Gastroresistant Microcapsules for Intestinal Delivery of Biomolecules

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Advanced Delivery Science

Background

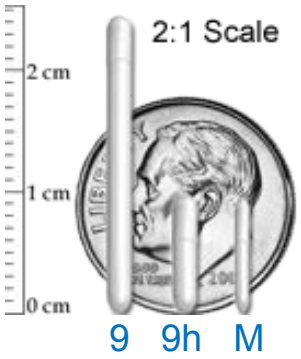
Consistency & Reproducibility

AIM – To provide safe intestinal delivery of sensitive drugs like peptides

Background

Pre-clinical Testing → Clinical Trials → Manufacturing → Market Surveillance

Consistency & Reproducibility



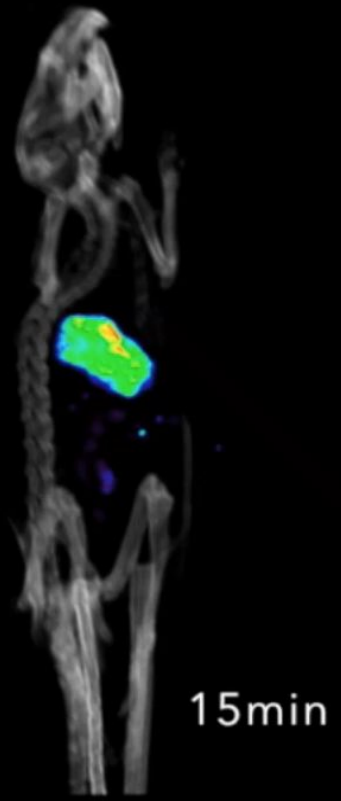
Rodent capsule[1]

Surgical insertion[2]

Human capsule

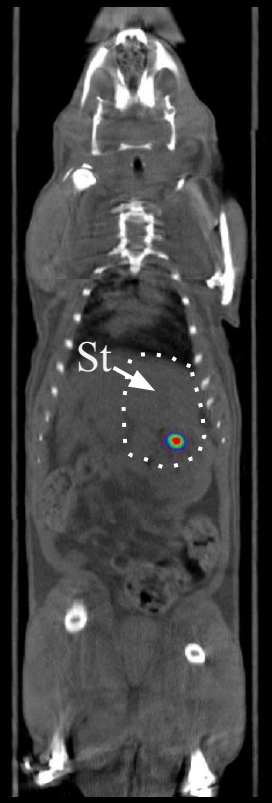
[1] Torpac®
[2] Ha *et al.* 2018

Pre-Clinical Oral Delivery



Polymer Excipient[1]

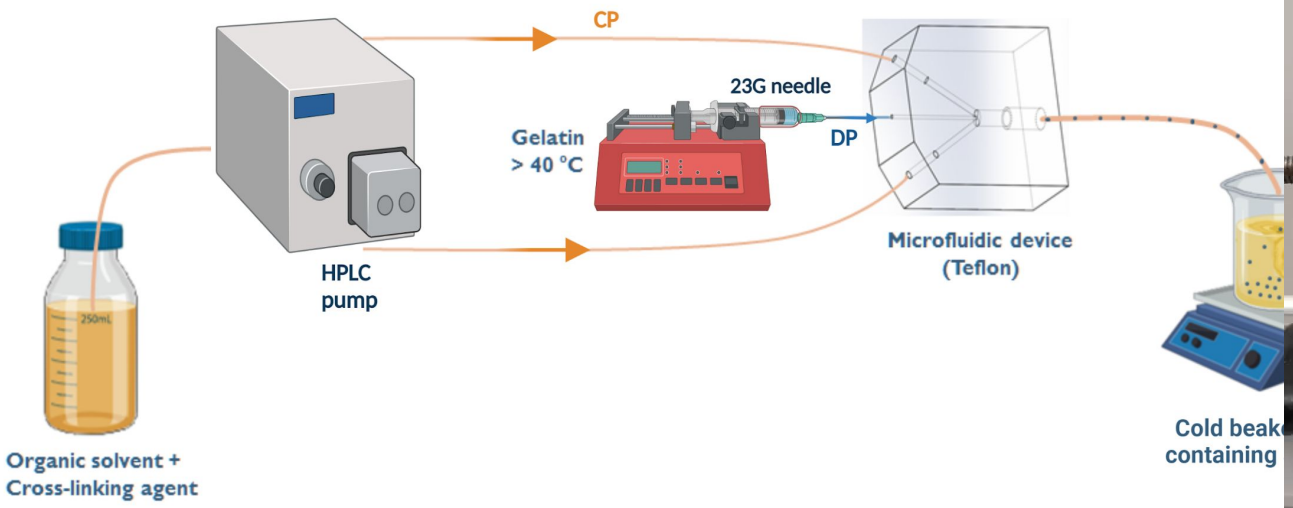
Size M
MCap[2]
Mice

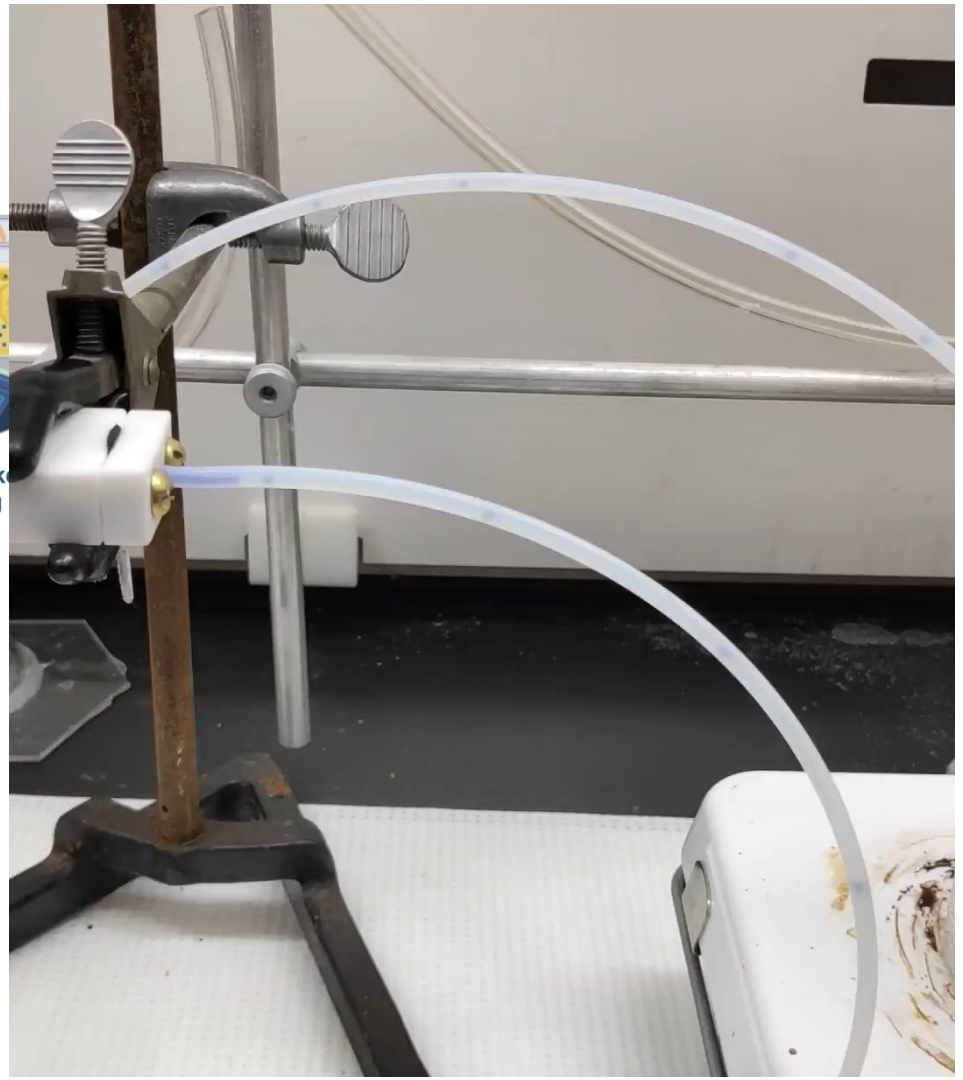


Size 9h[2]
Rats

[1] ©Tullio Esposito
[2] Torpac®

Gelatin Microcapsules – Sorbops (SB)





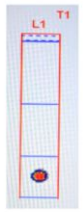
Benefits:

1. Absorption/adsorption of drugs
2. Multiple drug delivery
3. Long shelf life
4. Patient compliance

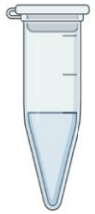
In vitro Testing

Drug
+
Radioisotope

Purify

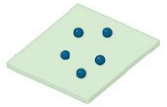


iTLC

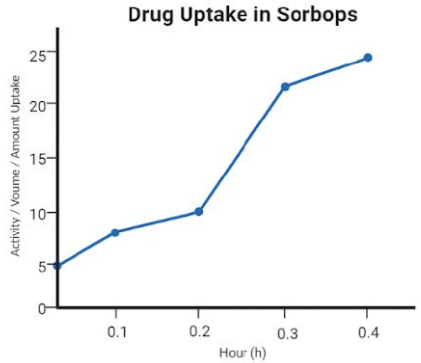


Radiolabeled drug solution

Sorbops dipped into drug solution

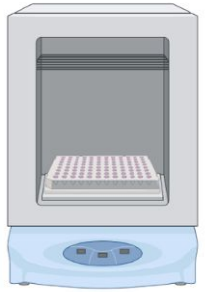


Sorbops air dried

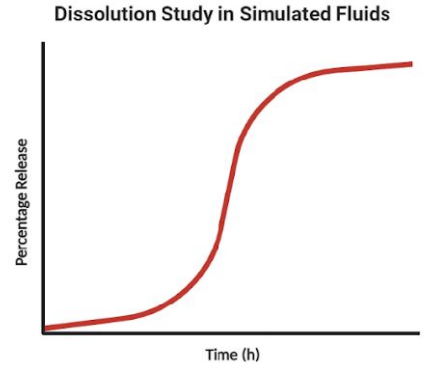


Uptake and Release Studies

Spray coating on Drug loaded Sorbops



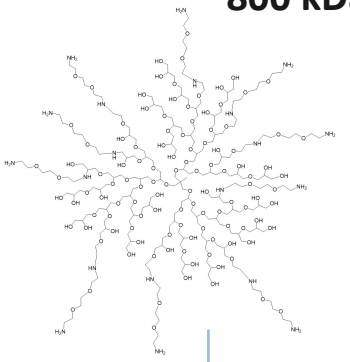
Release of drug in SGF and SIF using shaking incubator at 37 °C



Drug Release Curve

Molecules Tested

Hyperbranched Polyglycerol
800 kDa

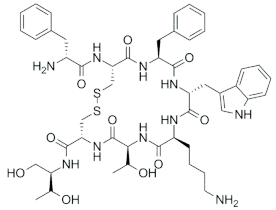


Bovine Serum Albumin
66.4 kDa

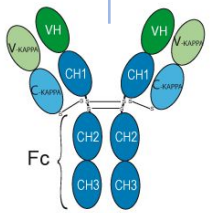
Indium
0.22 kDa

$^{111}InCl_3$

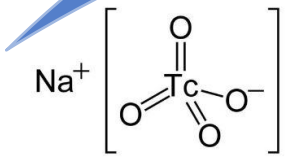
Molecular Weight



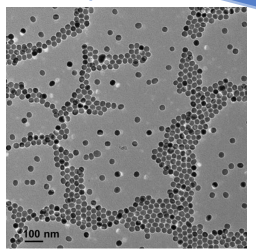
Octreotide
1.2 kDa



Trastuzumab
148 kDa

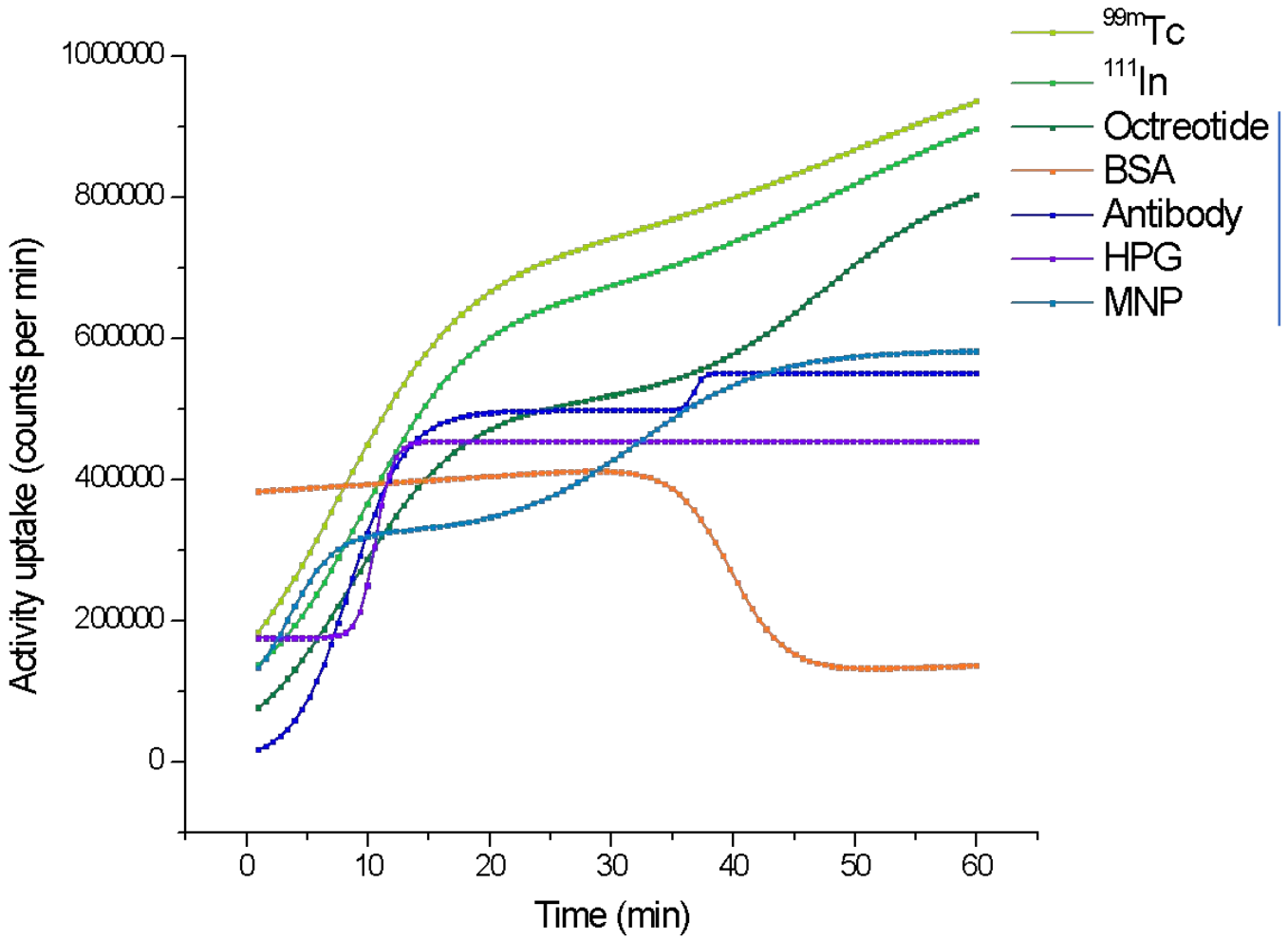


Technetium Pertechnetate
0.22 kDa



Magnetic Nanoparticles
Diameter 70 nm (micromod)

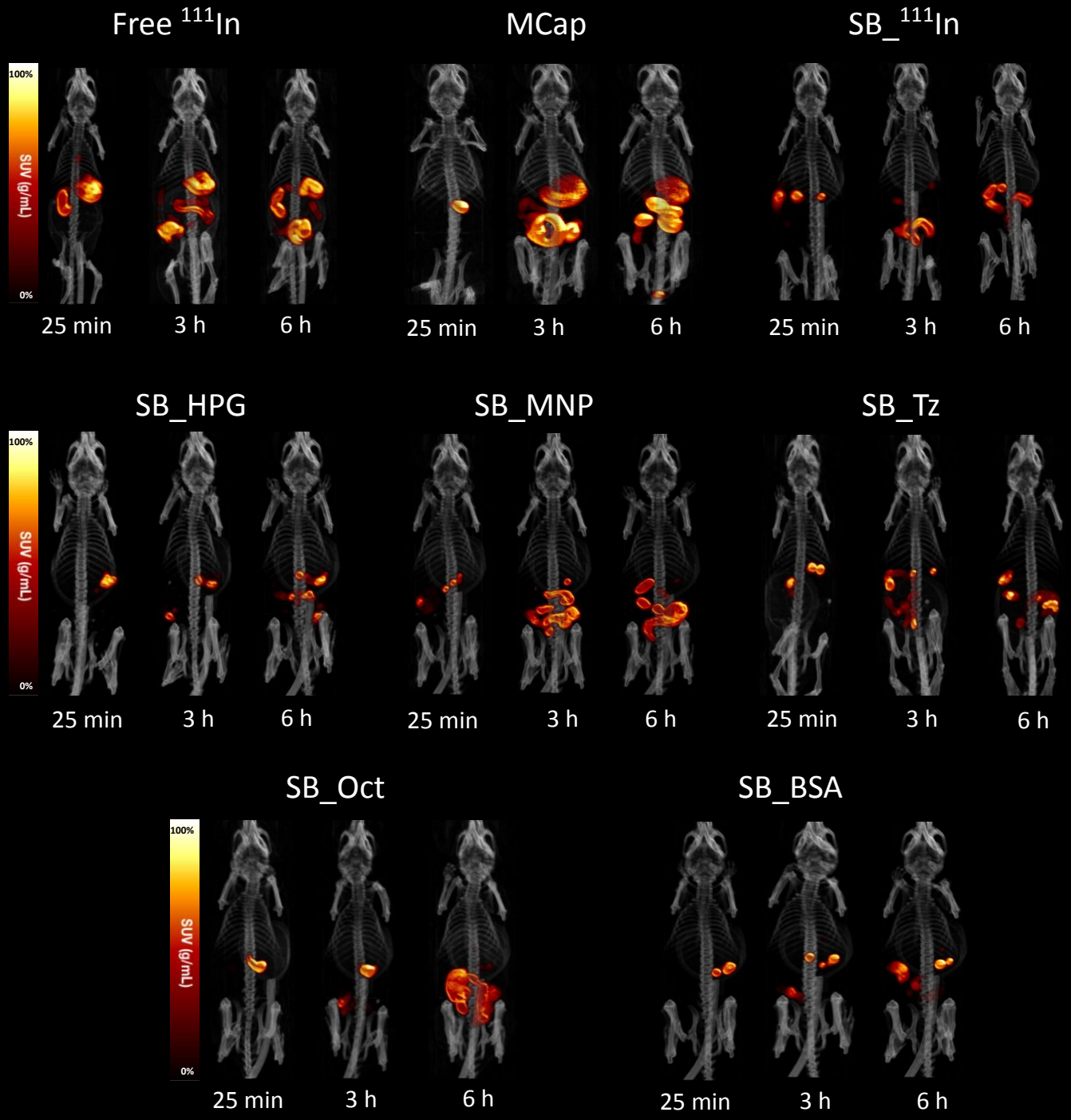
Uptake Study in Sorbops



Labeled with ^{111}In

Drug uptake is size dependent

BSA: Bovine Serum Albumin; HPG: Hyperbranched Polyglycerol; Oct: Octreotide; Tz: Trastuzumab; MNP: Magnetic nanoparticles



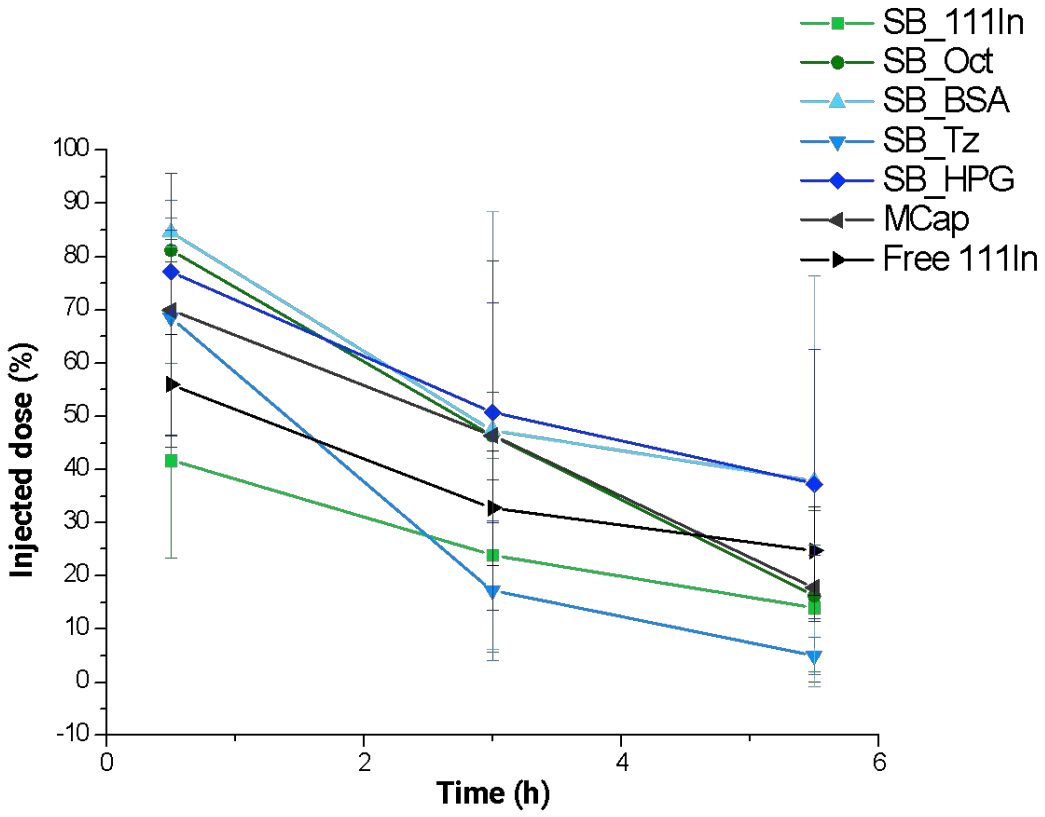
Real Time Imaging

- Good resistance to acidic degradation in stomach
- Intestinal delivery by 3h
- Burst release of cargo in the intestine

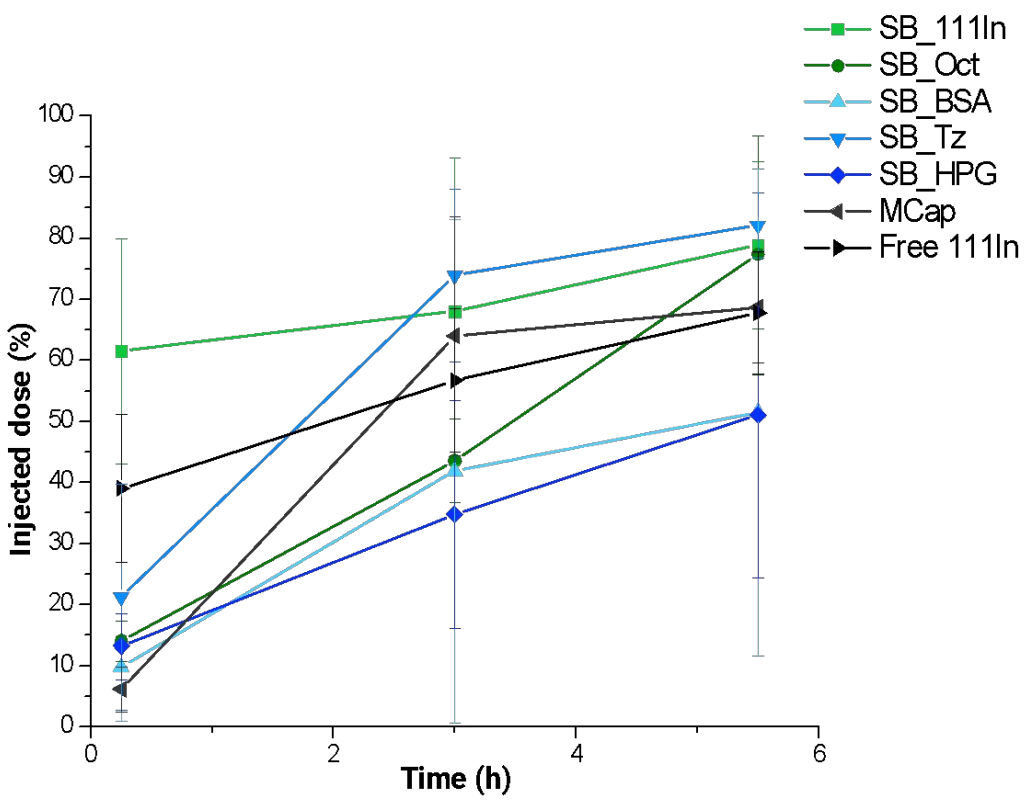
BSA: Bovine Serum Albumin; HPG: Hyperbranched Polyglycerol; Oct: Octreotide; Tz: Trastuzumab; MNP: Magnetic nanoparticles

Quantitative Analysis

Stomach – Drug decreases

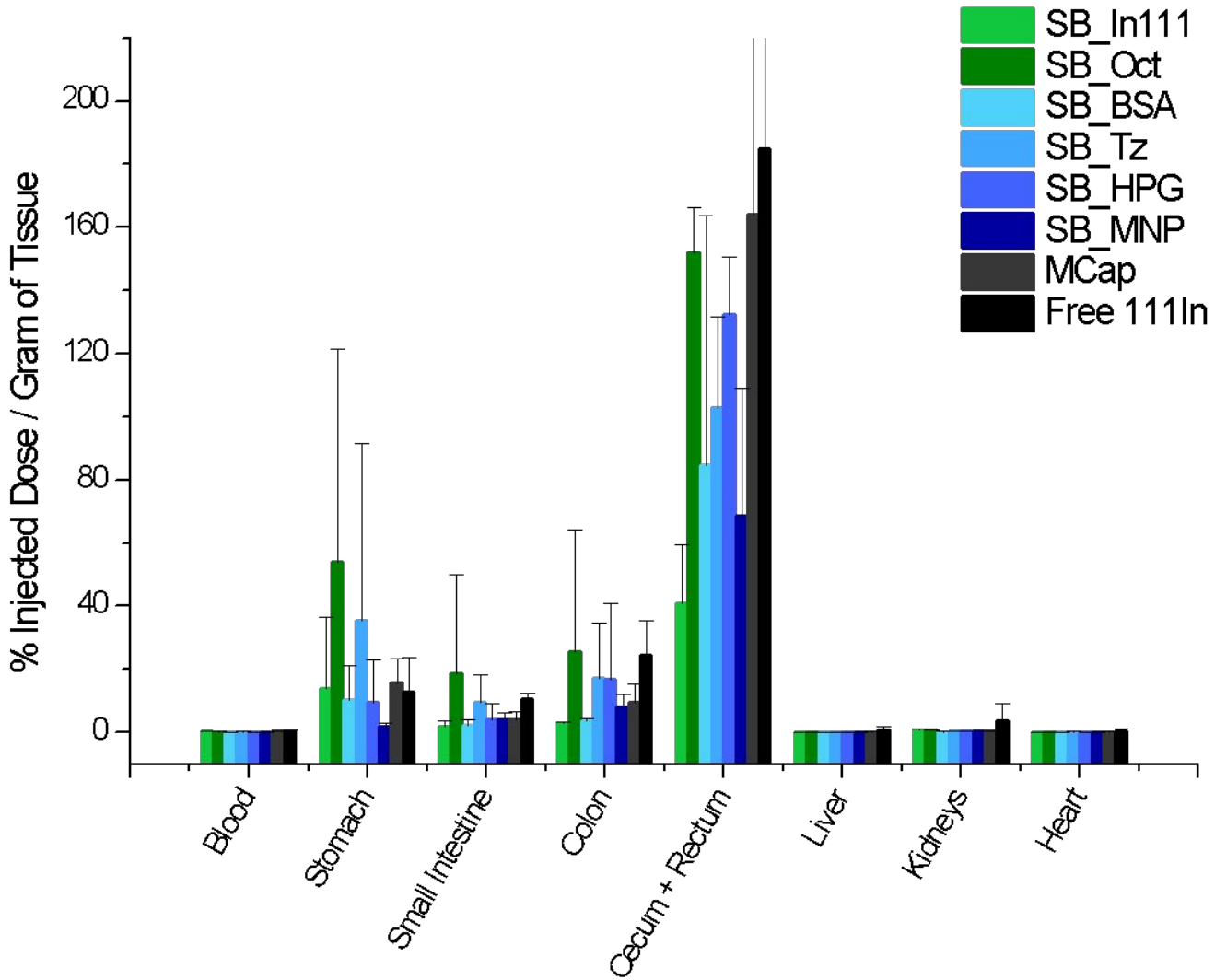


Intestine – Drug increases



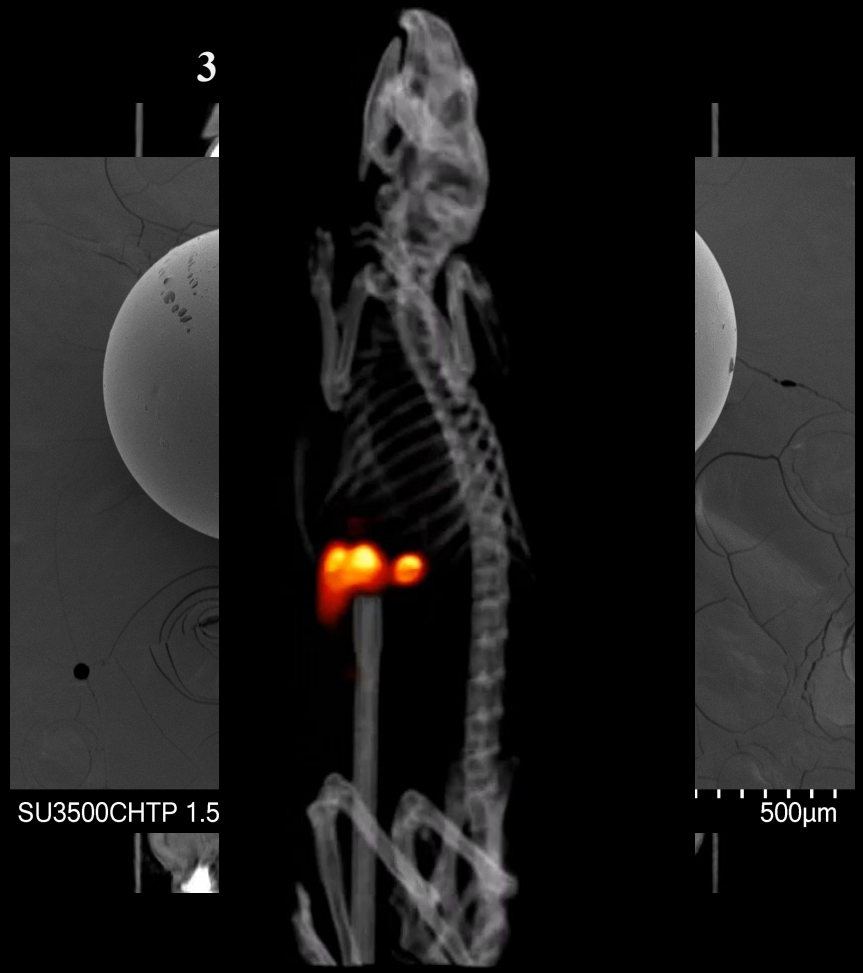
BSA: Bovine Serum Albumin; HPG: Hyperbranched Polyglycerol;
Oct: Octreotide; Tz: Trastuzumab; MNP: Magnetic nanoparticles

Biodistribution – 24 h



Conclusion

1. Commercial capsules get stuck in stomach – inserted surgically in the intestine
2. Uniform sized sorbops generated by microfluidics
3. Safe intestinal delivery of different cargo by oral gavage in mice
4. Future plan – study oral bioavailability of peptides delivered in enterically coated sorbops



Acknowledgement

Supervisory Committee

Dr. Urs O. Häfeli (Supervisor)
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Dr. Charles Haynes
Dr. Colin Ross (Chair)
Dr. Karla Williams

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Dr. Zeynab Nosrati
Maryam Osooly
Dr. Cristina Rodriguez-Rodriguez
Dr. Kathy Saatchi
& other lab members

Des Lovrity & Team

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Collier Lab

Dissolution study

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Faculty of Pharmaceutical Sciences

UNIVERSITY OF COPENHAGEN

Funding Agencies

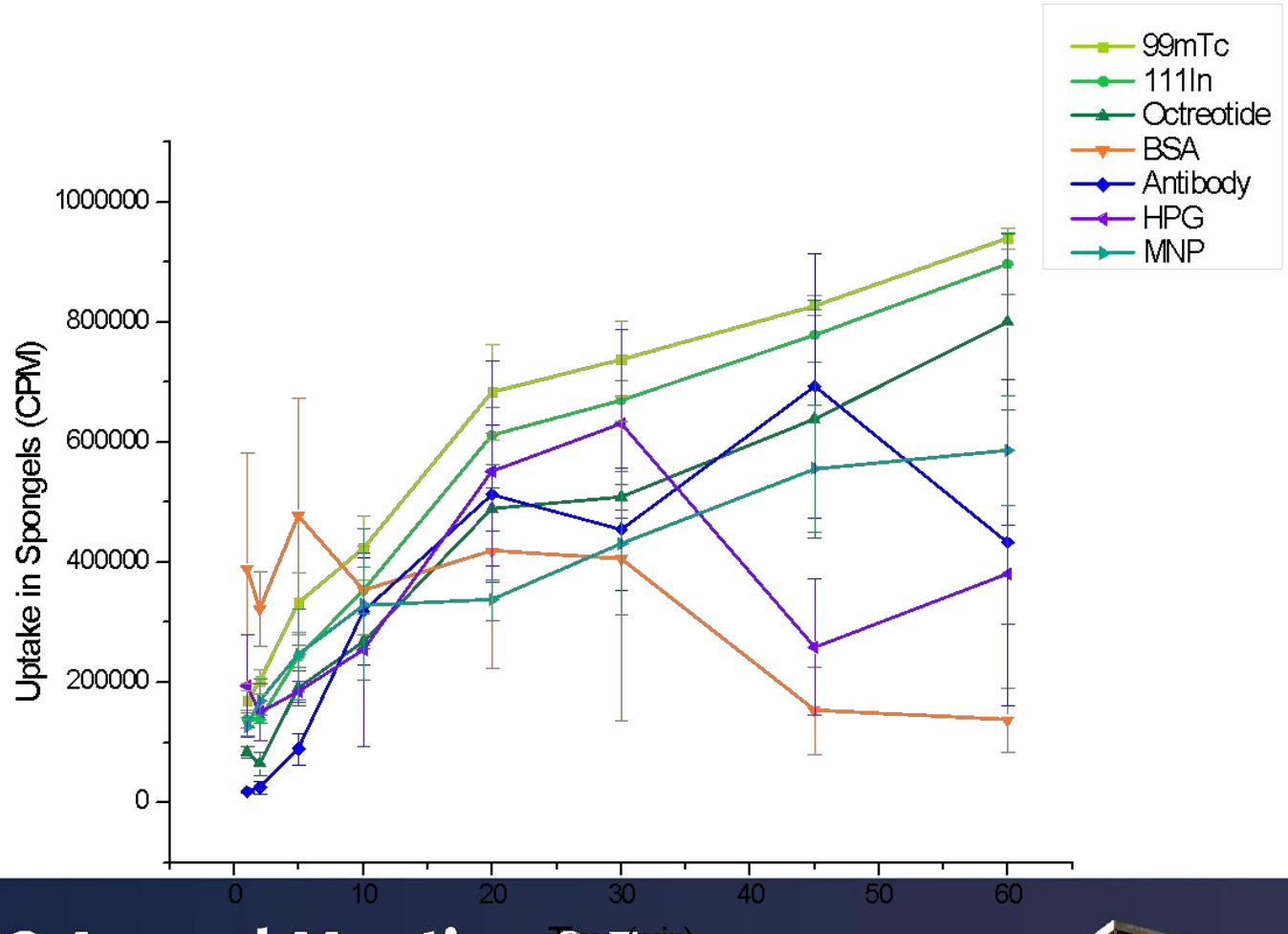
BioDelivery Center

novo nordisk®

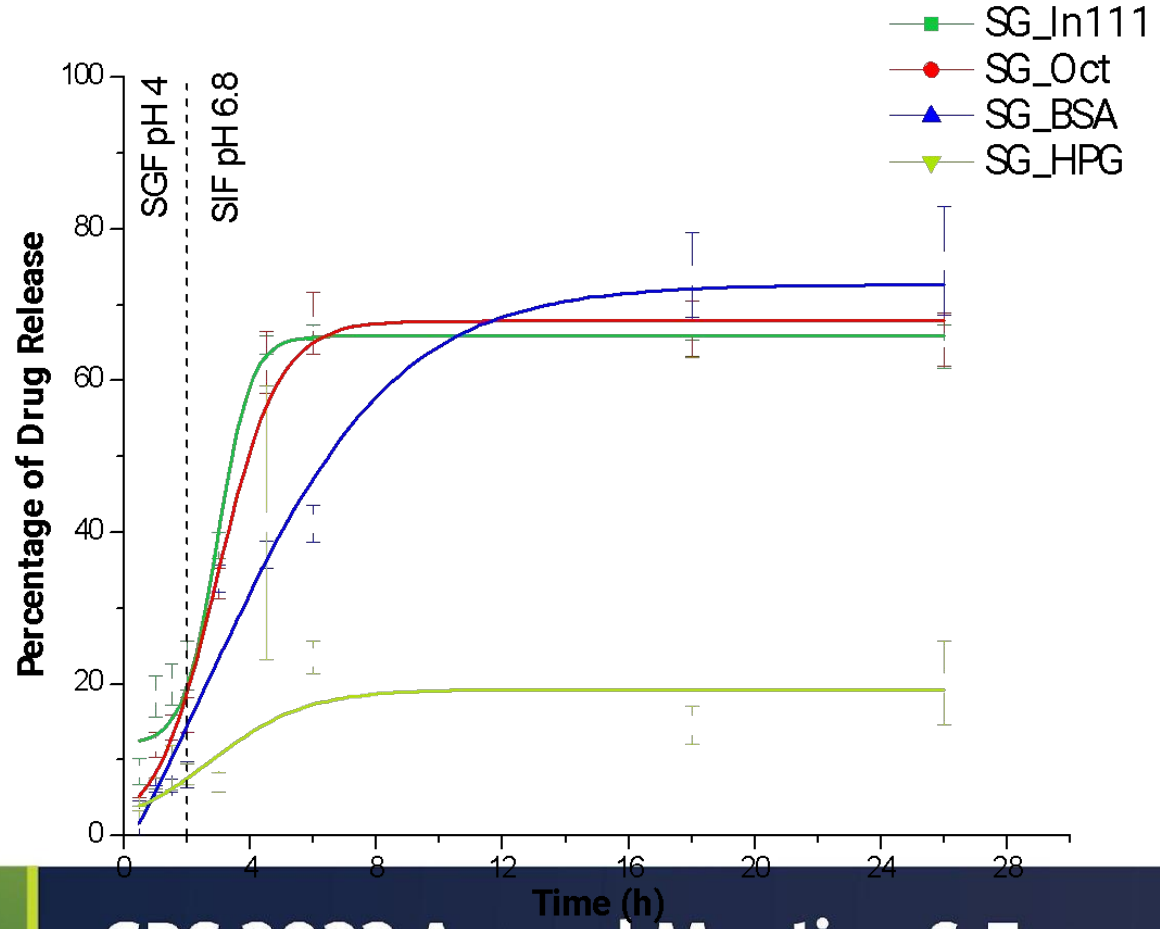
SERB DIA

Thank you for listening!

Drug Uptake



Drug Release Study



No release in SGF

Burst release in SIF

SGF: Simulated Gastric Fluid; SIF: Simulated Intestinal Fluid