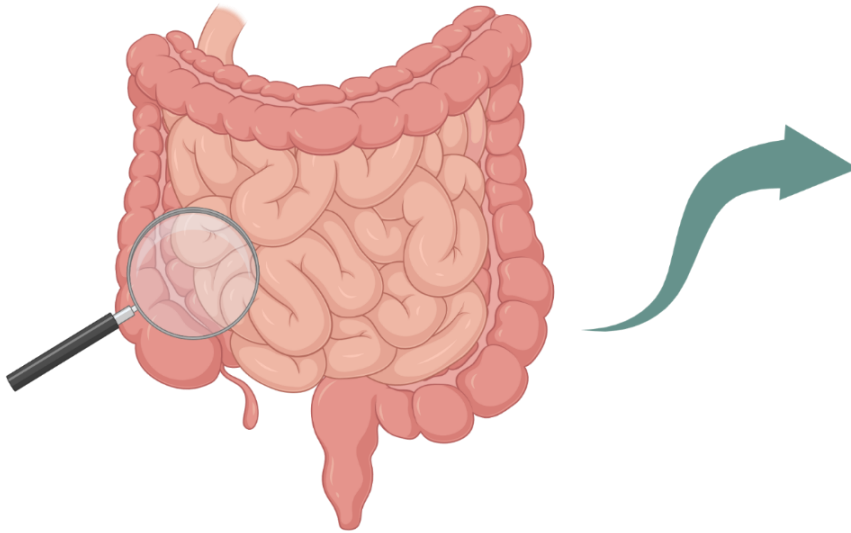


Colonic capsules for bacterial suspensions

Fatma Abdi
Drug Formulation & Delivery

Prof. Dr. Jean-Christophe Leroux

The gut microbiome: the hidden organ



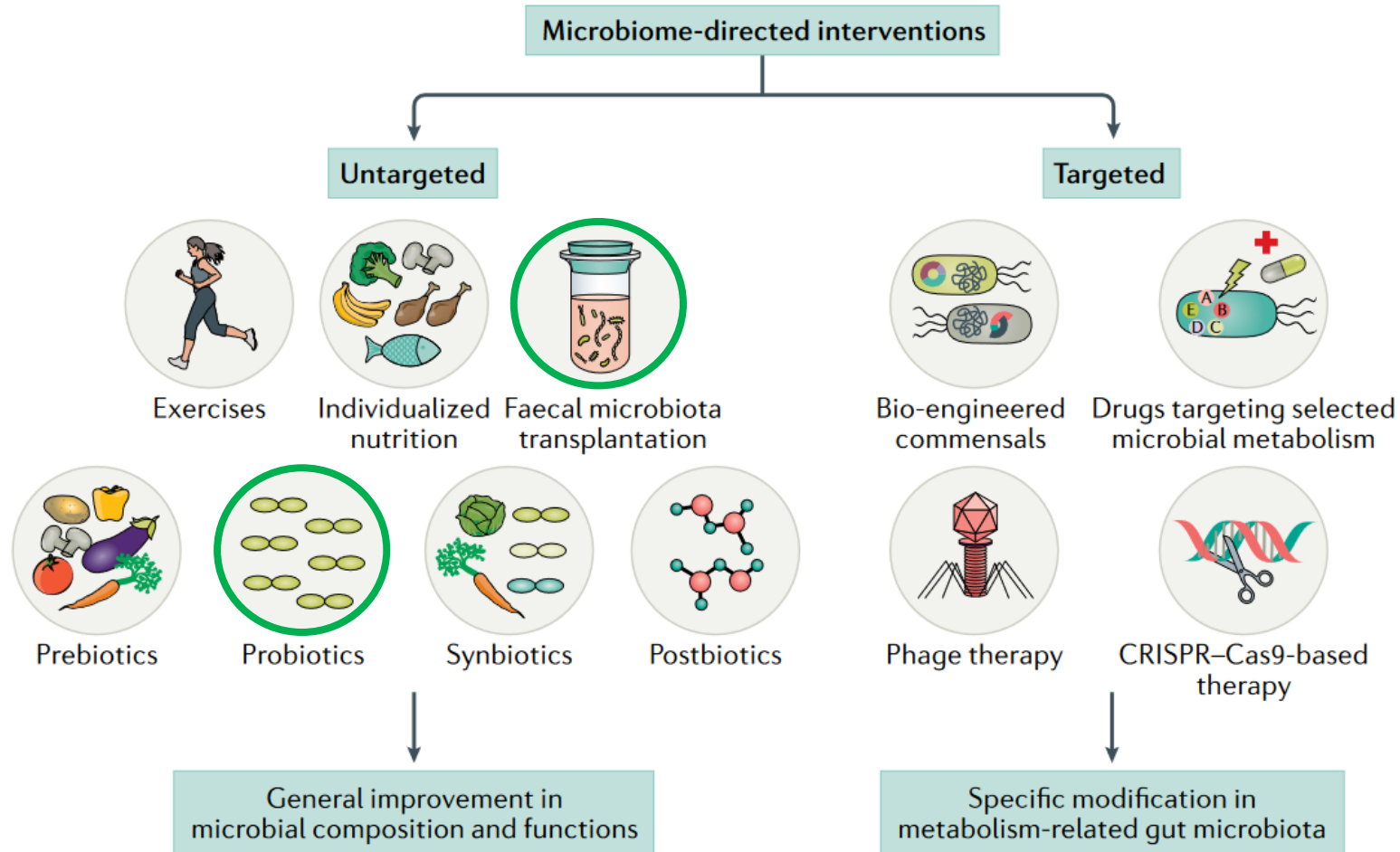
Zoom into the Ileum/colon



**A stable community of >1000
bacteria, eukaryotes, archaea and
viruses**

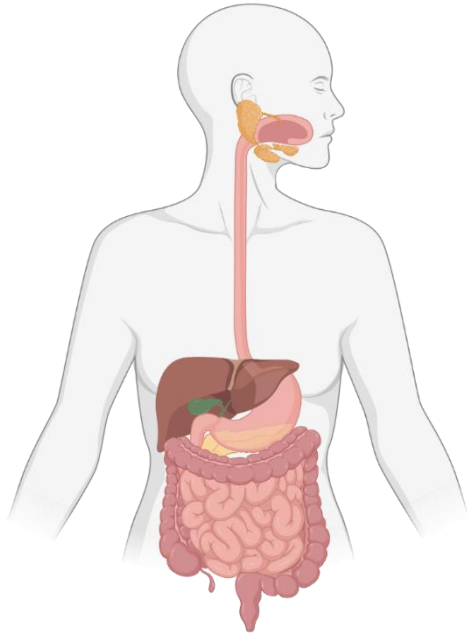
**Phylogenetically diverse
3 million (non-redundant) genes**

Interventions on the microbiome: restoring a healthy microbiome



Oral delivery systems for bacteria: challenges and approach

GI transit



Harsh conditions

Acid, enzymes and bile acids

Strategies

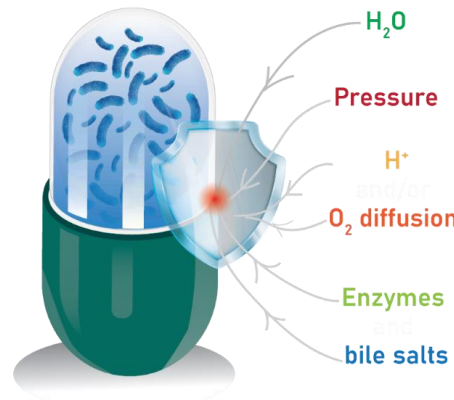


Tablets



Capsules

Live bacteria in
aqueous suspension



Functional composite
capsule



Loss of bacterial survival

Manufacturing hurdles

Freeze drying (powder)

Compression and heat generation (tablets)

Exposure to oxygen (anaerobic strains)



High bacterial viability

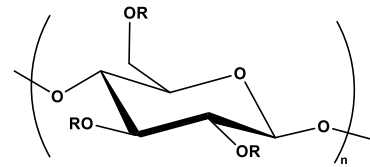
Fast encapsulation of a bacterial suspension

No processing (freeze-drying,
compression, etc.)

Convenient solution for research purposes

Capsule design: rational and methods

Step 1: Hydrophobic coating

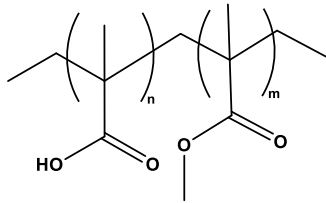


R= H or CH₂-CH₃

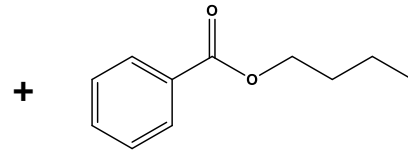
Ethyl cellulose derivatives (EC)

Allows encapsulation of bacterial suspension
Thin layer, breaks under pressure in the colon/ileum

Step 2: Enteric coating



Eudragit S100



Butyl benzoate (BB)

Protects from acidity
Dissolves at a pH >7

Dip-coating method

Type 1

EnC 1
13.6 % wt. Eudragit S 100
27 % wt. BB

HC 1
4.5 % wt. EC

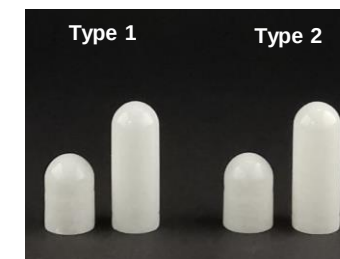


Hydrophobic Ethyl
Cellulose coating

HC 2
6.6 % wt. EC

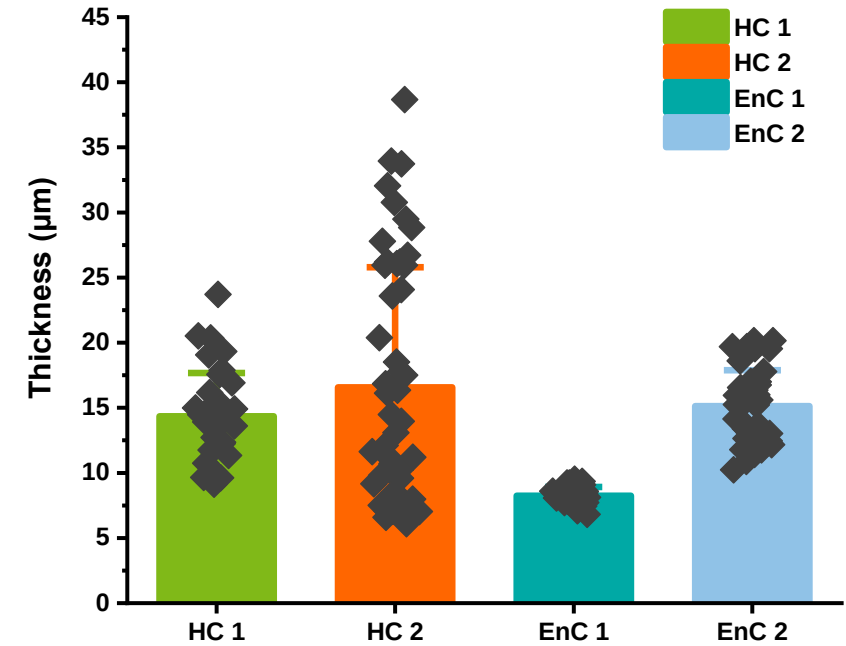
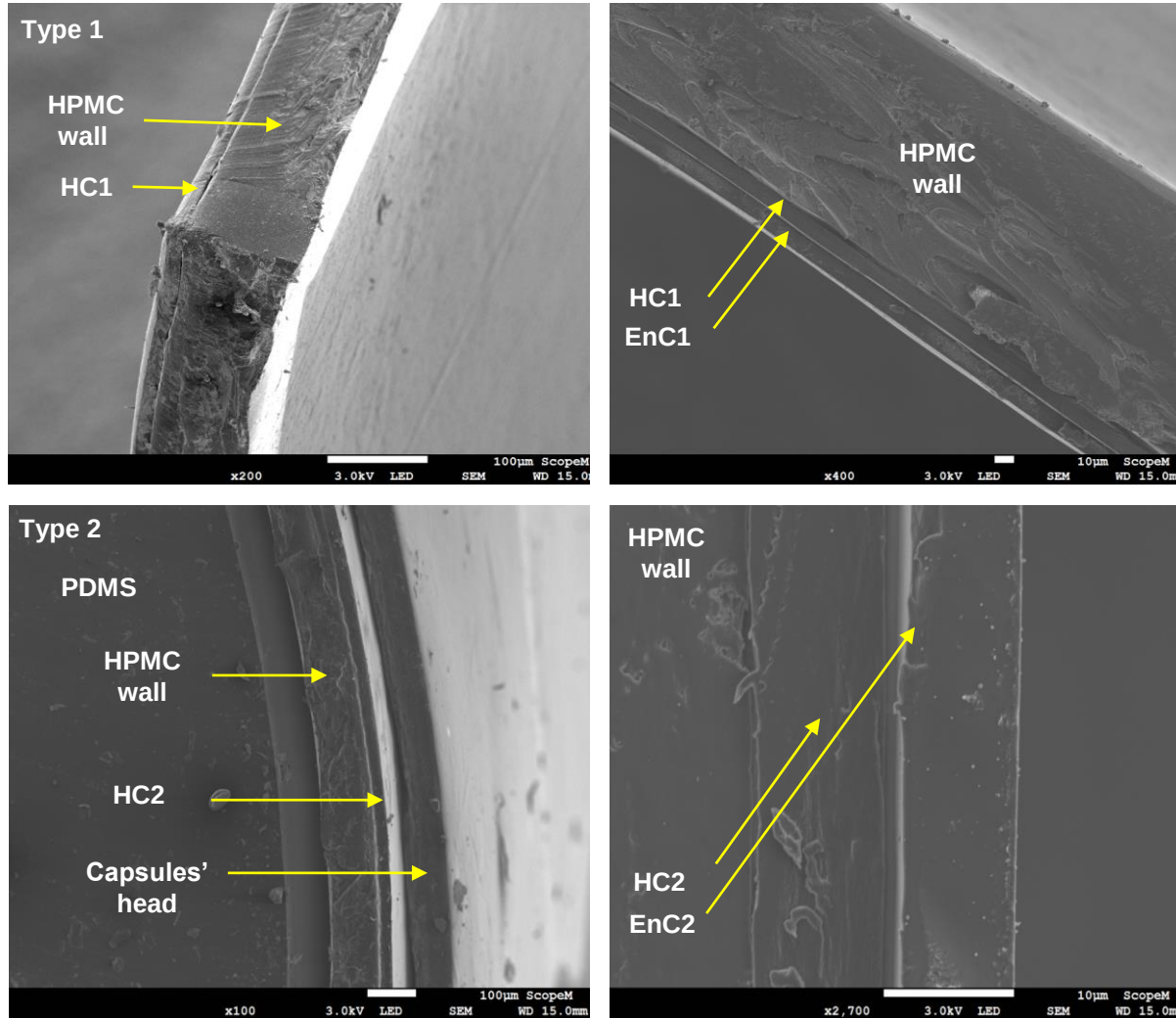
EnC 2
10 % wt. Eudragit S 100
3 % wt. BB

Type 2



Coating characterization: thickness

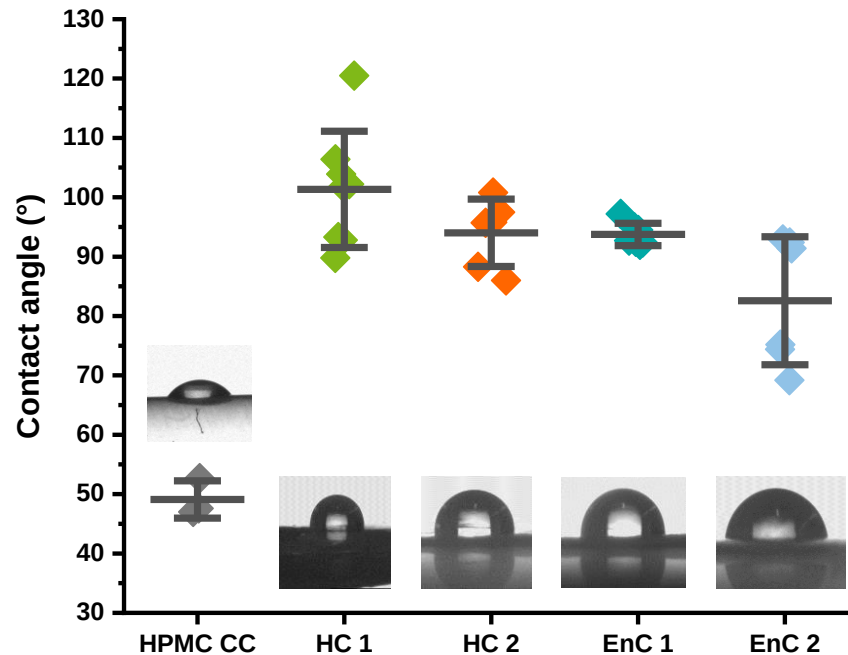
Scanning electron microscopy



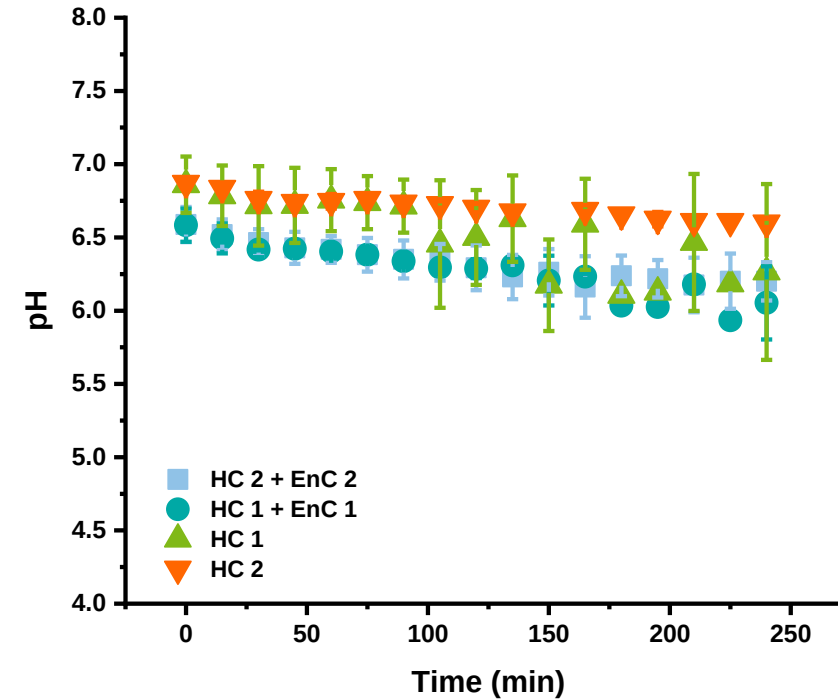
Type 1: 22.5 µm thick
Type 2: 30 µm thick

Coating properties and functionalities

Hydrophobicity and resistance to acidity



n=3

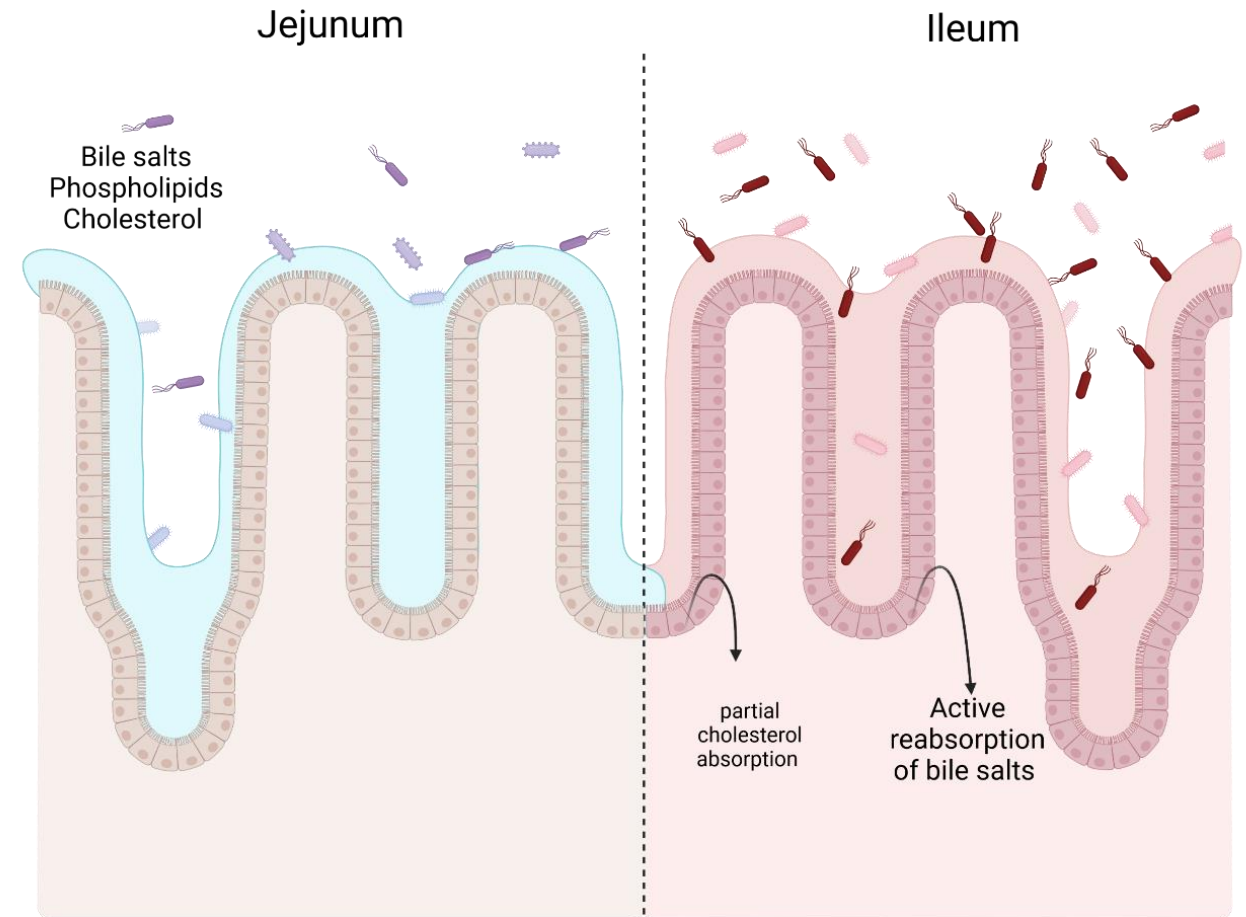
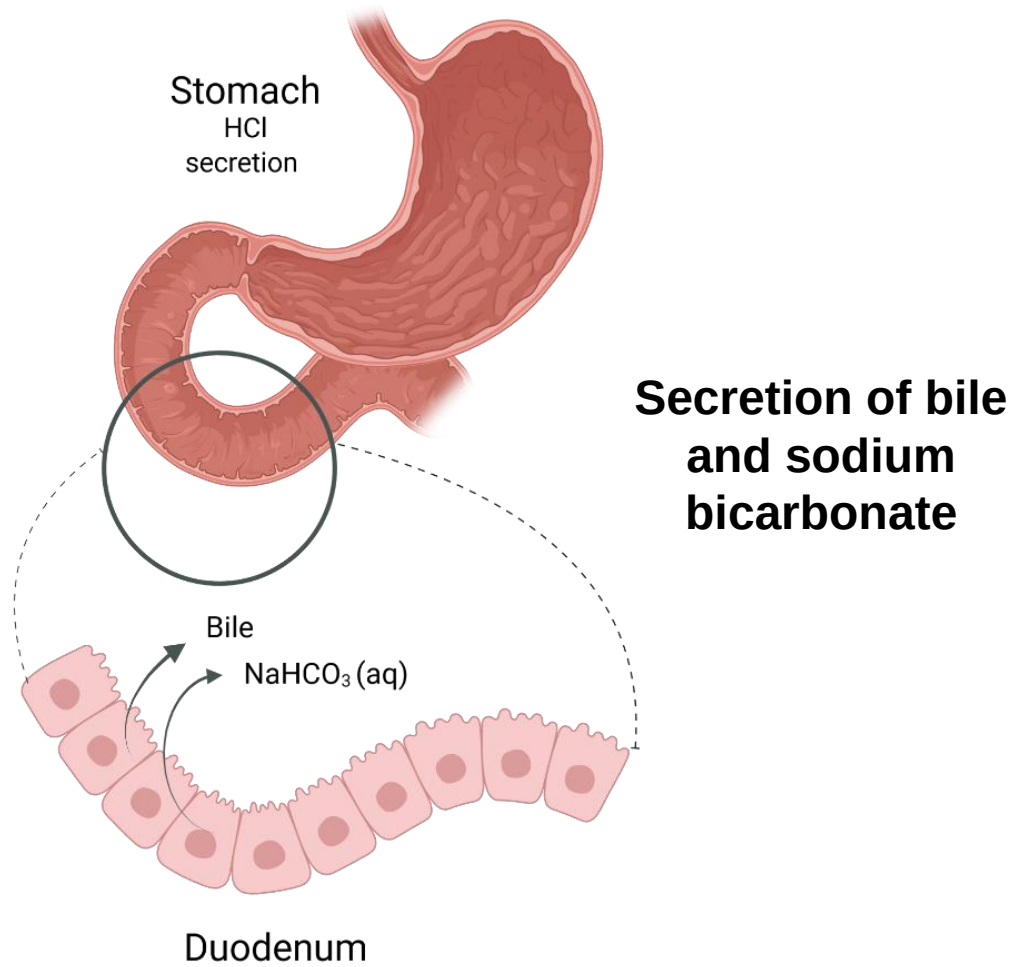


n=9

Diffusion of protons is hindered in simulated gastric fluid for 4 h
HC 1, HC 2 and EnC 1 are largely more hydrophobic than HPMC capsule shell

The GI tract physiology

Under fasted conditions

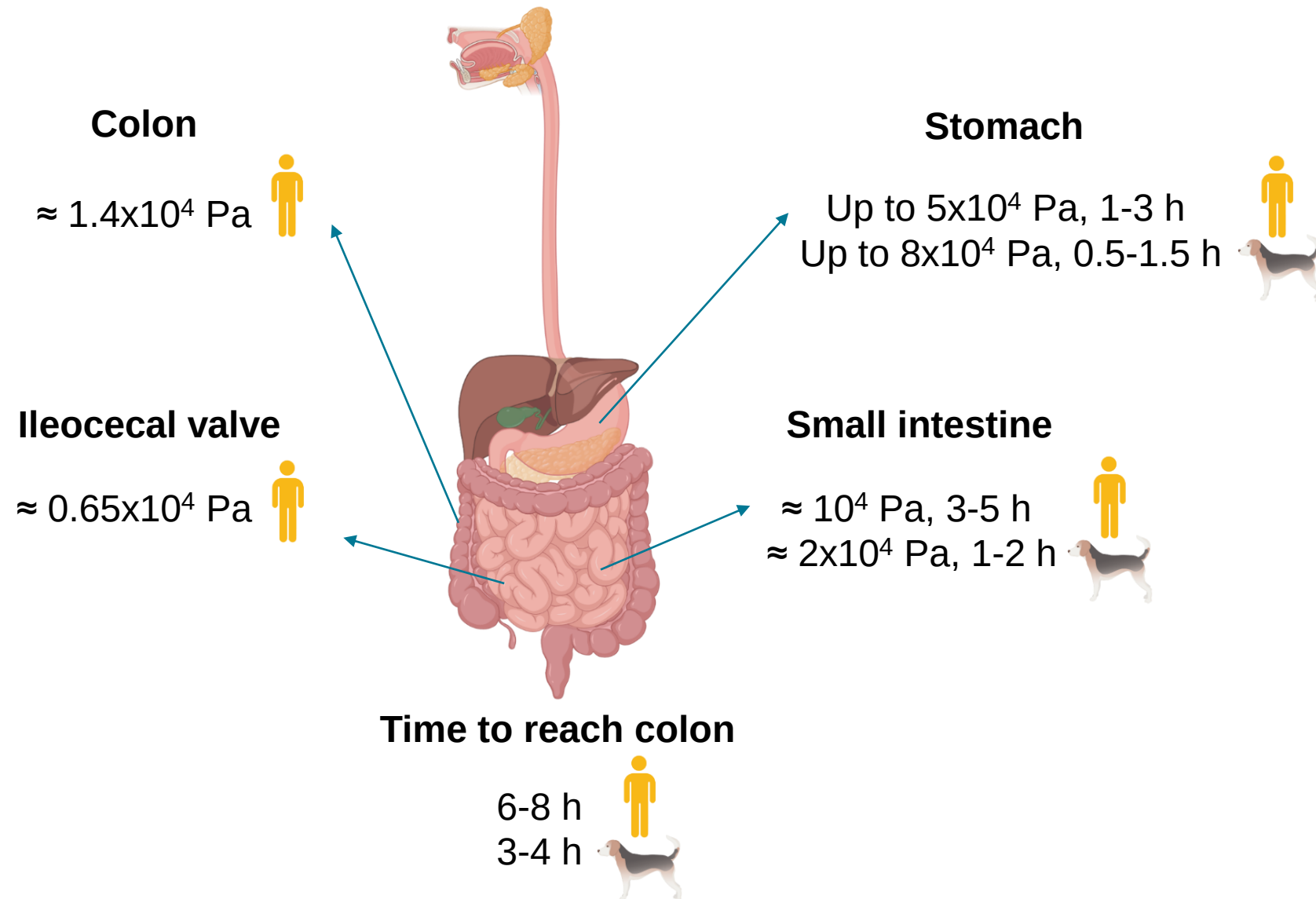


Circulation of bile

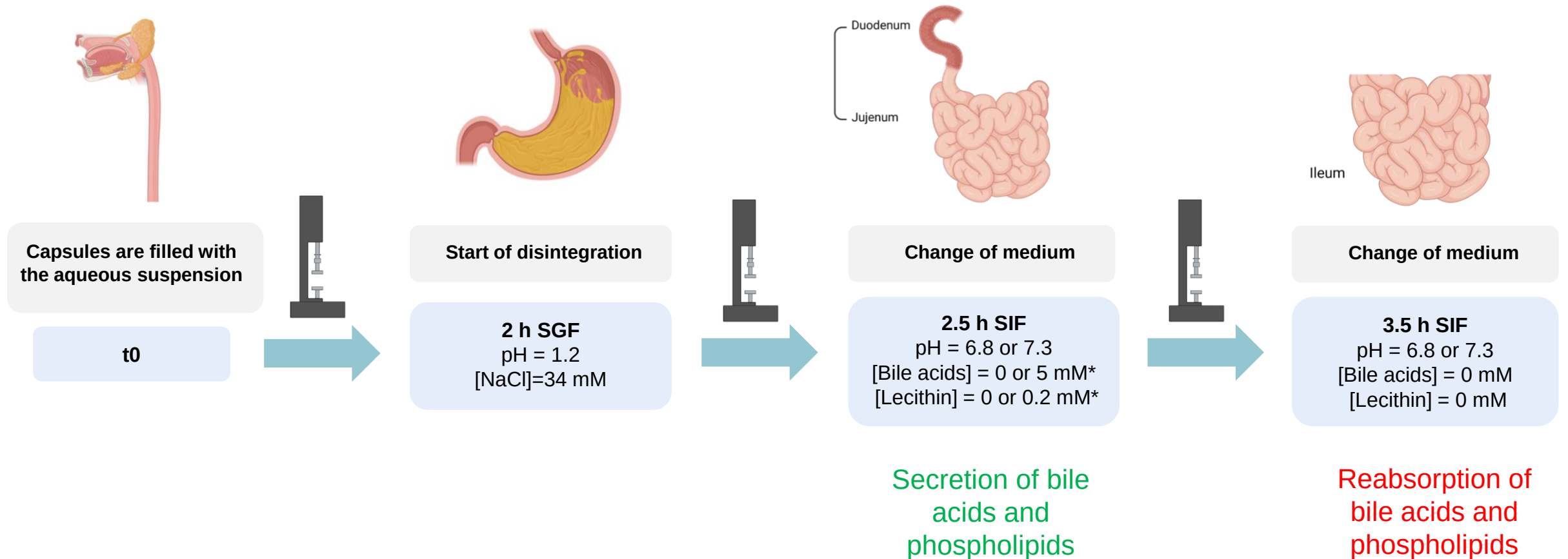
Enterohepatic
reabsorption of bile
(95%)

The GI tract physiology: pressure events and transit time

Under fasted conditions

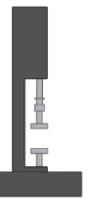


In-vitro disintegration testing coupled with mechanical compression

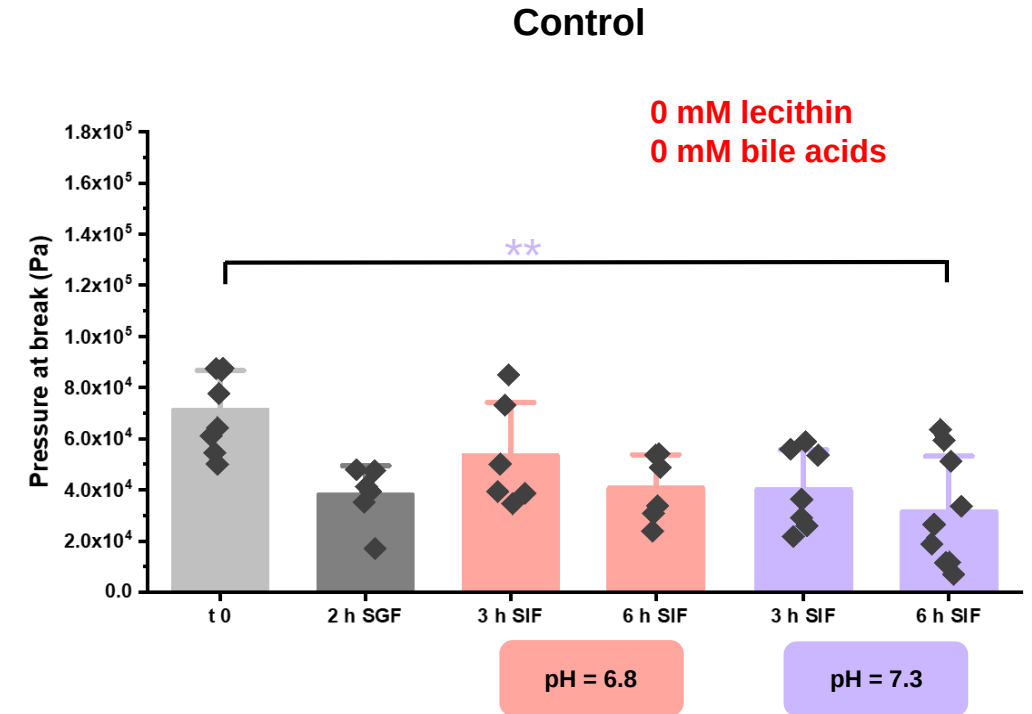
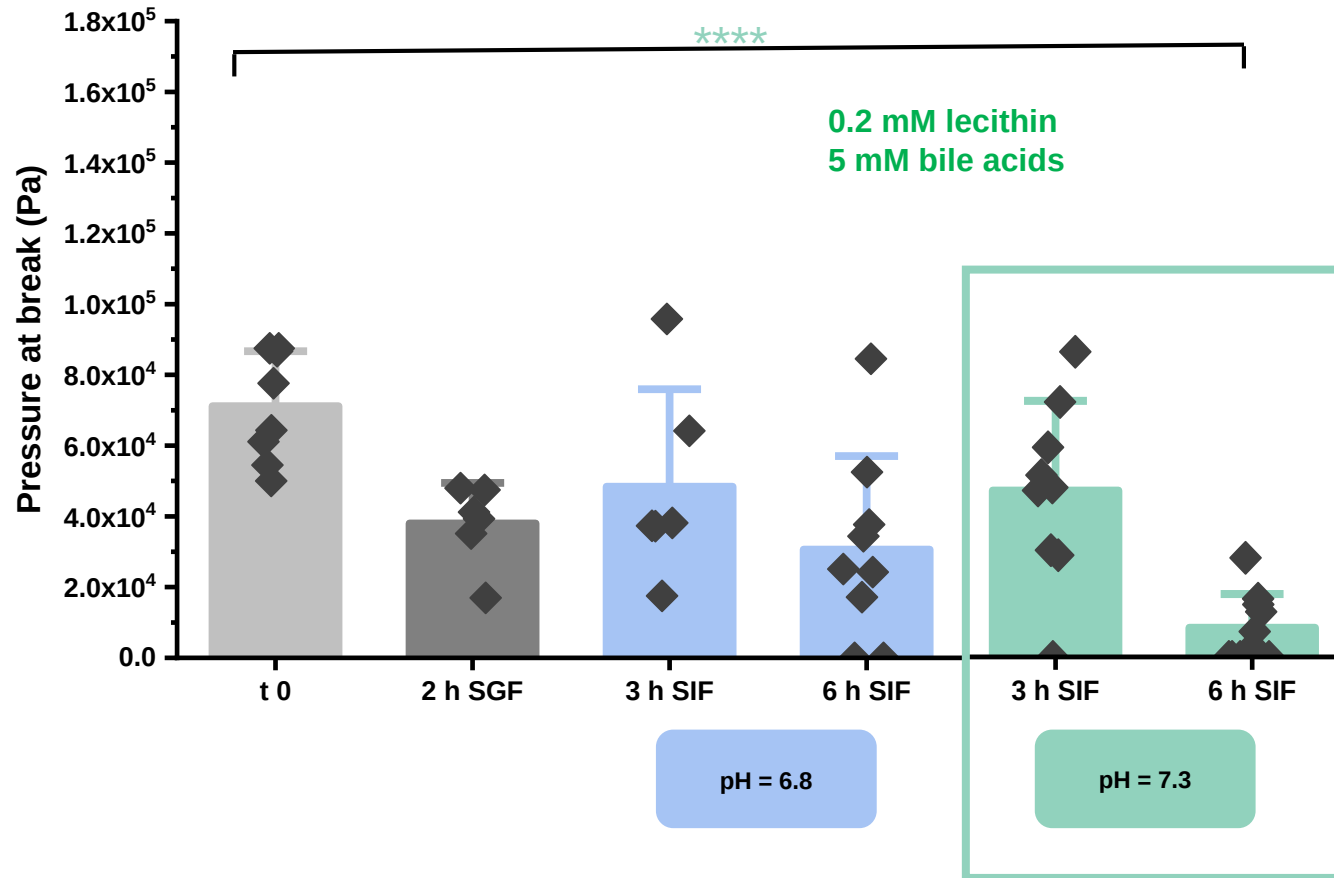


Mechanical properties: pressure at break

Mimicking the GI tract conditions: effect of lecithin, bile acids and pH on the capsules



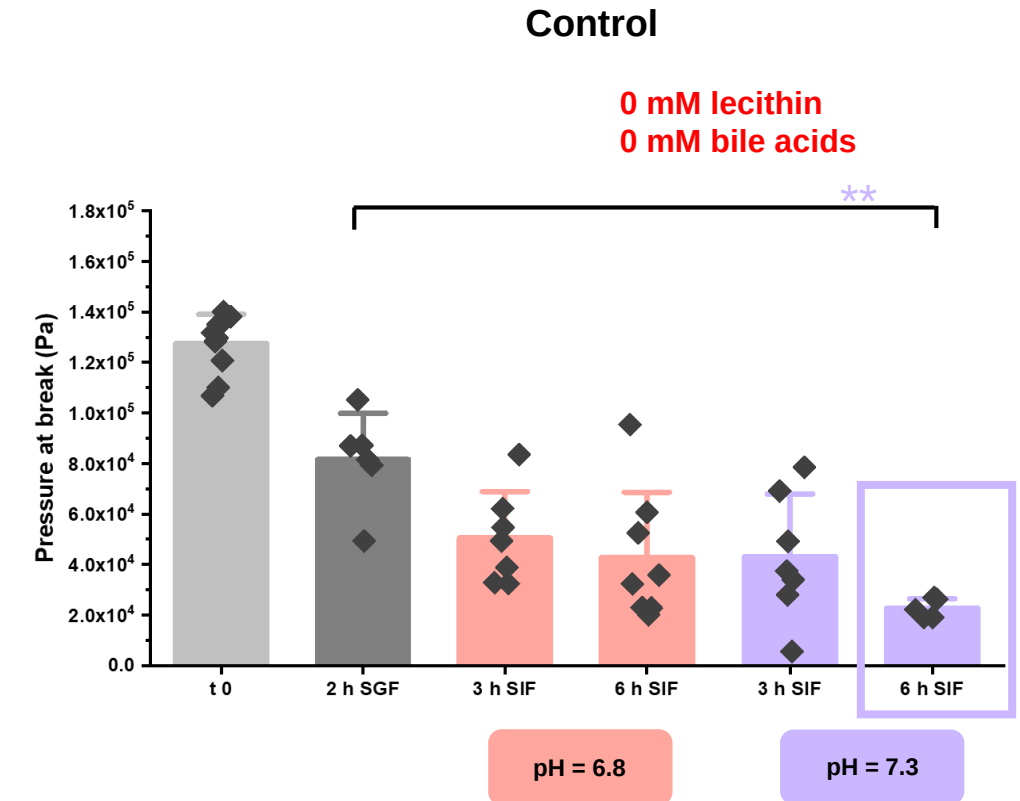
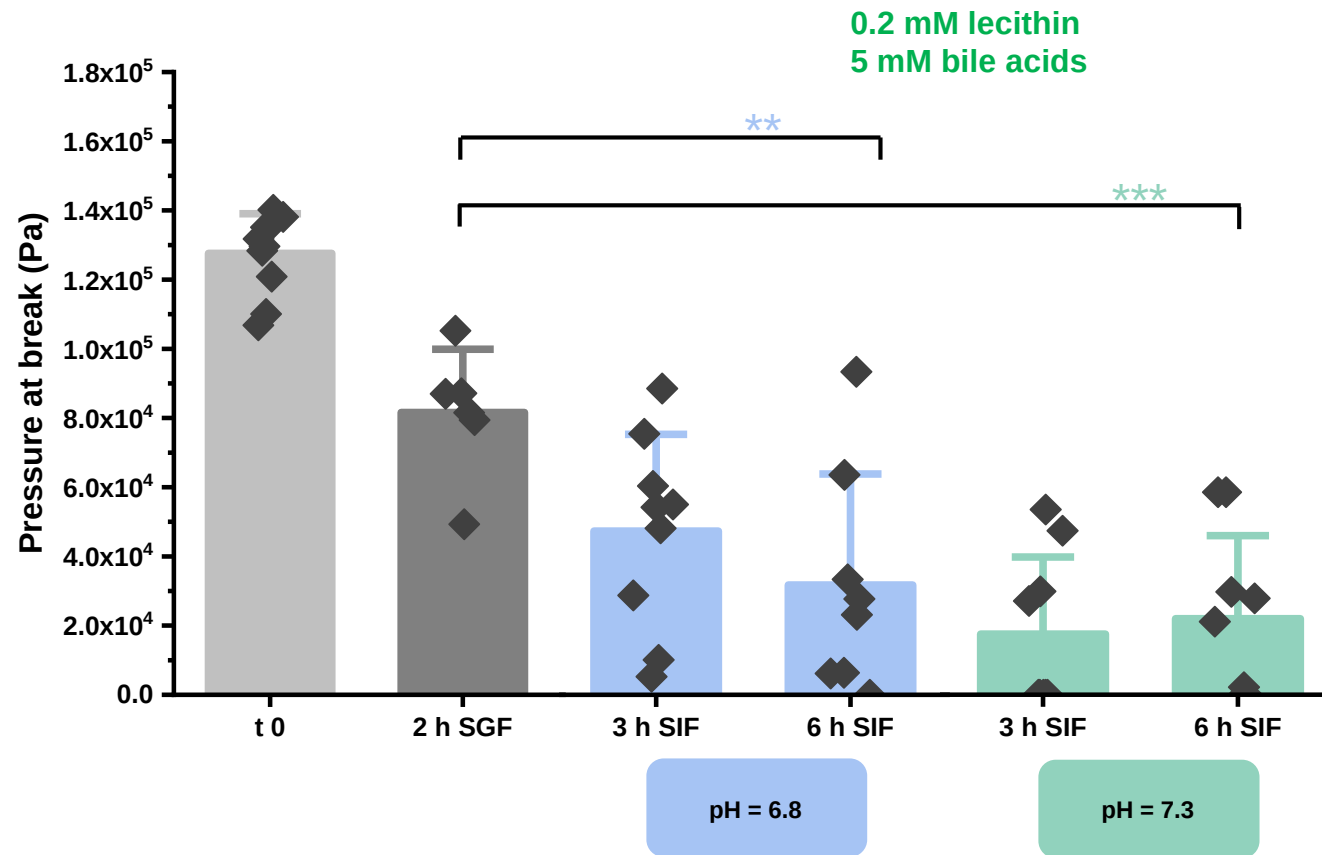
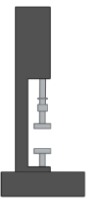
Type 1



Mechanical properties: pressure at break

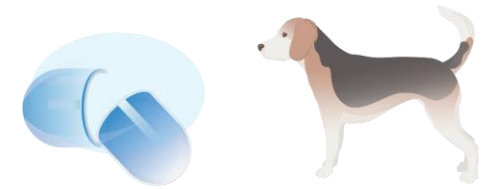
Mimicking the GI tract conditions: effect of lecithin, bile acids and pH on the capsules

Type 2

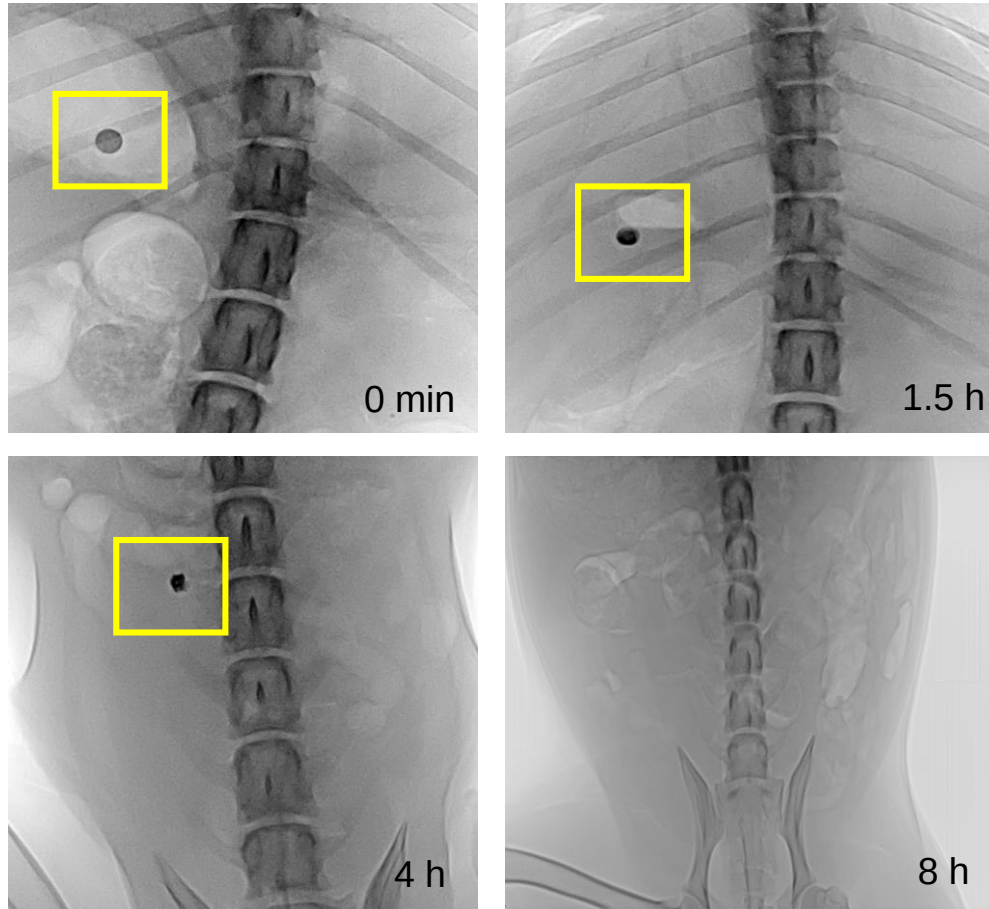


In-vivo study

Gastrointestinal transit in beagle dogs: X-ray investigation using BaSO₄ suspension

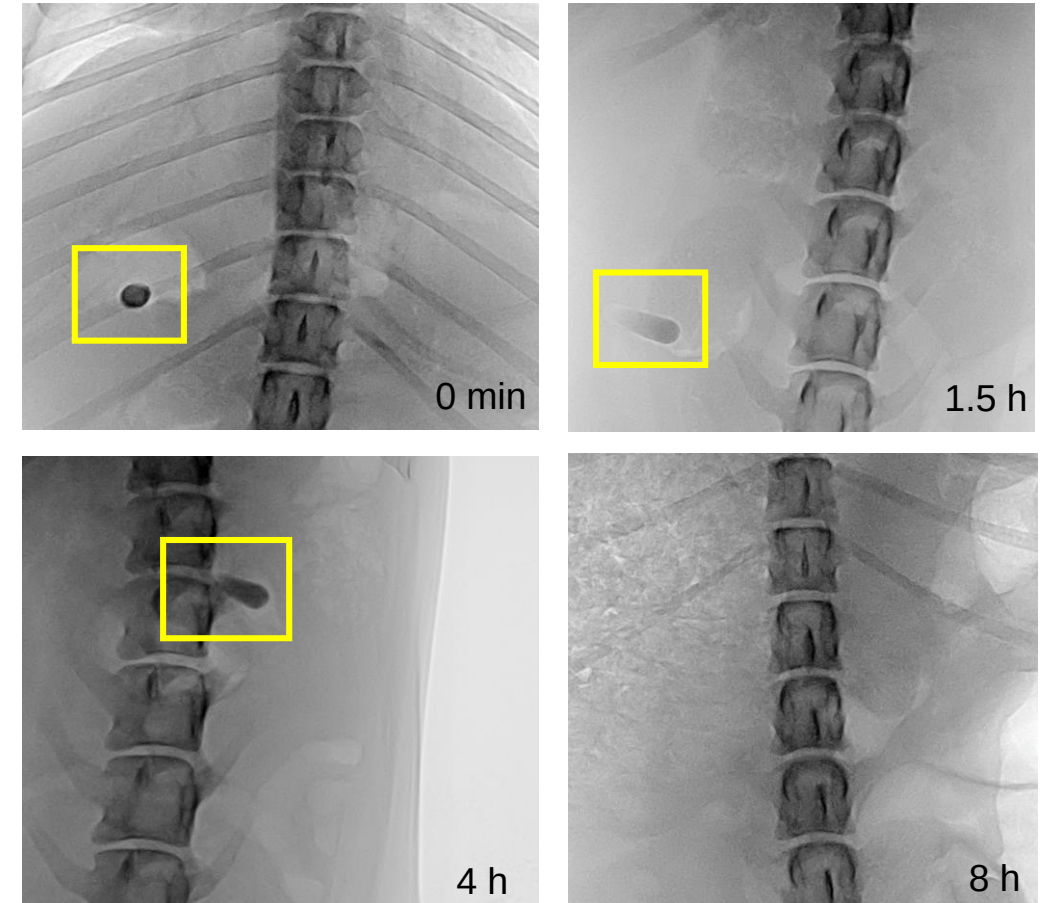


Type 1



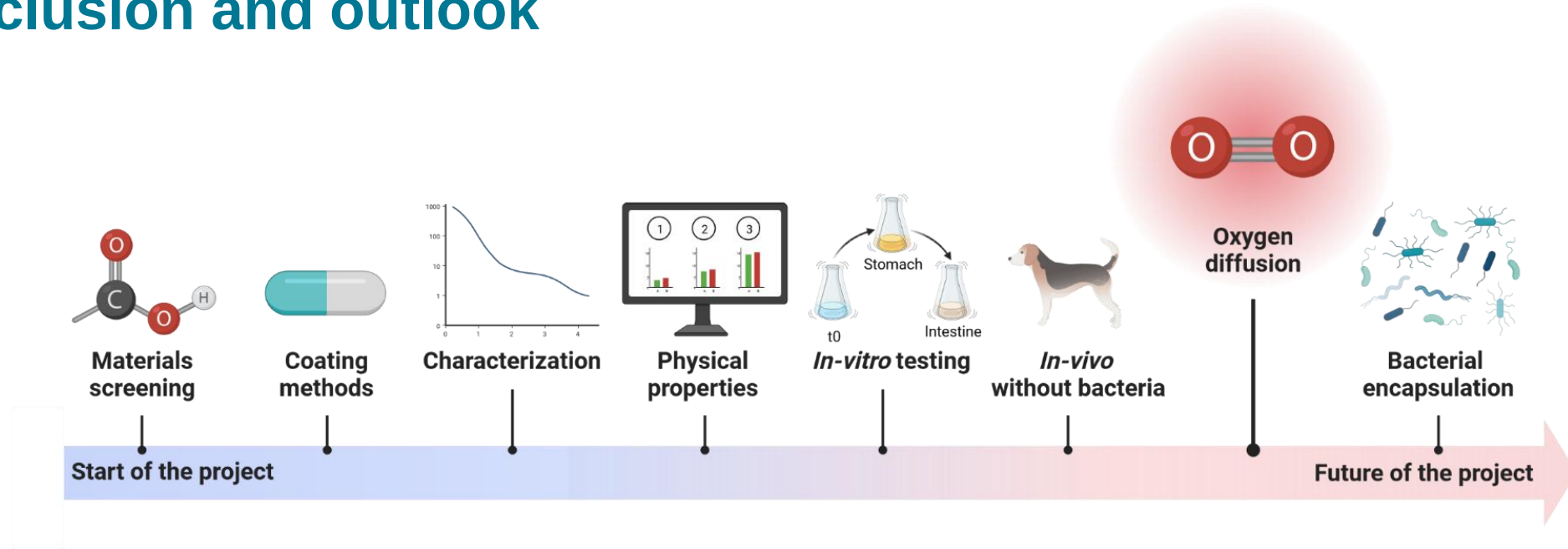
The average opening time is 4.2 h

Type 2



The average opening time is 3.2 h

Conclusion and outlook



Successful encapsulation of aqueous suspensions
Protection against harsh GI conditions
Opening *in-vivo* between 3-4 h
Assessing O₂ diffusion: versatile platform for strict anaerobes

Acknowledgments

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Valentine Berger

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In-vivo studies

Prof. Dr. Luo Zhi

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Thank you for your attention !
Questions ?

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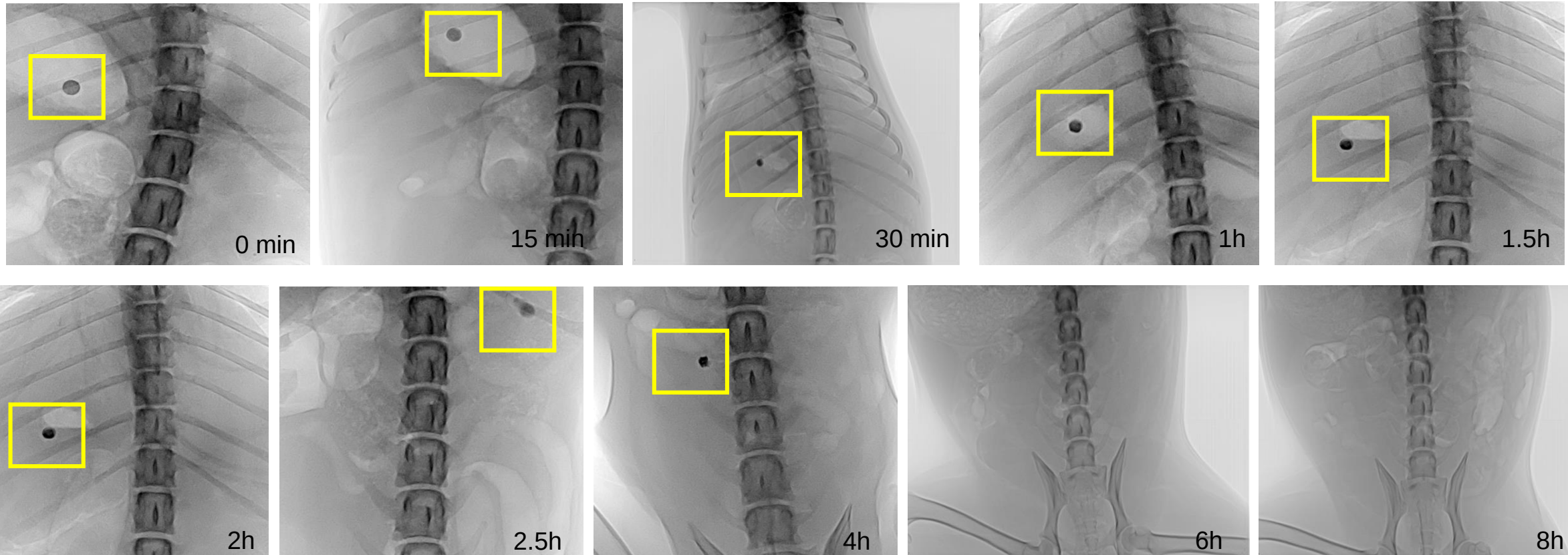
<https://galenik.ethz.ch/>



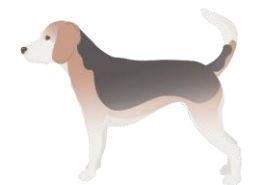
Back up slides

In vivo results:

Gastrointestinal transit in beagle dogs: X-ray investigation using BaSO₄ suspension : type 1

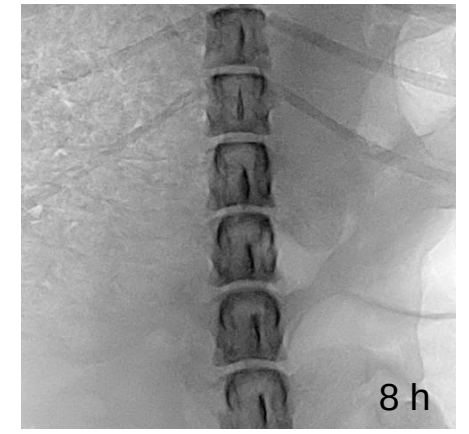
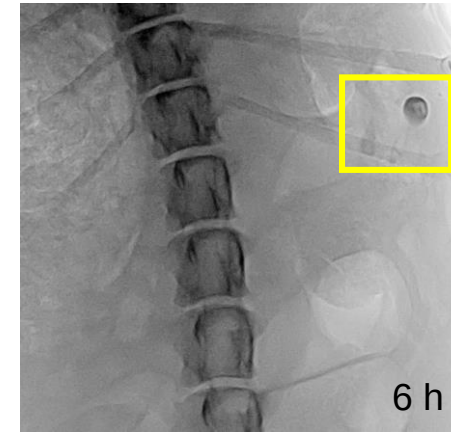
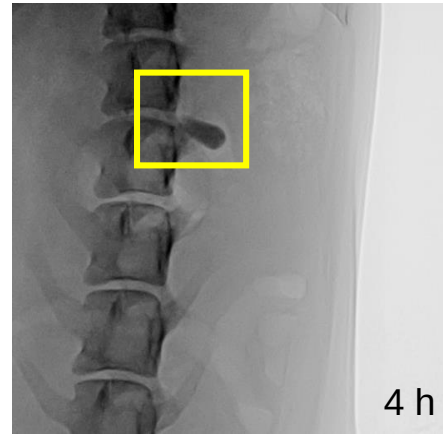
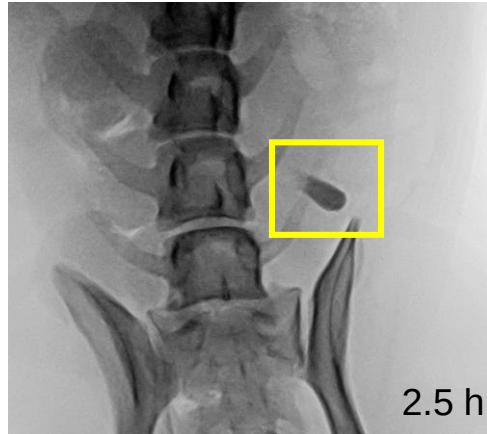
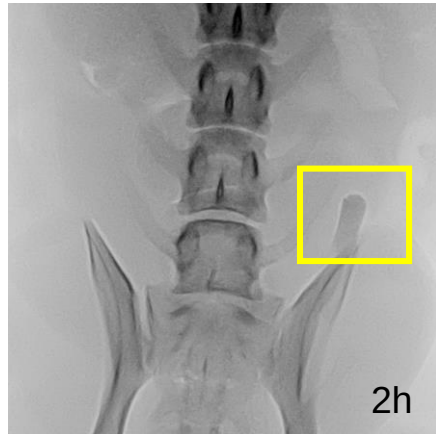
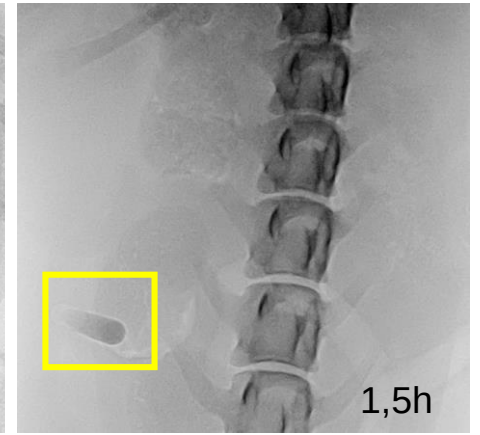
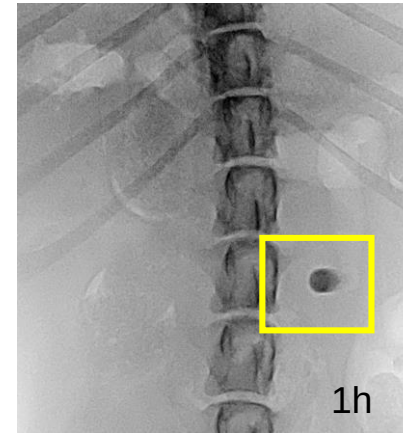
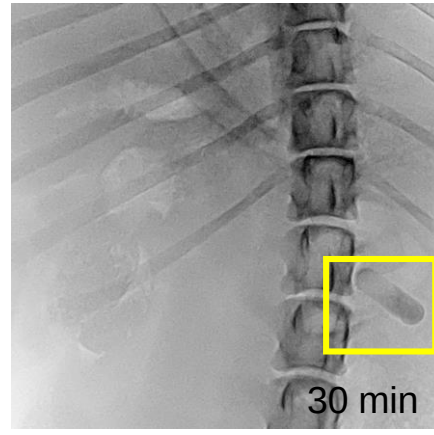
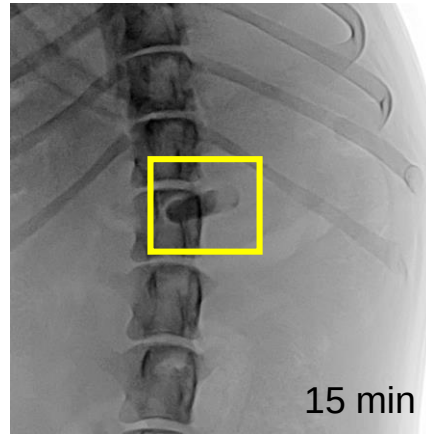
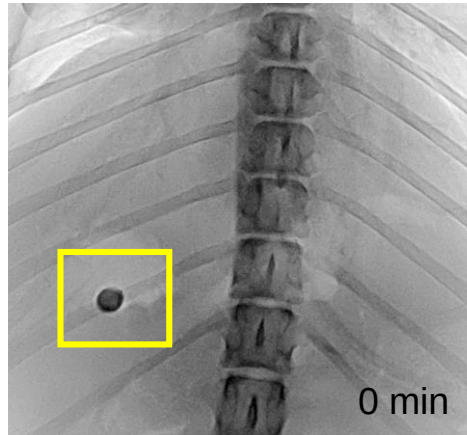


The average opening time is **4.16 h**



In vivo results:

Gastrointestinal transit in beagle dogs: X-ray investigation using BaSO₄ suspension : type 2



The average opening time is 3.16 h

