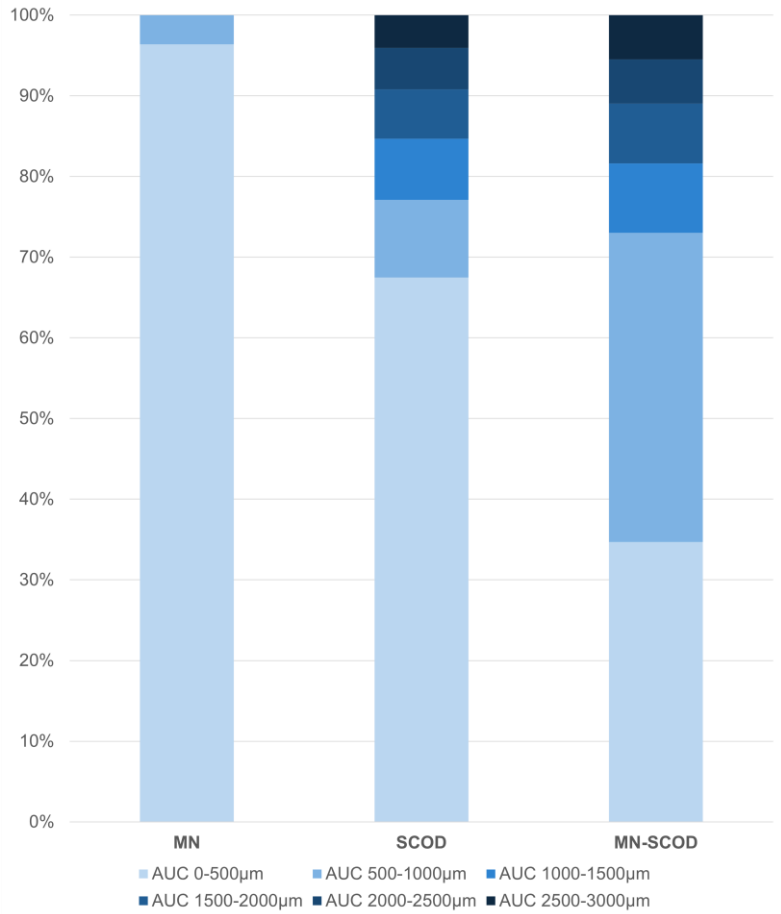
MN



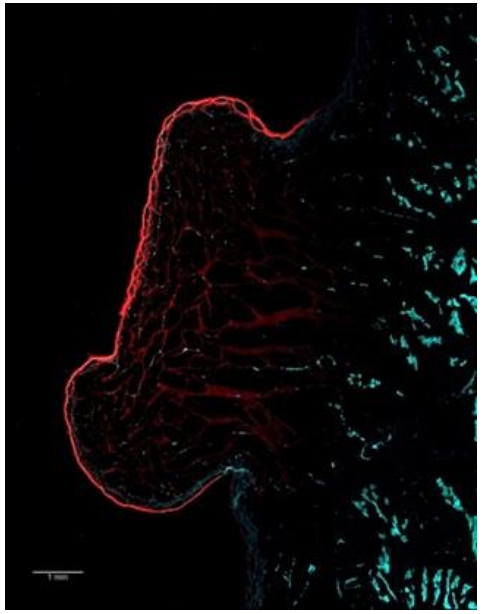
SCOD



Porcine mucosa



MN-SCOD



Unpublished data