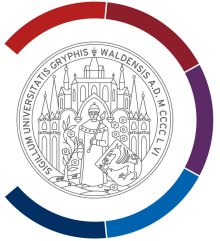


[Center of Drug Absorption and Transport]
Center of Competence of the University of Greifswald

UNIVERSITÄT GREIFSWALD
Wissen lockt. Seit 1456



Current developments in oral drug delivery concepts

Werner Weitschies

werner.weitschies@uni-greifswald.de

The holy grails of oral drug delivery

1. GASTRIC RETENTION

Why?


Promises of gastro-retentive dosage forms:

Release inside the stomach provides (continuous?) delivery to the small intestine:

- the only chance for extended absorption of drugs with absorption limited to the upper GI tract (e.g. frusemide, levodopa, many antibiotics, antivirals..)
- Duration of oral drug delivery no longer limited by GI transit times: Long lasting oral drug delivery (days – weeks?)

Review

In Vitro and In Vivo Test Methods for the Evaluation of Gastroretentive Dosage Forms

Felix Schneider, Mirko Koziolk and Werner Weitschies * 

Department of Biopharmaceutics and Pharmaceutical Technology, Institute of Pharmacy,
University of Greifswald, 17489 Greifswald, Germany

* Correspondence: werner.weitschies@uni-greifswald.de

Received: 10 July 2019; Accepted: 12 August 2019; Published: 16 August 2019



Mucoadhesion



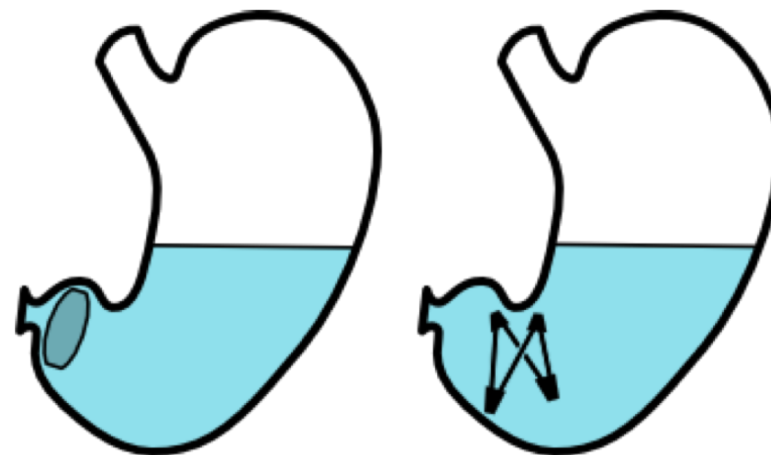
Floating



Sinking



Expansion (Blocking)



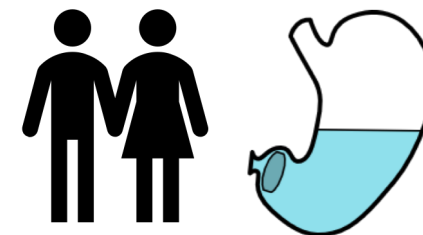


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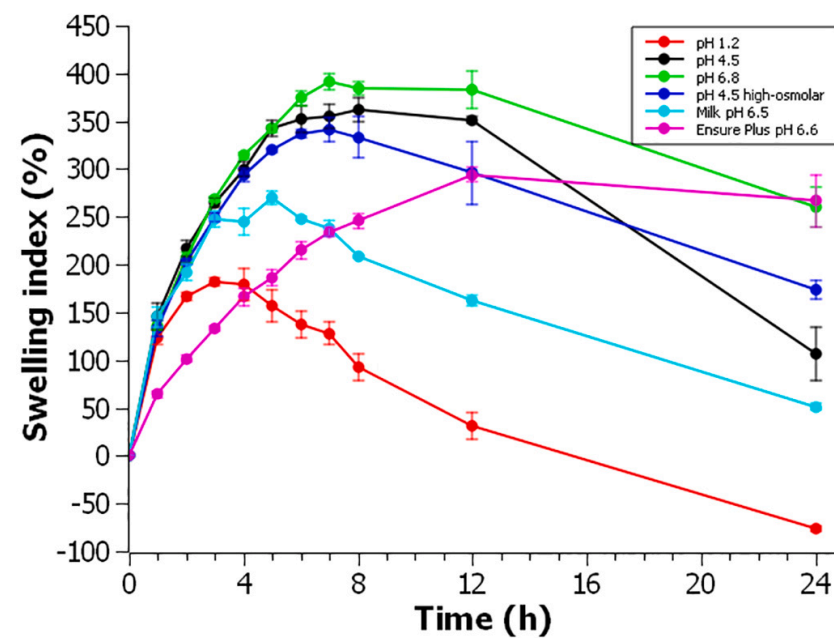
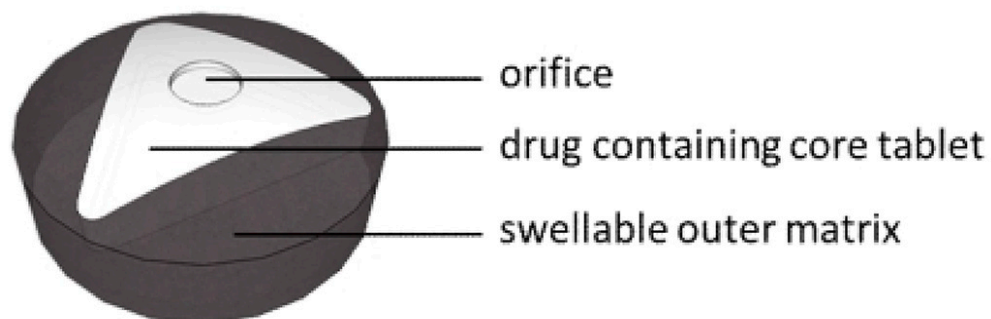
Journal of Controlled Release

journal homepage: www.elsevier.com/locate/jconrel



Development of a furosemide-containing expandable system for gastric retention

Marco Neumann^a, Claudia Heimhardt^a, Knut Seidlitz^b, Mirko Koziol^a, Felix Schneider^a, Christiane Schiller^b, Ulrike Hanke^b, Maria Anschutz^c, Christian Knopke^c, Frank Donath^c, Rudy Thoma^d, Christian Brätter^d, Barbara Schug^c, Hanshermann Franke^b, Werner Weitschies^{a,*}

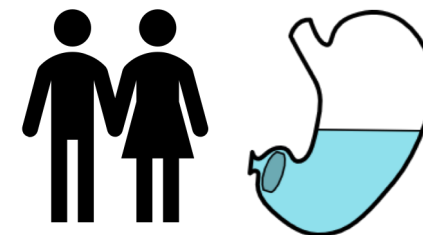




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Journal of Controlled Release

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Development of a furosemide-containing expandable system for gastric retention

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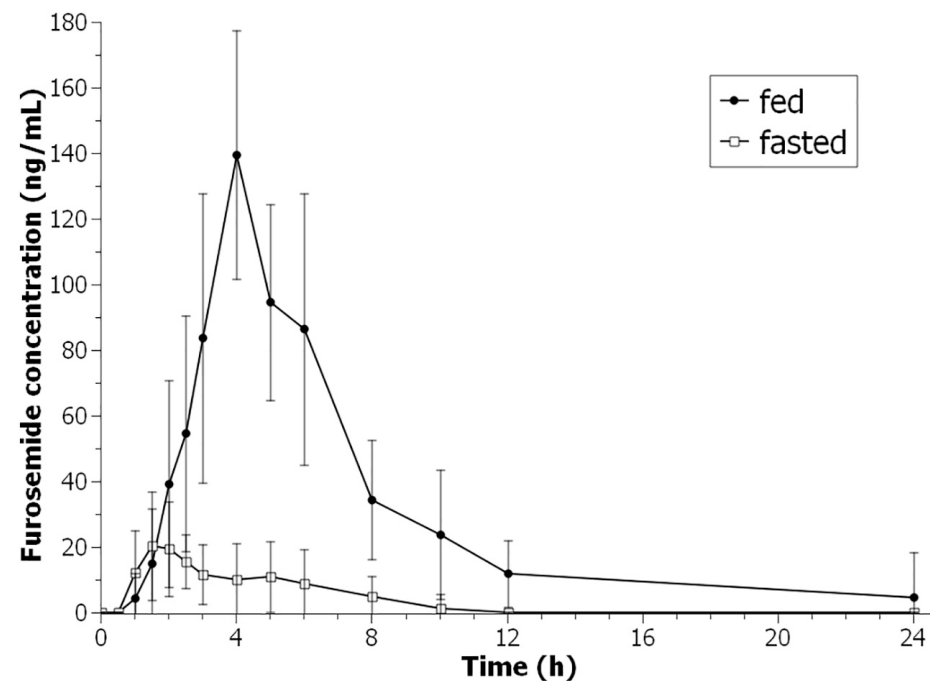
Table 4

Gastric emptying time of the swellable gastroretentive system for each subject after fasted and fed state administration.

Subject	GE “fasted” (min)	GE “fed” (min)
1	37	>748 ^a
2	55	279
3	47	533
4	37	>720 ^b
5	48	277
6	37	383
7	18	624
8	26	348
9	49	>569 ^b
10	23	>330 ^b
Mean	38	481
SD	12	180
Median	37	458

^a Last measurement after administration of the tablet.

^b Remaining magnetic moment was too low to ensure a correct localization of the tablet.

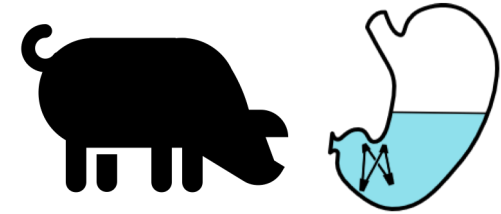


DRUG DELIVERY

Oral, ultra-long-lasting drug delivery: Application toward malaria elimination goals

Andrew M. Bellinger,^{1,2,3*} Mousa Jafari,^{1*} Tyler M. Grant,^{1,3*} Shiyi Zhang,^{1*†} Hannah C. Slater,⁴ Edward A. Wenger,⁵ Stacy Mo,¹ Young-Ah Lucy Lee,¹ Hormoz Mazdiyasni,¹ Lawrence Kogan,¹ Ross Barman,¹ Cody Cleveland,^{1,6} Lucas Booth,¹ Taylor Bensen,¹ Daniel Minahan,¹ Haley M. Hurowitz,¹ Tammy Tai,¹ Johanna Daily,⁷ Boris Nikolic,⁸ Lowell Wood,⁵ Philip A. Eckhoff,⁵ Robert Langer,^{1,9,10‡} Giovanni Traverso^{1,6,11‡}

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of Science.



NATURE COMMUNICATIONS | (2018)9:2

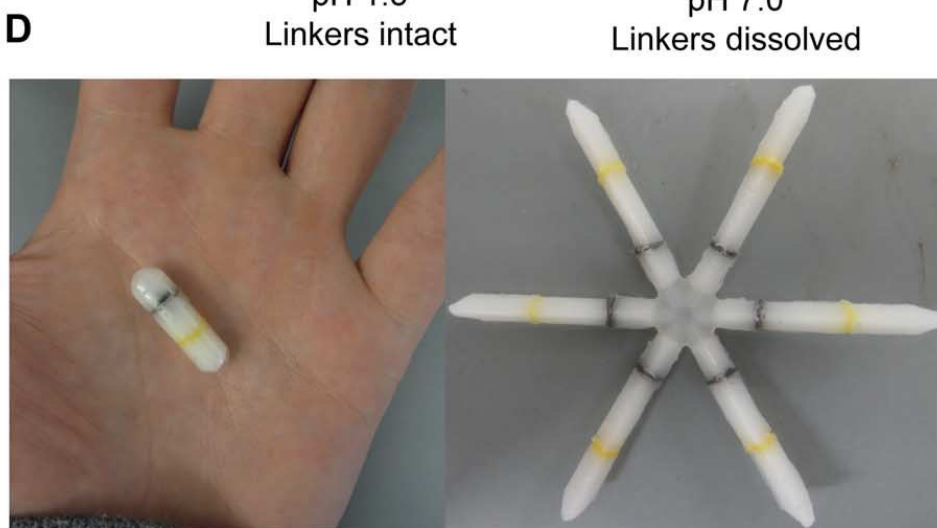
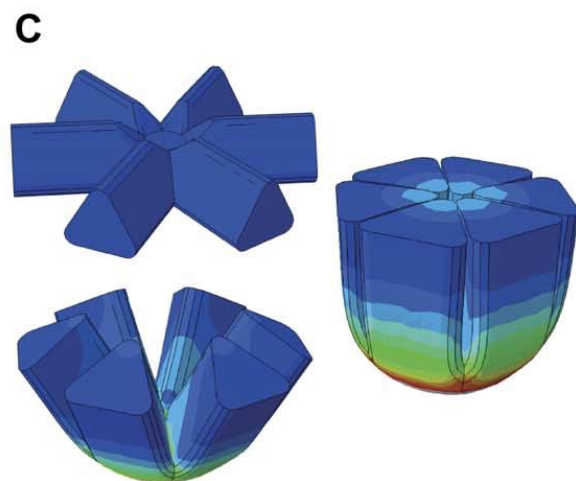
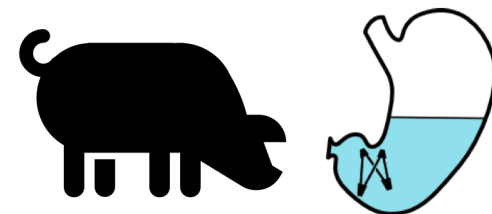
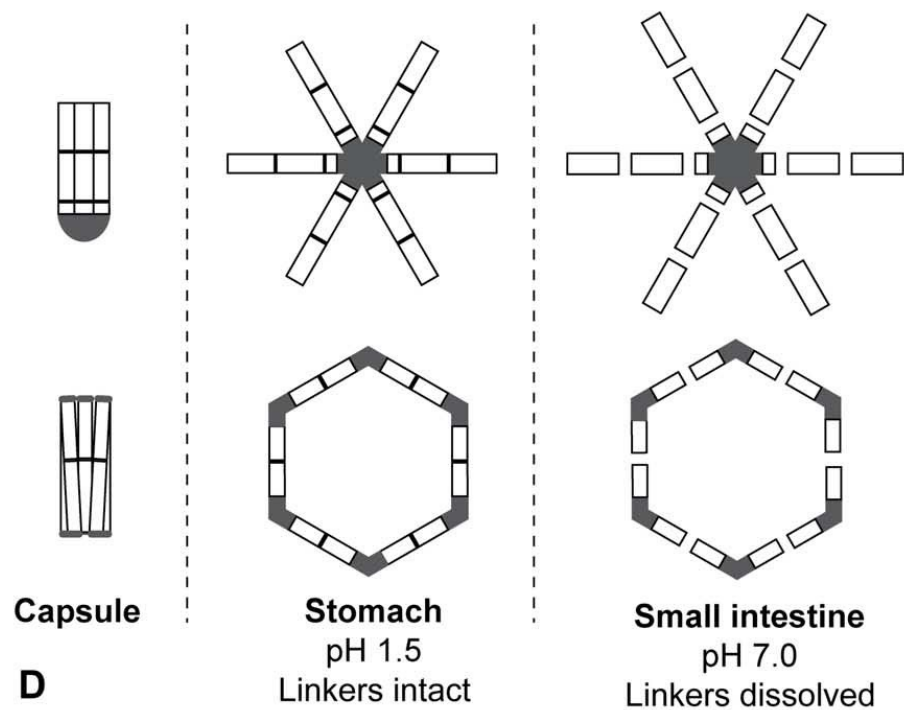
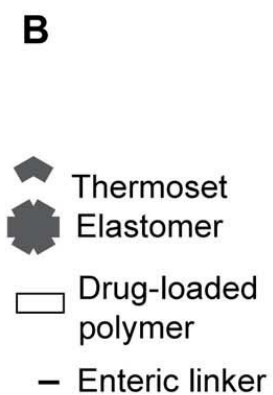
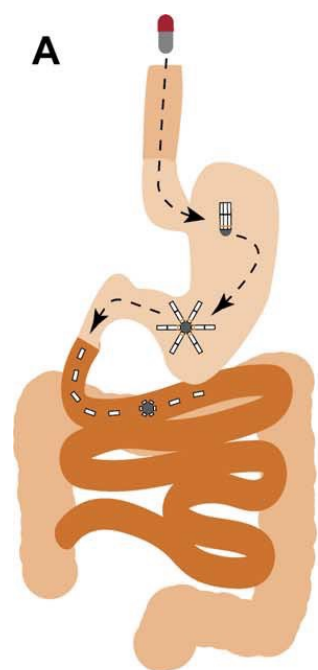
ARTICLE

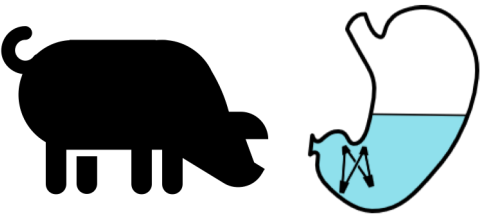
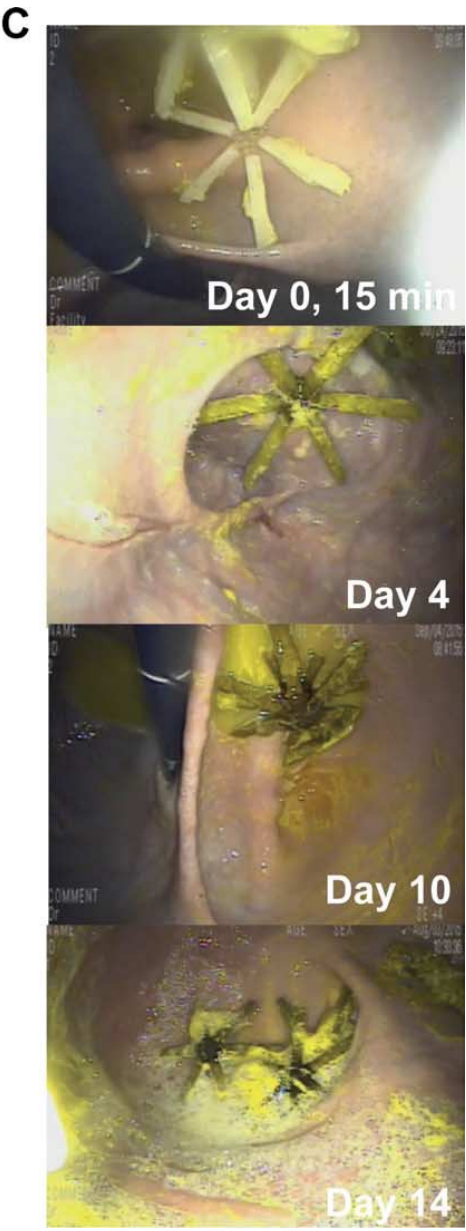
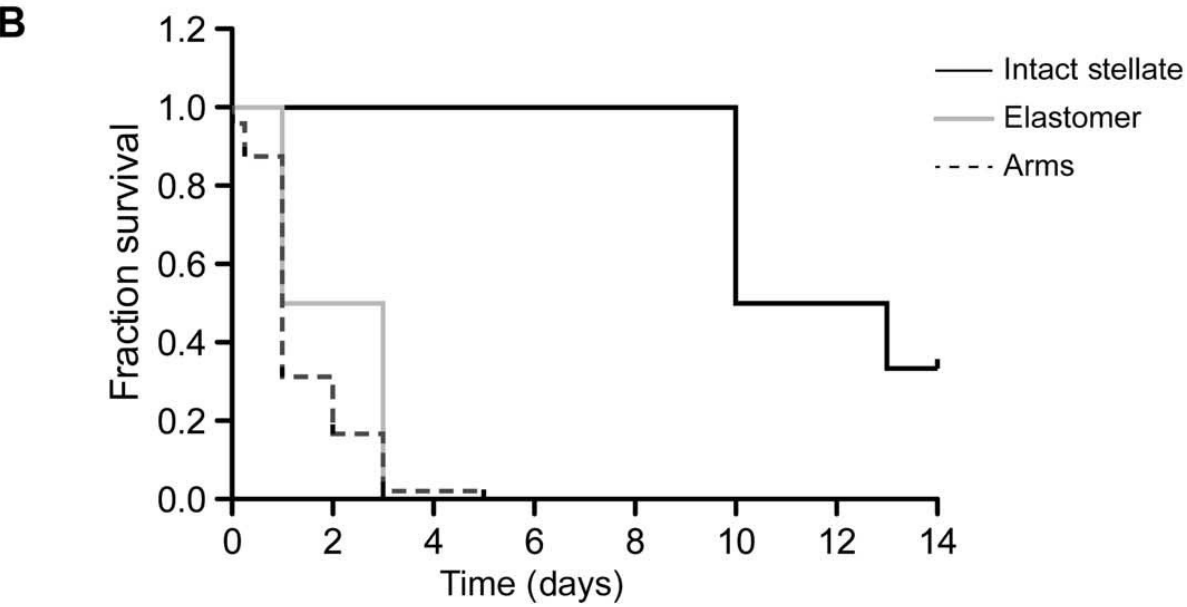
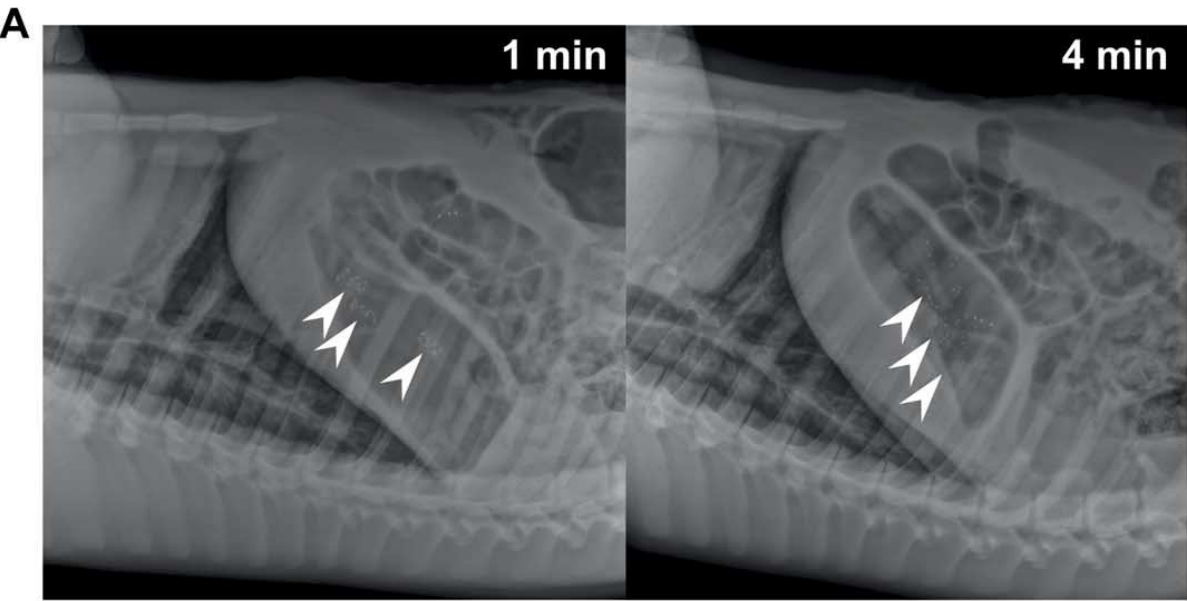
DOI: 10.1038/s41467-017-02294-6

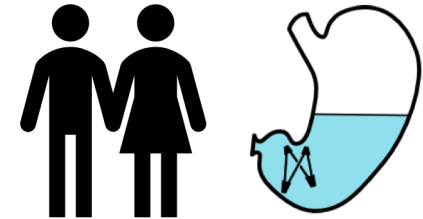
OPEN

Development of an oral once-weekly drug delivery system for HIV antiretroviral therapy

Ameya R. Kirtane¹, Omar Abouzid^{1,2}, Daniel Minahan¹, Taylor Bensen¹, Alison L. Hill³, Christian Selinger⁴, Anna Bershteyn⁴, Morgan Craig³, Shirley S. Mo³, Hormoz Mazdiyasni¹, Cody Cleveland^{1,5}, Jaimie Rogner¹, Young-Ah Lucy Lee¹, Lucas Booth¹, Farhad Javid, Sarah J. Wu⁶, Tyler Grant⁷, Andrew M. Bellinger⁷, Boris Nikolic⁸, Alison Hayward¹, Lowell Wood⁴, Philip A. Eckhoff⁴, Martin A. Nowak³, Robert Langer^{1,9,10} & Giovanni Traverso^{1,5}







Human/Human trials: Other

Ultra long-acting oral therapies for Alzheimer's: Proof of principle

Richard E. Scranton¹ | William Avery¹ | Cecilia Kruger¹ | Andrew Bellinger² |
Bernard Silverman¹

Method: The Lyndra ER capsule has modular features serving specific functions for extended delivery to the stomach. The features include a star-shaped drug-releasing formulation (stellate) with up to six drug-loaded polymer arms formulated to achieve controlled drug release while maintaining gastric residence. Polymer-coated arms yield a steady rate of drug release into the stomach. The formulation is designed to lose its structural integrity after a period of residence and to pass safely through the GI tract. To test the feasibility of this approach, 8 healthy volunteers received a single dose of LYN-157 containing 40 mg of memantine HCl and 38mg of donepezil HCl while under observation in a Phase 1 unit for 7 days.

Human/Human trials: Other

Ultra long-acting oral therapies for Alzheimer's: Proof of principle

Richard E. Scranton¹ | William Avery¹ | Cecilia Kruger¹ | Andrew Bellinger² | Bernard Silverman¹

Alzheimer's Dement. 2020;16(Suppl. 9):e043034.
<https://doi.org/10.1002/alz.043034>

[wileyonlinelibrary.com/journal/alz](https://onlinelibrary.com/journal/alz)

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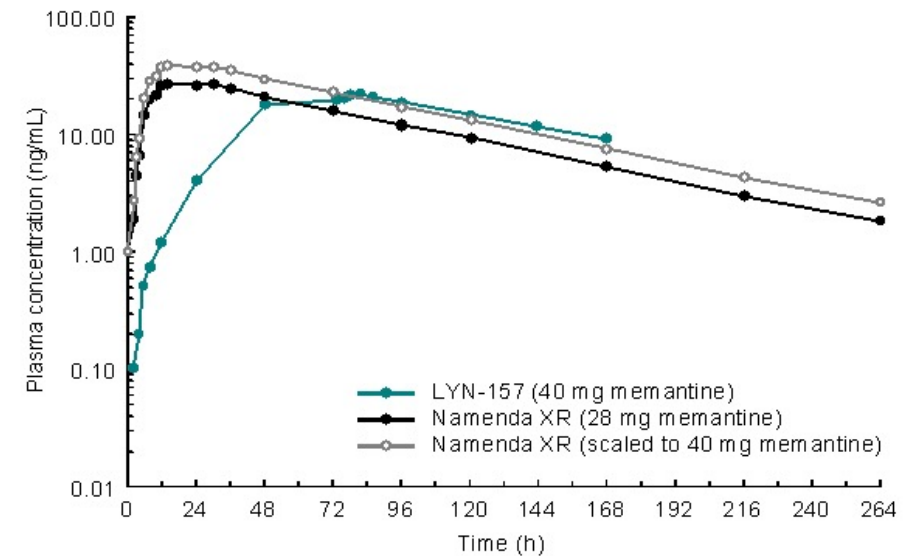
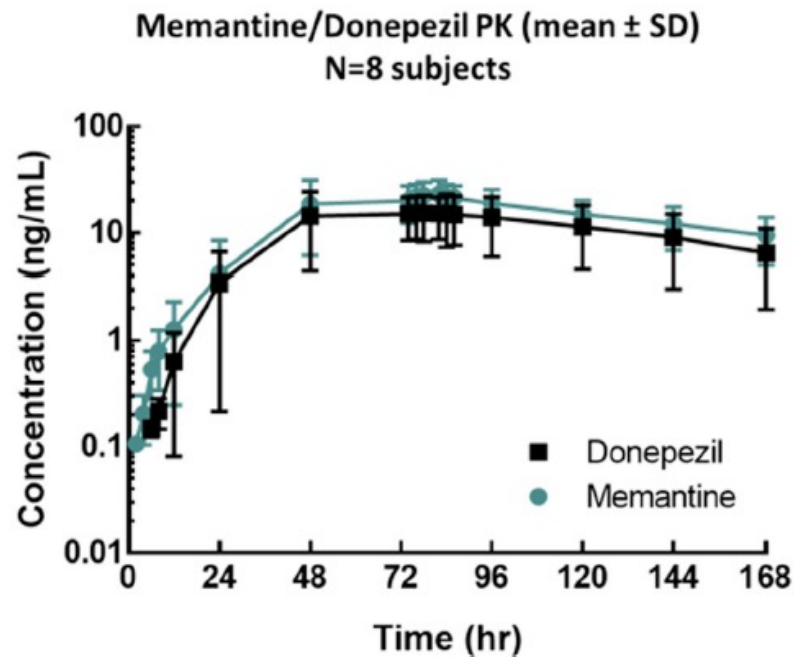
Clin Drug Investig (2015) 35:427–435
 DOI 10.1007/s40261-015-0296-4



ORIGINAL RESEARCH ARTICLE

A Novel Once-Daily Fixed-Dose Combination of Memantine Extended Release and Donepezil for the Treatment of Moderate to Severe Alzheimer's Disease: Two Phase I Studies in Healthy Volunteers

Ramesh Boipally¹ · Laishun Chen¹ · Stephen R. Zukin^{1,3} · Natalie McClure² · Robert K. Hofbauer¹ · Antonia Periclou¹



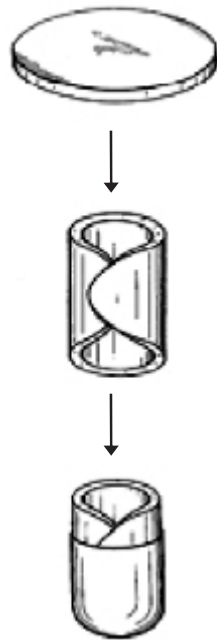
Expansion



4-lobed



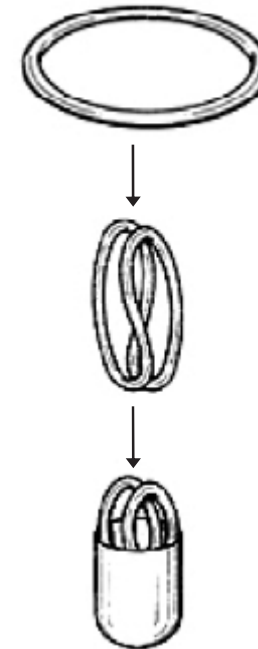
Disc



4-limbed cross



Ring



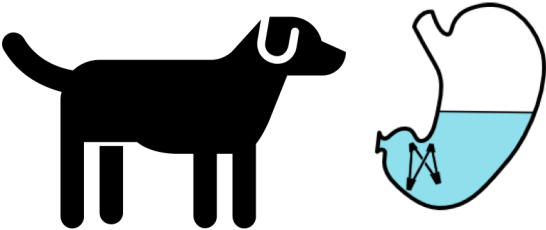
Tetrahedron



Caldwell et al. US Patent, 1988

Report

Controlled Gastric Emptying. II. *In Vitro* Erosion and Gastric Residence Times of an Erodible Device in Beagle Dogs



Robyn Cargill,^{1,4} Karen Engle,¹ Colin R. Gardner,^{1,2} Patricia Porter,^{1,3} Randall V. Sparer,¹ and Joseph A. Fix¹

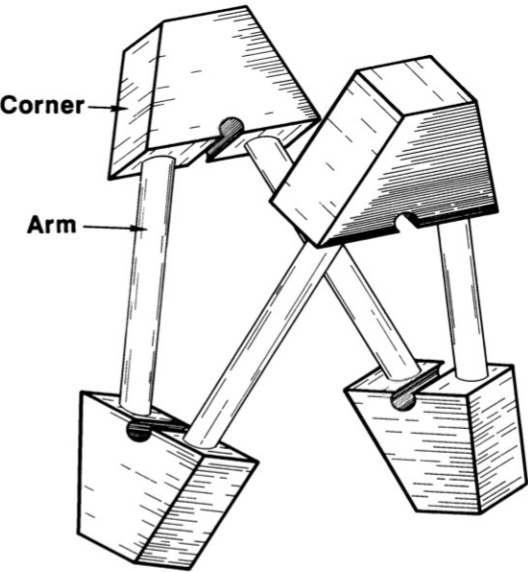


Fig. 1. Gastric drug platform. Tetrahedron-shaped devices formed by assembling two components, silastic corners and polymeric arms.

2 cm x 2 cm x 2 cm

Table II. *In Vivo* Gastric Retention of Poly(Ortho Ester)/Polyethylene Tetrahedral Devices

Polymer blend (ratio of POE/PE)	% retained in stomach at 24 hr	N
50/50	80	5
65/35	80	5
72/25	100	5
80/20	0	4
85/15	25	4
90/10	0	5

Controlled Gastric Emptying. III. Gastric Residence Time of a Nondisintegrating Geometric Shape in Human Volunteers

Joseph A. Fix,^{1,2} Robyn Cargill,¹ and Karen Engle¹

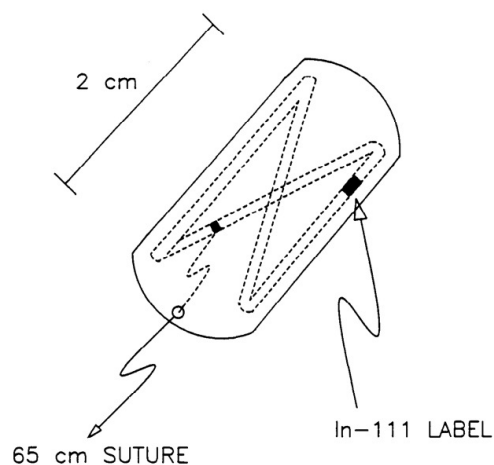


Fig. 1. Schematic of open tetrahedron compressed inside No. 000 hard gelatin capsule.

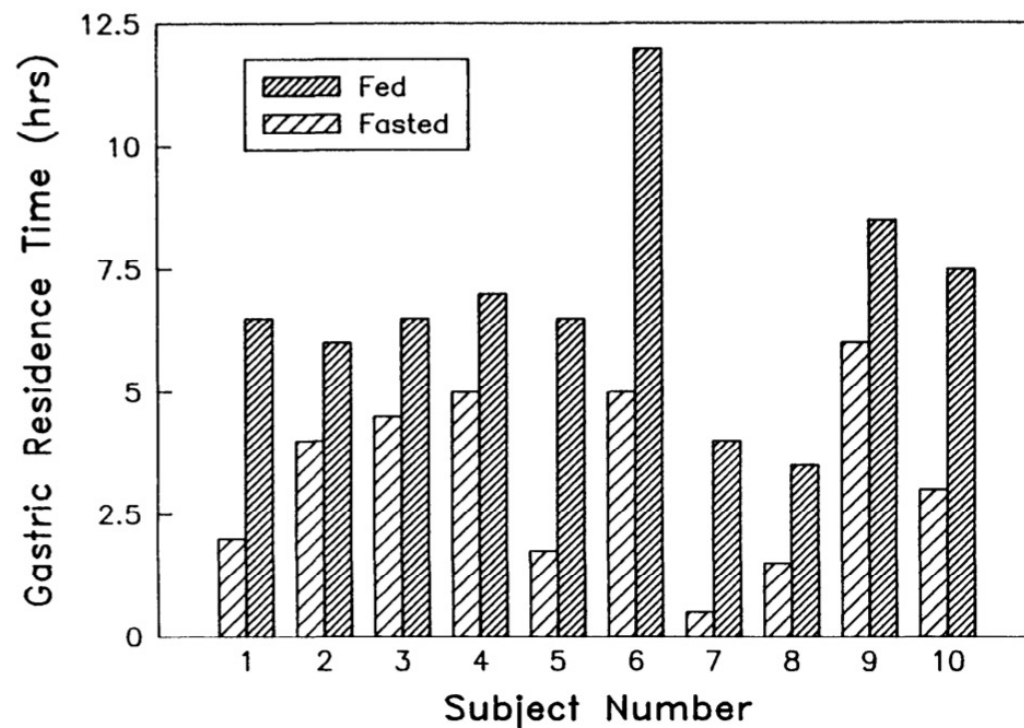
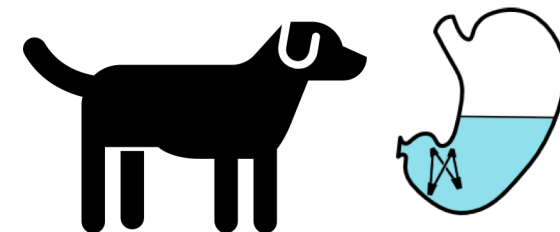
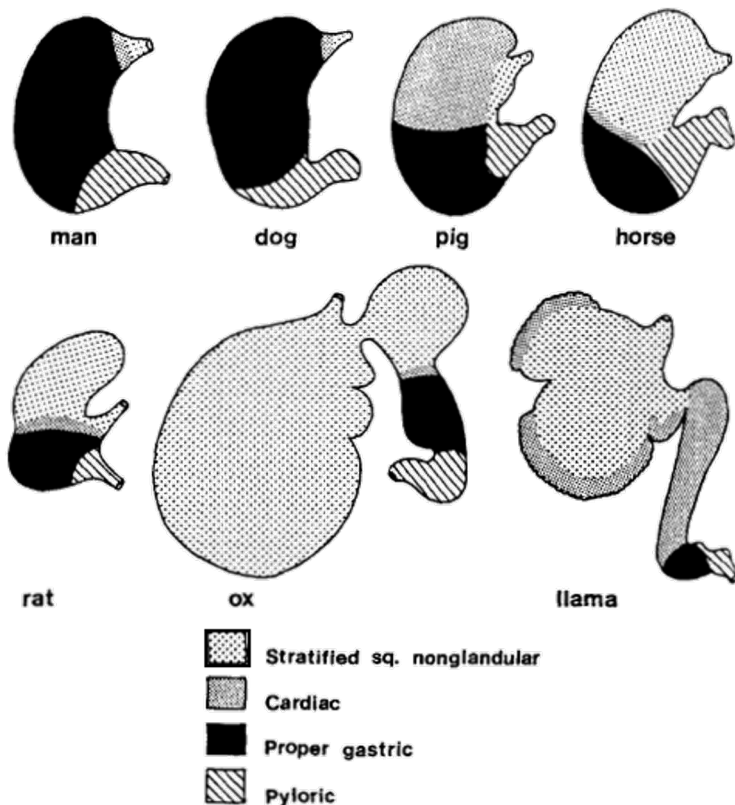


Fig. 2. Individual data for gastric residence time of open tetrahedron in human volunteers.

Animal models für human GI-tract?

GI anatomy and physiology: Different species



BIOPHARMACEUTICS & DRUG DISPOSITION, VOL. 16, 351-380 (1995)

REVIEW ARTICLE

COMPARISON OF THE GASTROINTESTINAL ANATOMY, PHYSIOLOGY, AND BIOCHEMISTRY OF HUMANS AND COMMONLY USED LABORATORY ANIMALS

TUGRUL T. KARARLI

Figure 1. Variations in the type and distribution of gastric mucosa. Stomachs are not drawn to scale. From reference 1, with permission

Report

Gastrointestinal Transit of Nondisintegrating, Nonerodible Oral Dosage Forms in Pigs

Mohammad Hossain,¹ Wattanaporn Abramowitz,¹ Barbara J. Watrous,² Gregory J. Szpunar,³ and James W. Ayres^{1,4}

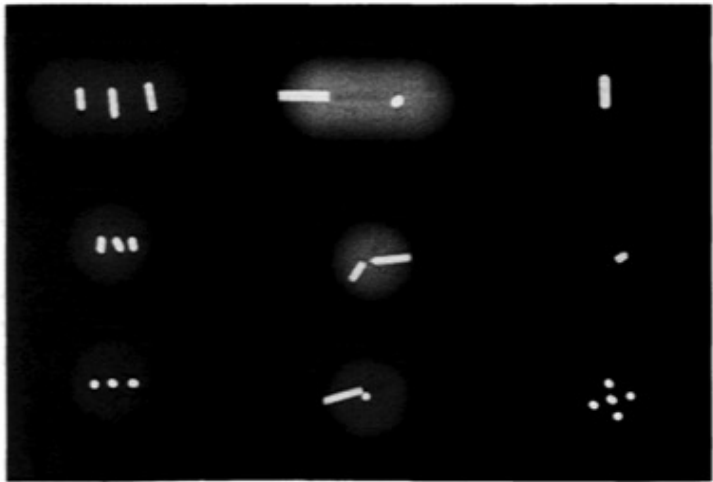
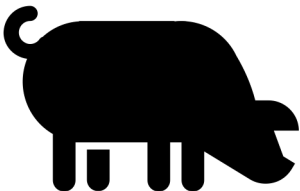


Fig. 1. X-ray photograph of dosage forms used in the study. Small stainless-steel rods inserted in dosage forms help radiographic visualization and identification. Left to right (density): Teflon, 2.30 g/ml; PVC, 1.45 g/ml; nylon, 1.25 g/ml. Top to bottom (size): large, 20 × 10 mm; medium, 10 × 10 mm; small, 5 × 10 mm.

Table II. Transit Time in Pigs for High-, Medium-, and Low-Density Nonerodible, Rigid Oral Dosage Forms Having Large, Medium, and Small Sizes

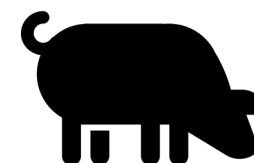
Subject	Density	Transit time (days)		
		Gastric	Small intestine	Large intestine
Large caplet				
1	Low	1	<1	<1
2	"	5	<1	>2
1	Medium	10	2	19
2	"	5	1	1
	"	24 ^a	<1	<1
1	High	13	2	4
2	"	5	2	3
	"	29 ^a	<1	>3
Medium caplet				
1	Low	4	<1	>1
2	"	4	<1	>1
1	Medium	2	1	3
2	"	1	<1	<1
1	High	7	<1	>3
2	"	5	2	1
Small caplet				
1	Low	1	<1	>1
2	"	10	1	1
1	Medium	1	<1	<1
2	"	2	1	1
1	High	24	1	1
2	"	3	2	2

^a Repeat experiment in same animal.



Contents lists available at ScienceDirect

European Journal of Pharmaceutical Sciences

journal homepage: www.elsevier.com/locate/ejps

Characterization of gastrointestinal transit and luminal conditions in pigs using a telemetric motility capsule

Laura J. Henze^a, Niklas J. Koehl^a, Harriet Bennett-Lenane^a, René Holm^{b,c}, Michael Grimm^d, Felix Schneider^d, Werner Weitschies^d, Mirko Koziol^d, Brendan T. Griffin^{a,*}

^a School of Pharmacy, University College Cork; Cork, Ireland

^b Drug Product Development, Janssen Research and Development, Johnson & Johnson, Turnhoutseweg 30, 2340 Beerse, Belgium

^c Department of Science and Environment, Roskilde University, Universitetsvej 1, DK-4000 Roskilde, Denmark

^d Department of Biopharmaceutics and Pharmaceutical Technology, Institute of Pharmacy, University of Greifswald, Felix-Hausdorff-Strasse 3, 17489 Greifswald, Germany

Table 2

Individual transit times of the SmartPill® administered in four male landrace pigs under fasted and fed conditions. GET – gastric emptying time; CAT – colonic arrival time; SITT – small intestinal transit time; CTT – Colon transit time; WGT – whole gut transit time.

Pig	GET		SITT		CAT		CTT		WGT	
	fasted	fed	fasted	fed	fasted	fed	fasted	fed	fasted	fed
1	92 h	22 h	2.6 h	2.3 h	95 h	25 h	83 h	169 h	177 h	194 h
2	68 h	43.4 h	3.2 h	2.6 h	71 h	46 h	32 h	83 h	103 h	129 h
5	233 h	118 h	3.2 h	n.a. *	235 h	n.a. *	21 h	> 140 h *	257 h	262 h
48	94 h	20 h	4.0 h	3.8 h	98 h	24 h	79 h	55 h	177 h	79 h

* Signal loss



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Characterization of gastrointestinal transit and luminal conditions in pigs using a telemetry system

Laura J. Henze^a, Nil
Felix Schneider^d, W

^a School of Pharmacy, University of

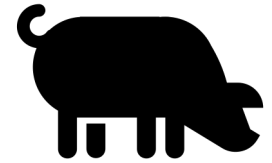
^b Drug Product Development, Janssen

^c Department of Science and Environ

^d Department of Biopharmaceutics o
Germany

3. Results

Overall whole gut transit time (WGTT) was successfully determined using SmartPill® capsules in four landrace pigs (P1, P2, P5, P48) in a two-way crossover of fasted and fed state. The fasted and fed study conditions were based on previous established study protocols, utilizing a standard high-caloric, high-fat FDA breakfast (Henze et al., 2019). Individual profiles of SmartPill® data obtained are illustrated in Fig. 2. As explained in the methods, in three pigs (P3, P6 & P44) the SmartPill® capsule remained in the stomach for more than a week until the battery was completely discharged. They were therefore excluded from the study.

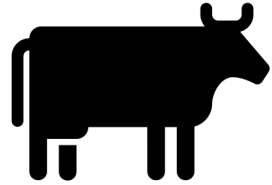




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Livestock Science

journal homepage: www.elsevier.com/locate/livsci



Measurement of abomasal conditions (pH, pressure and temperature) in healthy and diarrheic dairy calves using a wireless ambulatory capsule

Thomas Hildebrandt^a, Eberhard Scheuch^b, Werner Weitschies^c, Michael Grimm^c,
Felix Schneider^c, Lisa Bachmann^d, Ingrid Vervuert^{a,*}

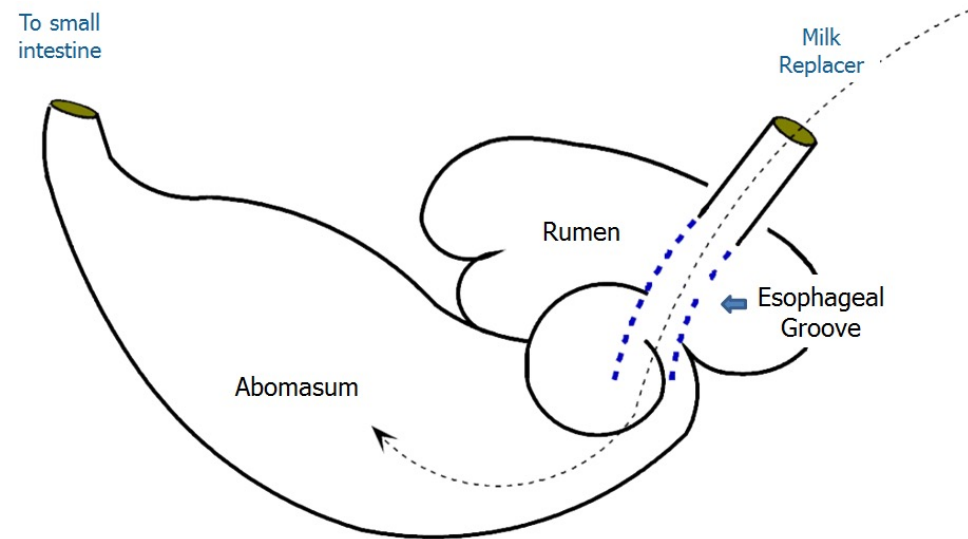
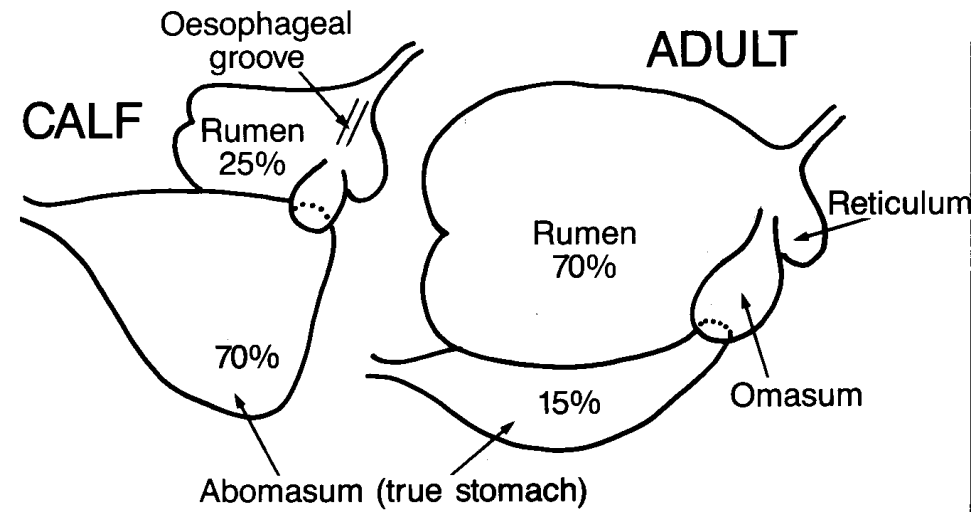
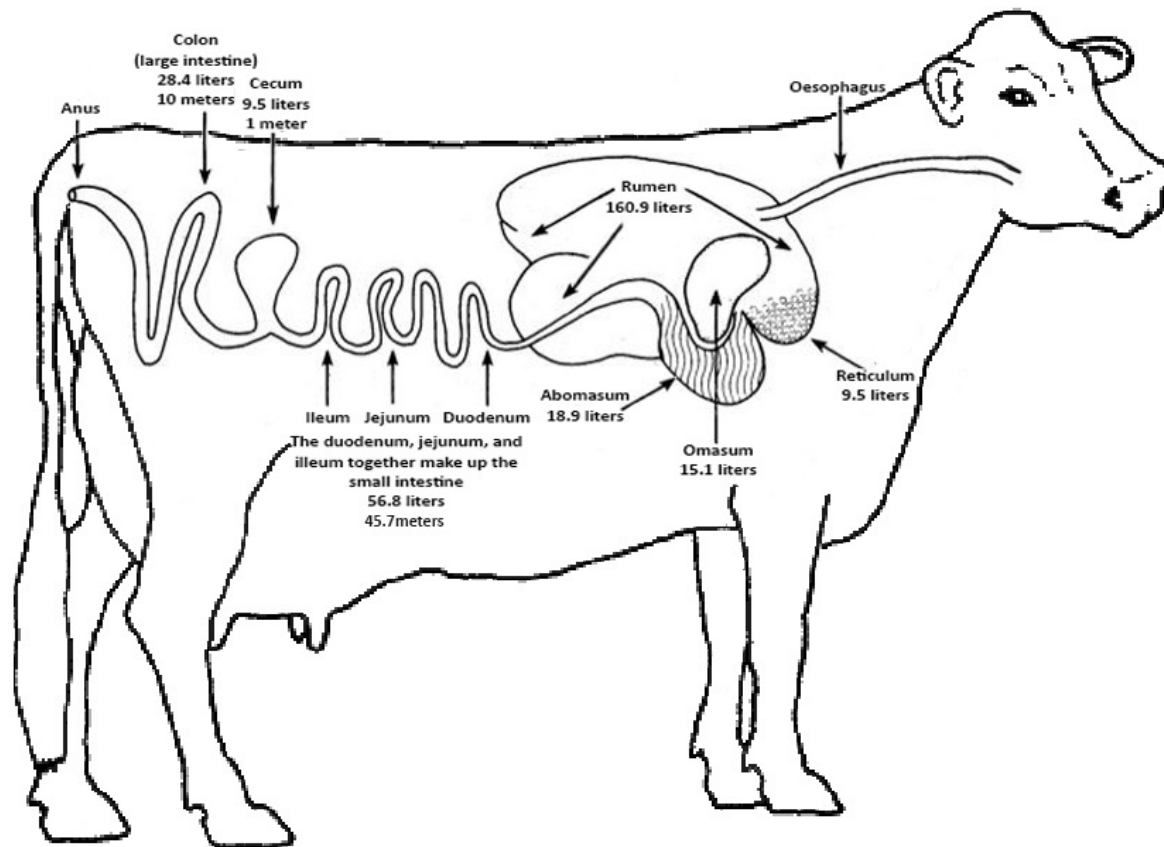
^a Faculty of Veterinary Medicine, University of Leipzig, Institute of Animal Nutrition, Nutrition Diseases and Dietetics, An den Tierkliniken 9, D-04103 Leipzig, Germany

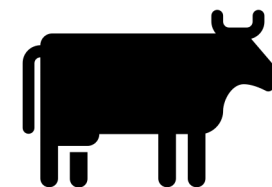
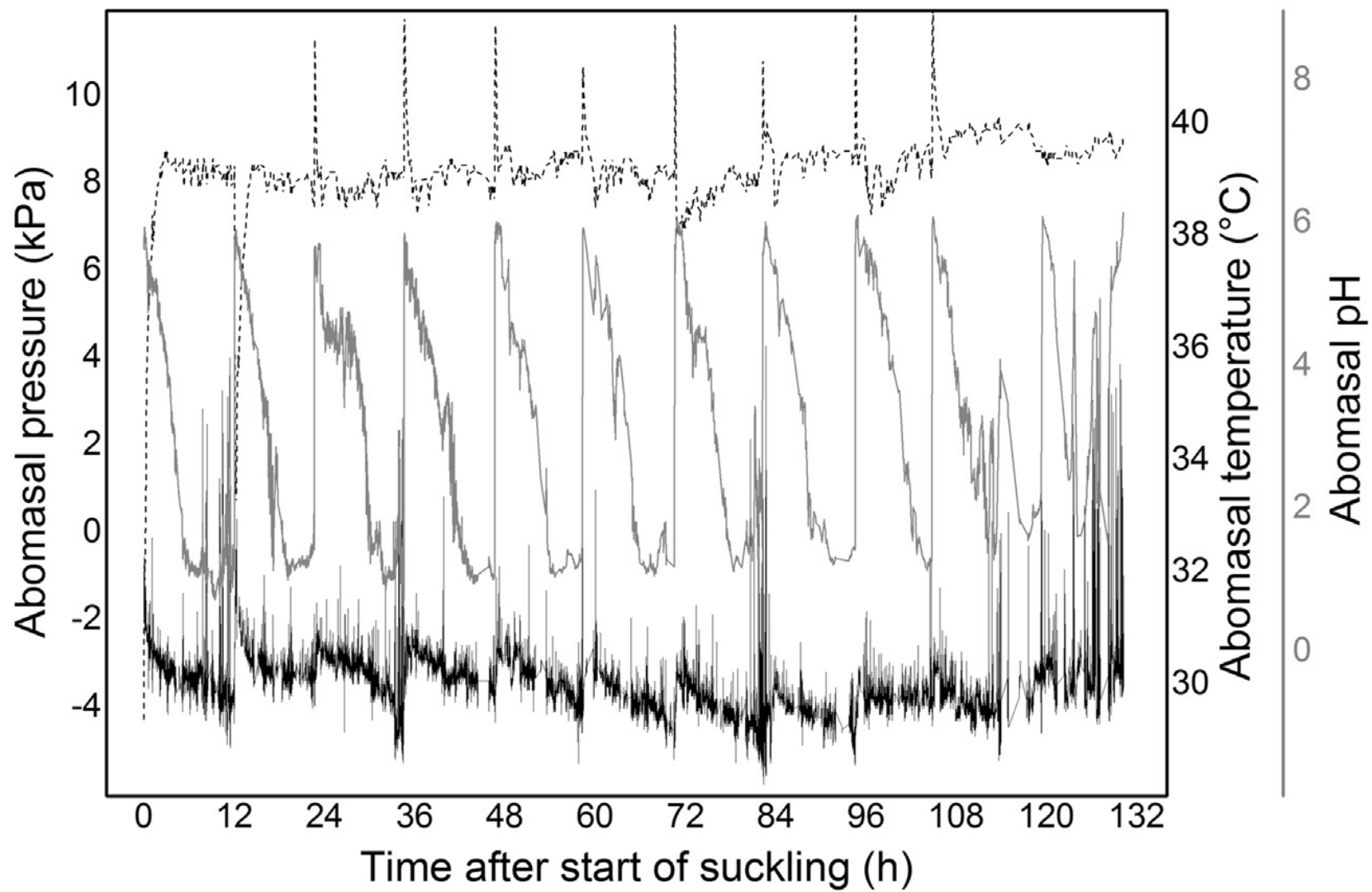
^b Center of Drug Absorption and Transport, Ernst Moritz Arndt University of Greifswald, Department of Clinical Pharmacology, Felix-Hausdorff-Straße 3, D-17487 Greifswald, Germany

^c Center of Drug Absorption and Transport, Ernst Moritz Arndt University of Greifswald, Department of Biopharmaceutics and Pharmaceutical Technology, Felix-Hausdorff-Str. 3, D-17487 Greifswald, Germany

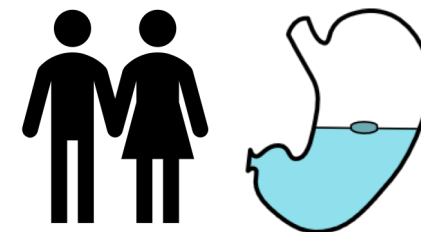
^d Alta Deutschland GmbH, Altes Dorf 1, D-29525 Uelzen, Germany







Floating instead of expanding? Density effects on gastric transit of capsules



European Journal of Pharmaceutical Sciences 129 (2019) 163–172



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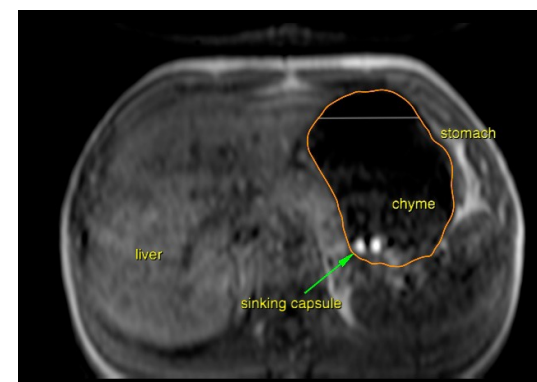
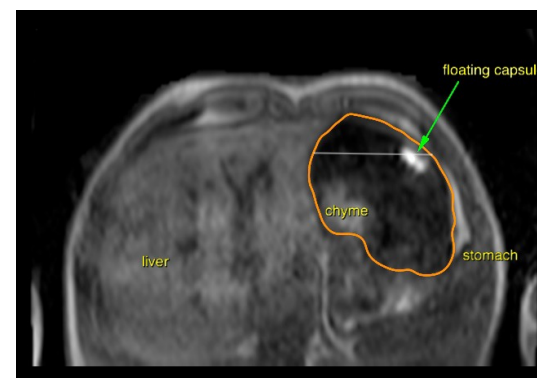
European Journal of Pharmaceutical Sciences

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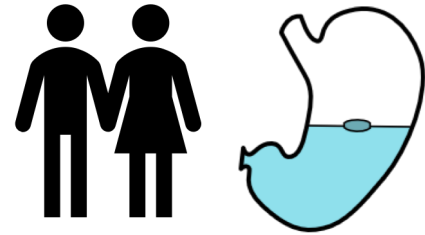
Characterization of the gastrointestinal transit and disintegration behavior of floating and sinking acid-resistant capsules using a novel MRI labeling technique

Michael Grimm^a, Katharina Ball^a, Elisabeth Scholz^a, Felix Schneider^a, Aurélien Sivert^b, Hassan Benameur^b, Marie-Luise Kromrey^c, Jens-Peter Kühn^{c,d}, Werner Weitschies^{a,*}

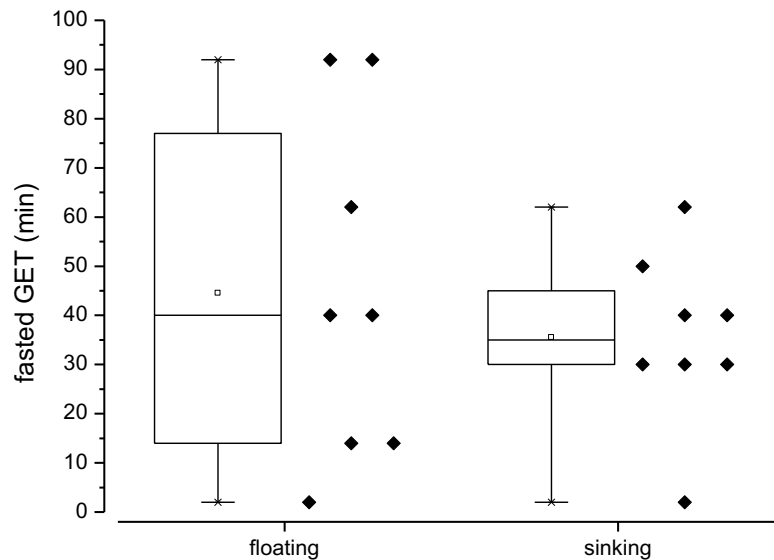


Floating instead of expanding?

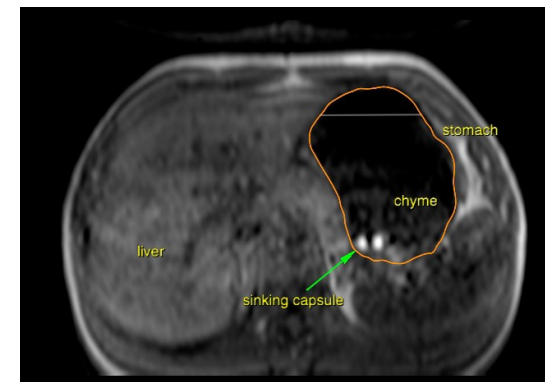
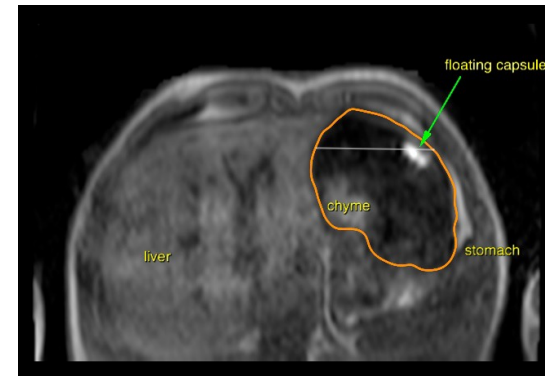
Density effects on gastric transit of capsules



→ no evidence for altered gastric transit due to lower density of capsules

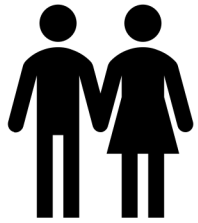


Distribution of gastric emptying times (GET) in fasted state of the floating and sinking formulation (whisker 0-100%; n=8)



MRI: Water in the stomach

Gastric fluid content volumes after drinking 240 mL of water



3 min: 247 mL

8 min: 137 mL

18 min: 3 mL



The holy grails of oral drug delivery

2. Oral Protein Delivery

Oral Delivery of Peptides/Proteins

- Penetration enhancers
- Nano (-technology, -medicine, -materials)
- Intestinal patches
- (Micro)needles
- Combinations thereof

Problems of oral peptide/protein delivery

- Enzymatic degradation (digestion)
- Low permeability
- ☞ Very high variability

Penetration enhancers (PE)



In clinical use:

- SNAC (Salcaprozate sodium, in: Vit. B₁₂ (Eligen™-B₁₂) and semaglutide (Rybelsus®))
- C₁₀ (Sodium caprate, in: rectal ampicillin (Doktacillin®), withdrawn)
- C₈ (Sodium caprylate, in: Octreotide (Mycapssa®))

Oral semaglutide (Rybelsus®)



SCIENCE TRANSLATIONAL MEDICINE | RESEARCH ARTICLE

DRUG MECHANISM

Transcellular stomach absorption of a derivatized glucagon-like peptide-1 receptor agonist

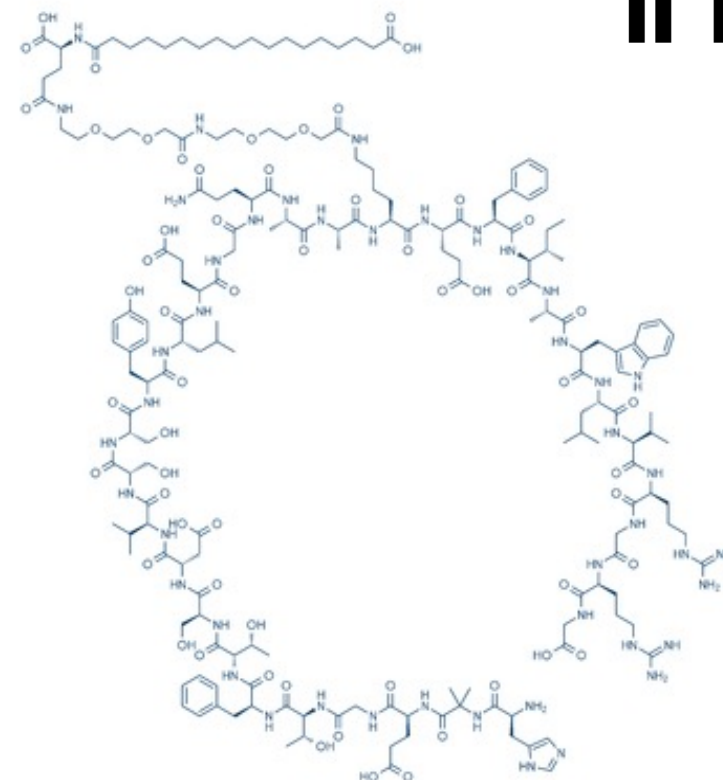
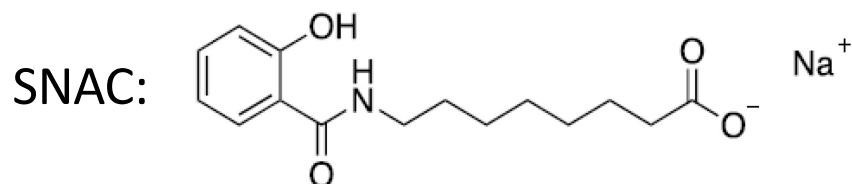
Stephen T. Buckley^{1*†}, Tine A. Bækdal^{2†}, Andreas Vegge^{1†}, Stine J. Maarbjer², Charles Pyke¹, Jonas Ahnfelt-Rønne¹, Kim G. Madsen¹, Susanne G. Schéele¹, Tomas Alanentalo¹, Rikke K. Kirk¹, Betty L. Pedersen¹, Rikke B. Skyggebjerg¹, Andrew J. Benie¹, Holger M. Strauss¹, Per-Olof Wahlund¹, Simon Bjerregaard¹, Erzsébet Farkas³, Csaba Fekete^{3,4}, Flemming L. Søndergaard², Jeanett Borregaard², Marie-Louise Hartoft-Nielsen², Lotte Bjerre Knudsen¹

Buckley *et al.*, *Sci. Transl. Med.* **10**, eaar7047 (2018) 14 November 2018

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American Association
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to original U.S.
Government Works

10 mg semaglutide and 300 mg SNAC
(Rybelsus®: 7 or 14 mg semaglutide and 300 mg SNAC)

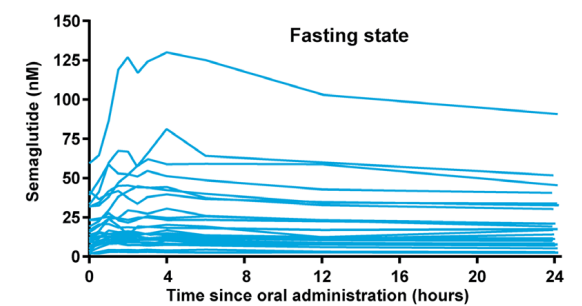
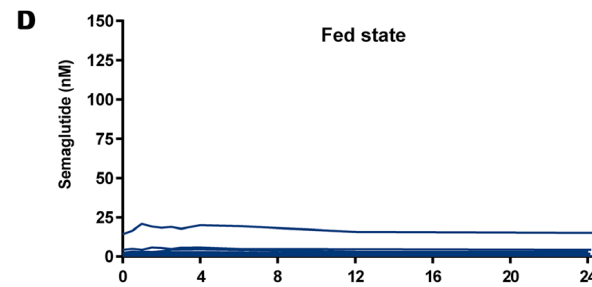
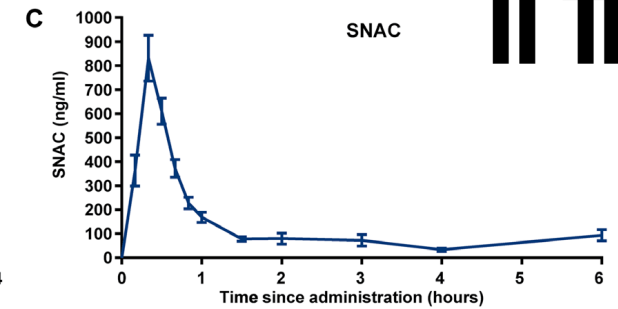
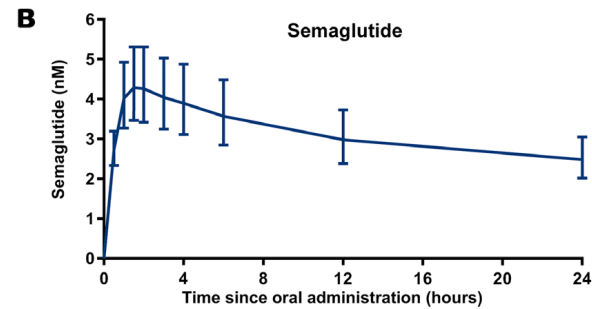
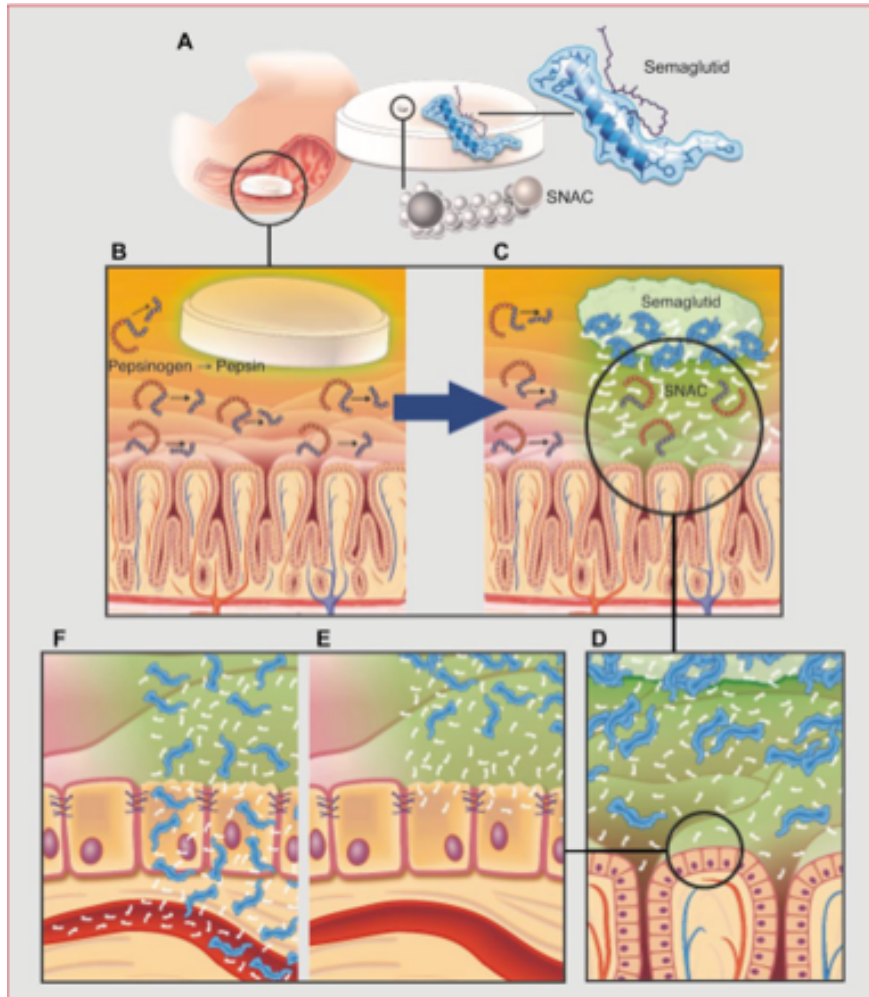
MW 301 Da, pKa = 5.0



semaglutide

MW 4114 Da

Oral semaglutide (Rybelsus®)



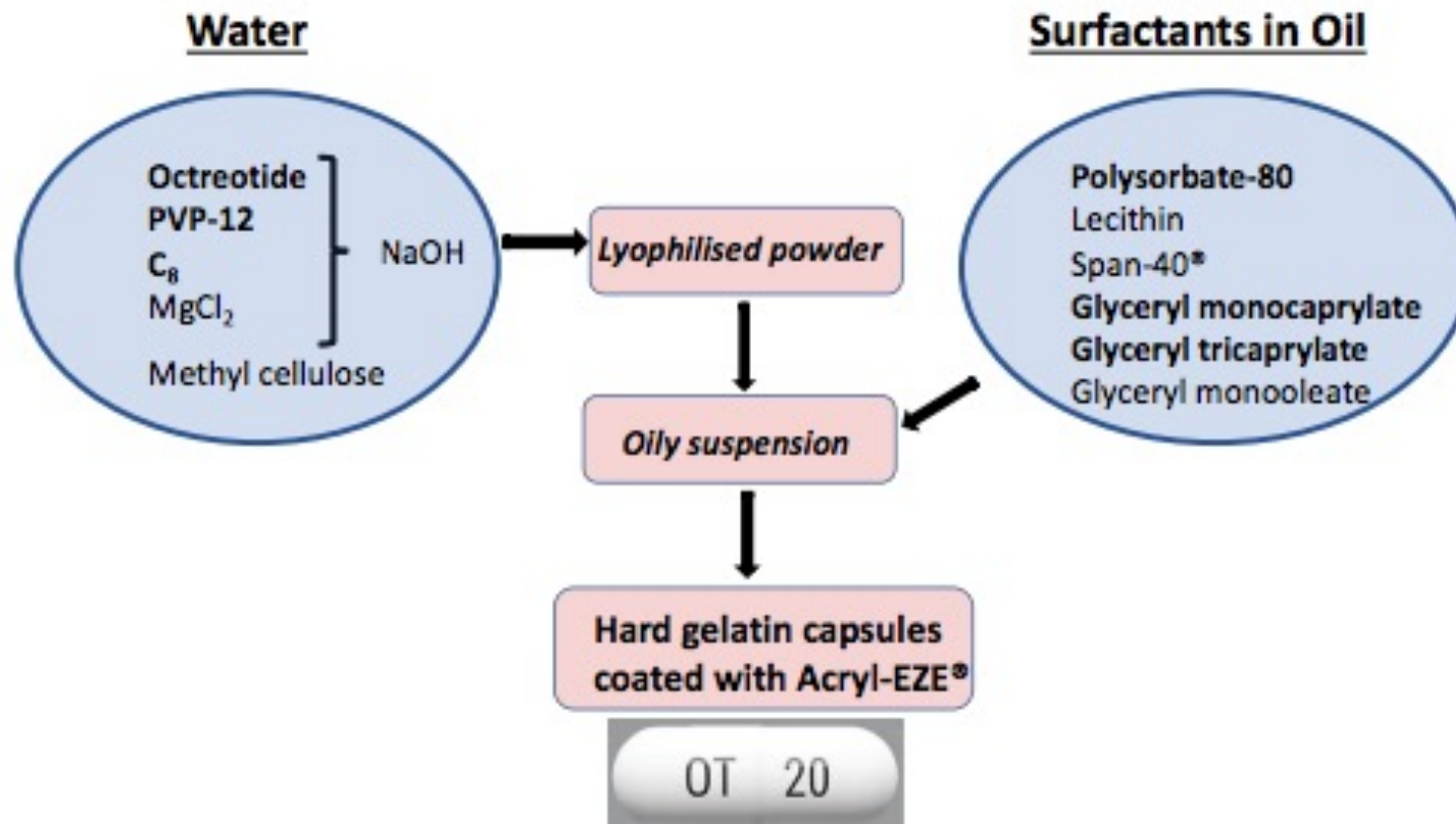
Oral bioavailability

Dog: $1.22\% \pm 0.25\%$

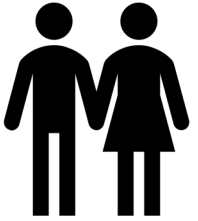
Human: 0.8%

Oral octreotide (Mycapssa®)

Soft capsule filled with the Transient Permeation Enhancer® (TPE®) system



Oral octreotide (Mycapssa®)



- 20 mg Octreotide per capsule
- Quantity of C_8 unknown
- Bioavailability: 20 mg < 1%; 80 mg < 0.2%
- Negative food effect (- 90%)

(Micro)needles

Expectations:

- High bioavailability (up to 100%?)
- Low variability

Questions:

- Reliability
- Dose
- Safety

Needle systems targeting the esophagus

“Esophageal flower-like system”

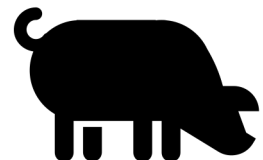
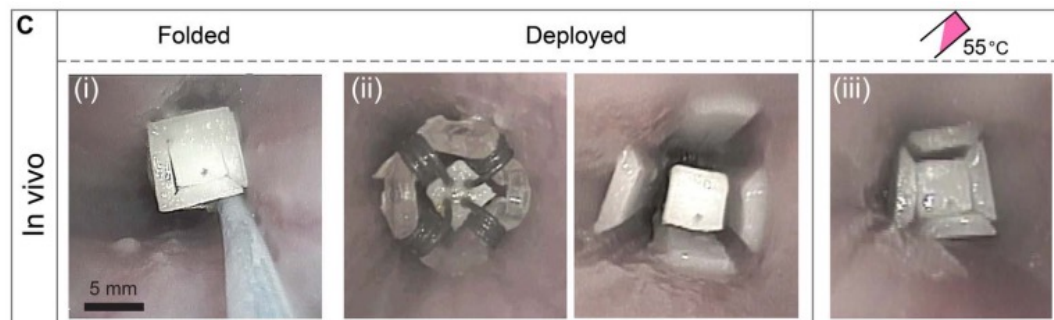
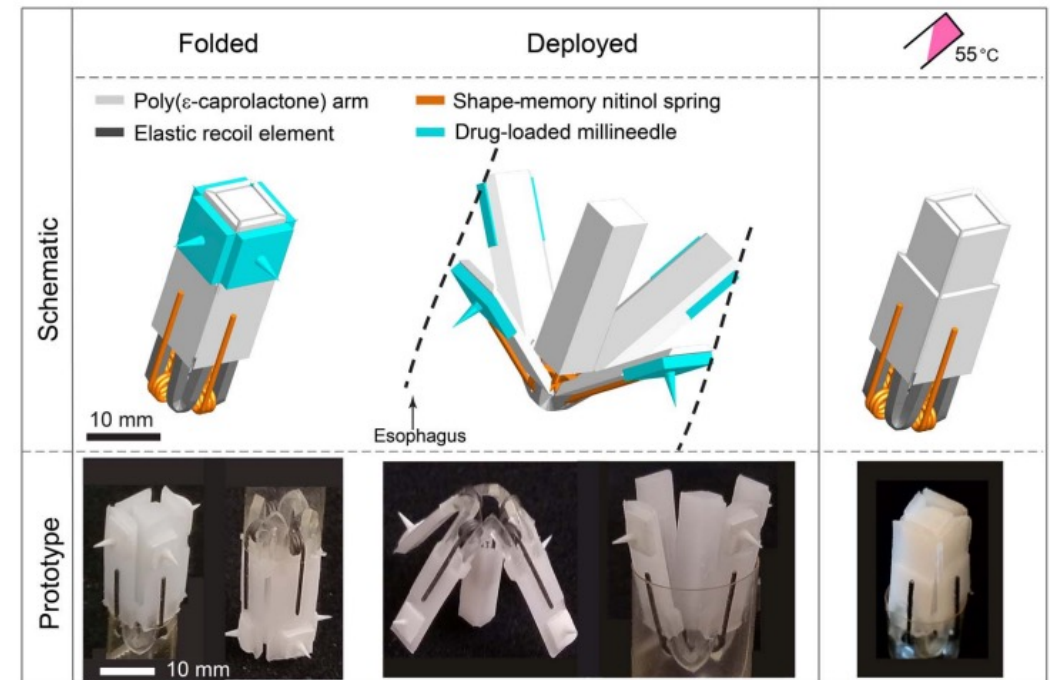
SCIENCE TRANSLATIONAL MEDICINE | RESEARCH ARTICLE

DRUG DELIVERY

Temperature-responsive biometamaterials for gastrointestinal applications

Sahab Babaee¹, Simo Pajovic¹, Ameya R. Kirtane¹, Jiuyun Shi¹, Ester Caffarel-Salvador^{1,2}, Kaitlyn Hess¹, Joy E. Collins¹, Siddhartha Tamang¹, Aniket V. Wahane¹, Alison M. Hayward^{1,3}, Hormoz Mazdiyasni^{1,4}, Robert Langer^{1,2*}, Giovanni Traverso^{1,4,5*}

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Needle systems targeting the esophagus

nature
materials

Nature Materials 20 (2021) 1085–1092

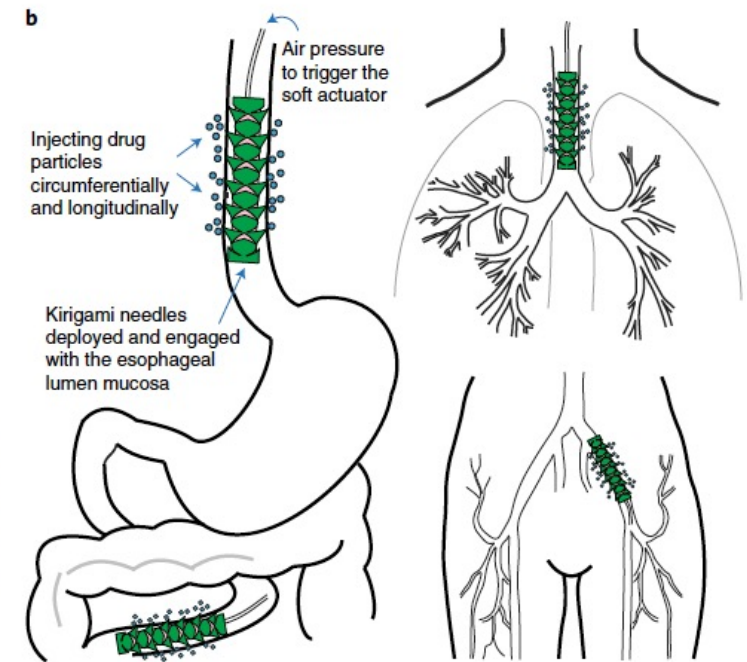
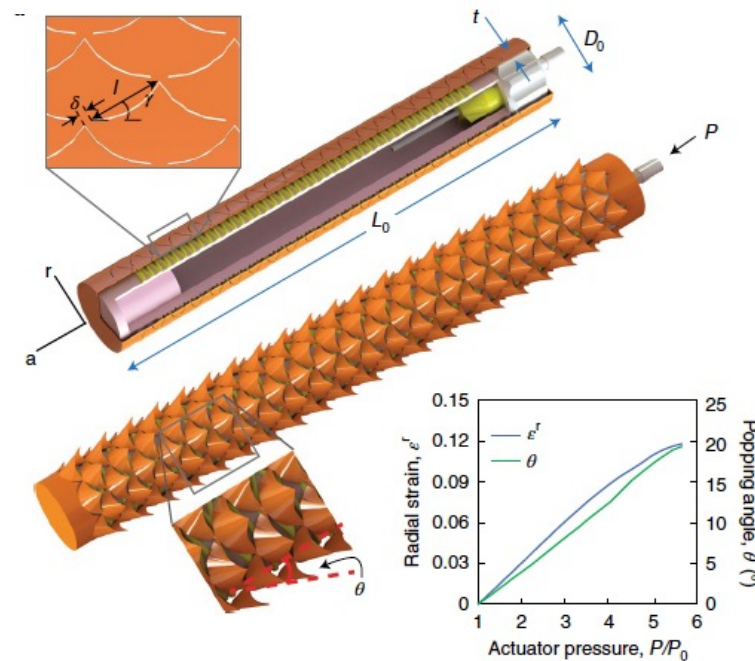
LETTERS

<https://doi.org/10.1038/s41563-021-01031-1>

Check for updates

Kirigami-inspired stents for sustained local delivery of therapeutics

Sahab Babae^{1,2,3}, Yichao Shi², Saeed Abbasalizadeh², Siddhartha Tamang^{1,2}, Kaitlyn Hess^{1,2}, Joy E. Collins^{2,3}, Keiko Ishida^{1,2,3}, Aaron Lopes^{1,2,3}, Michael Williams², Mazen Albaghdadi^{2,4}, Alison M. Hayward^{1,2,3} and Giovanni Traverso^{1,2,3} ✉



Needle systems targeting the stomach

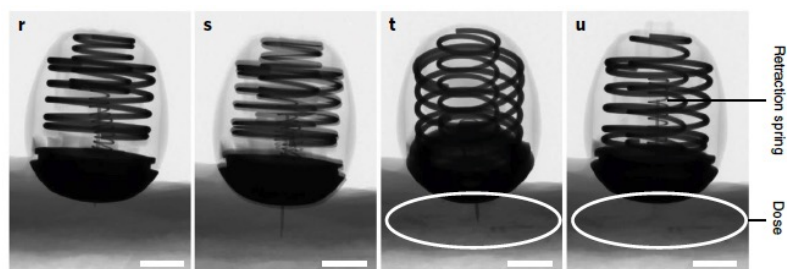
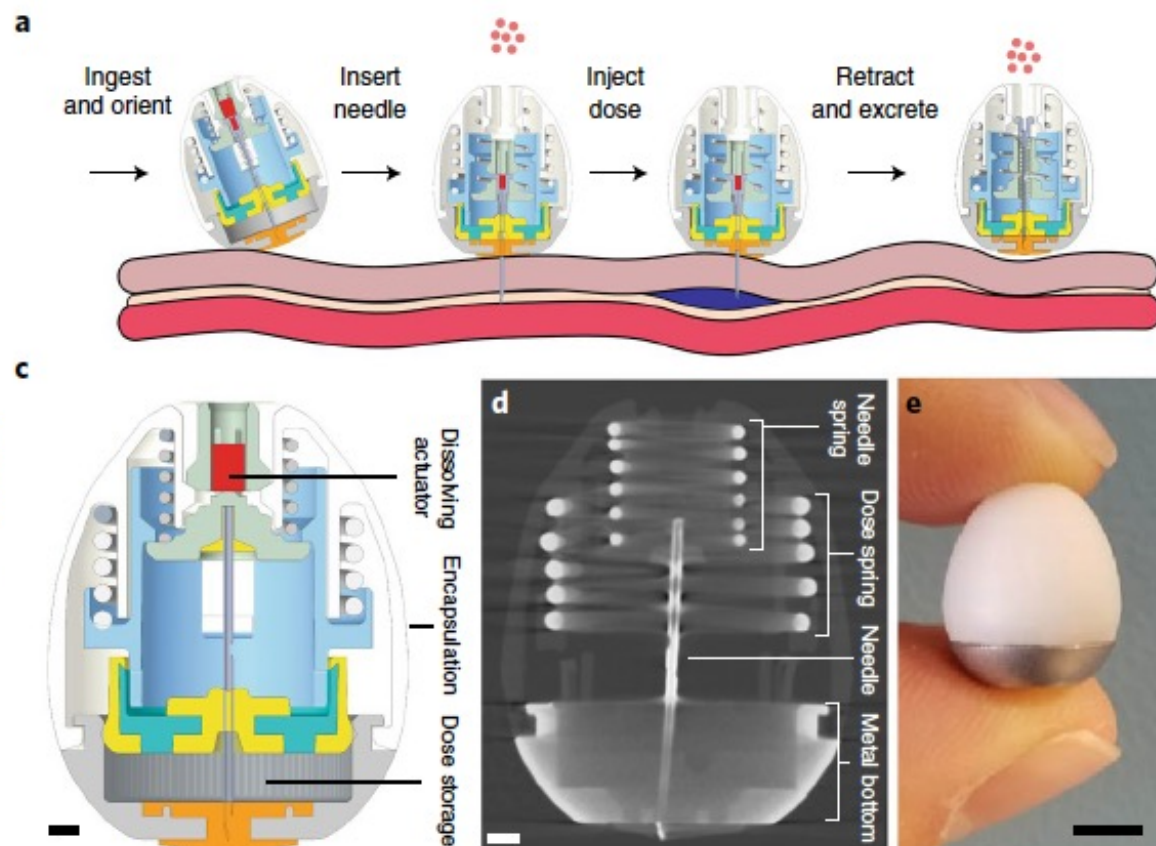
- Liquid-injecting self-orienting millimeter scale applicator (L-SOMA)
- BIONDD™



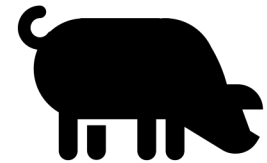
Oral delivery of systemic monoclonal antibodies, peptides and small molecules using gastric auto-injectors

Alex Abramson^{1,10,14}, Morten Revsgaard Frederiksen^{2,11,14}, Andreas Vegge^{3,14}, Brian Jensen², Mette Poulsen², Brian Mouridsen², Mikkel Oliver Jespersen², Rikke Kaae Kirk³, Jesper Windum², František Hubálek⁴, Jorrit J. Water⁴, Johannes Fels⁴, Stefán B. Gunnarsson⁴, Adam Bohr⁴, Ellen Marie Straarup³, Mikkel Wennemoes Hvitfeld Ley², Xiaoya Lu^{1,12}, Jacob Wainer^{1,13}, Joy Collins¹, Siddhartha Tamang¹, Keiko Ishida^{1,5}, Alison Hayward^{1,5,6}, Peter Herskind², Stephen T. Buckley⁴, Niclas Roxhed^{1,7}, Robert Langer^{1,8,9}, Ulrik Rahbek⁴ and Giovanni Traverso^{1,5,6}

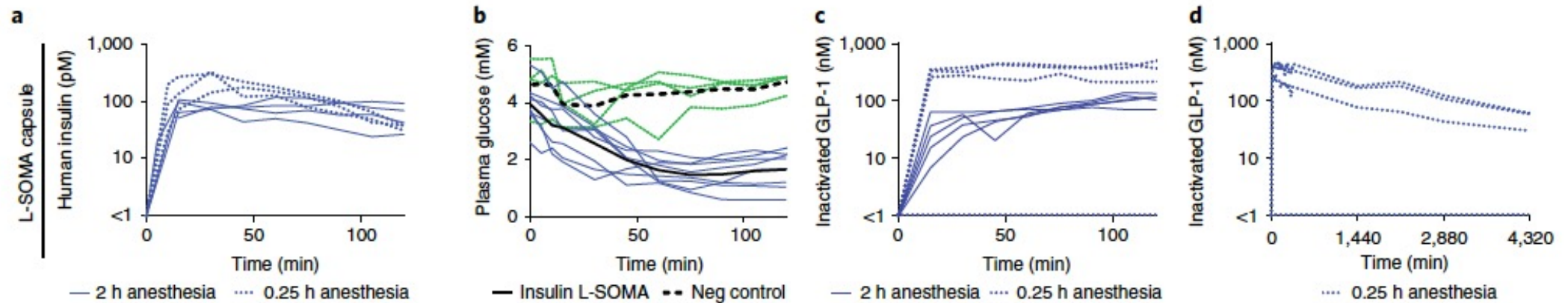
L-SOMA



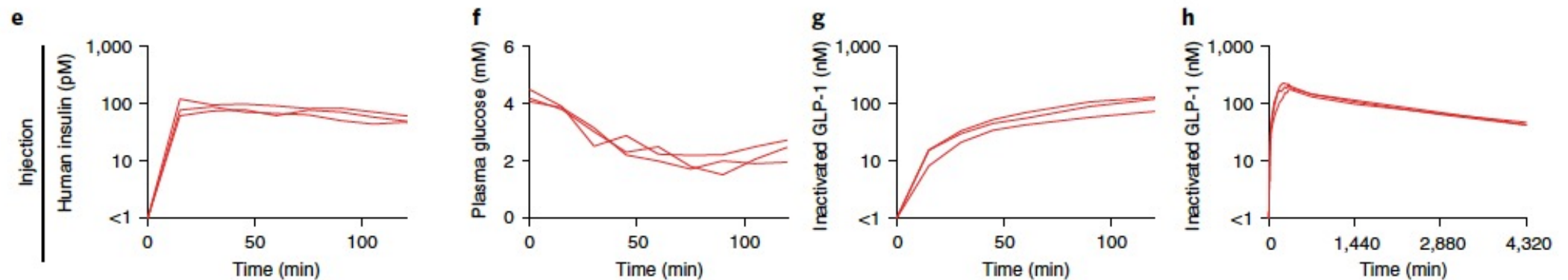
L-SOMA: In vivo data (aneasthetised pig)



L-SOMA:

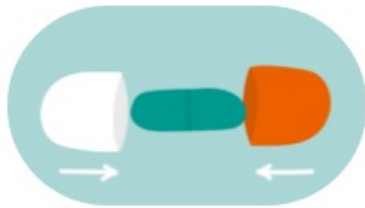


Subcutaneous injection:



<https://biograil.com/>

BIONDD™



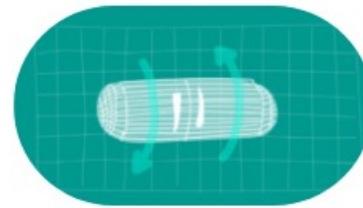
1

BIONDD™ in a standard size 00 capsule



2

...is swallowed and is activated after 3 minutes in the stomach



3

The device rotates two halves in opposite direction with small spikes extending



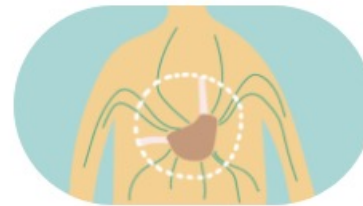
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The spikes embrace tissue from both sides and secure a safe and painless transient positioning of the spike inside the stomach wall



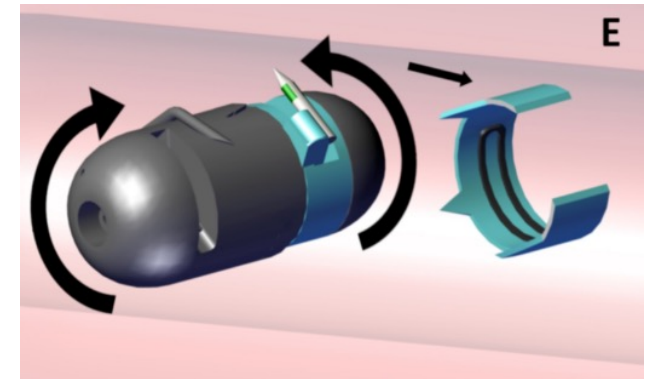
5

The biodegradable spikes detach, releasing drug from the spikes for effective distribution into the blood stream



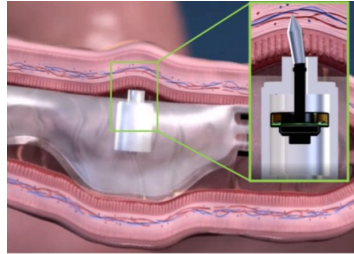
6

...and throughout the body

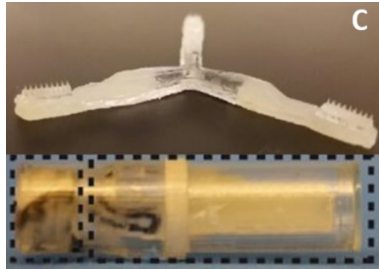


Needle systems targeting the small intestine

➤ RaniPill™

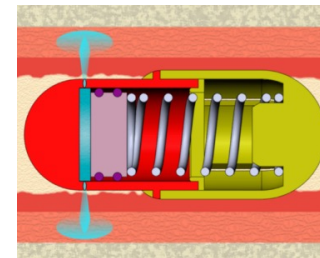


➤ Lumi



➤ Oral Biopharmaceutical Delivery System (OBDS; needle free)

➤ JetCAP™ (high pressure jet: needle free)



all pictures from: Sogaard et al., Pharmaceutics 13(10) 2021

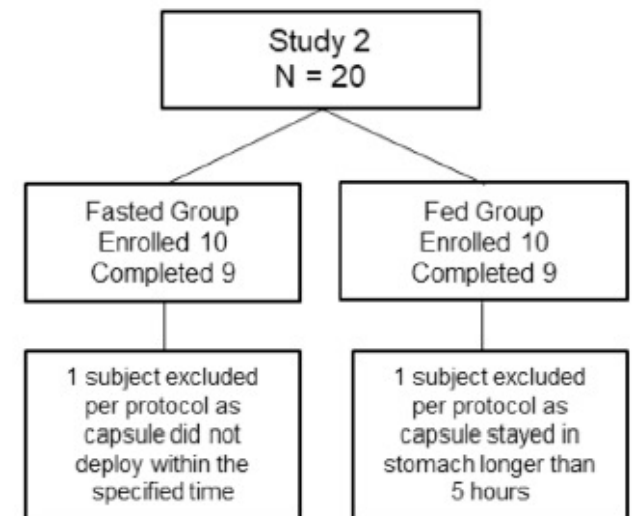
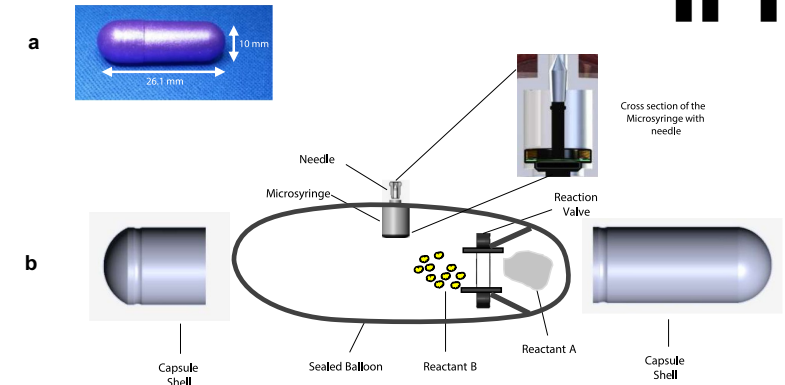
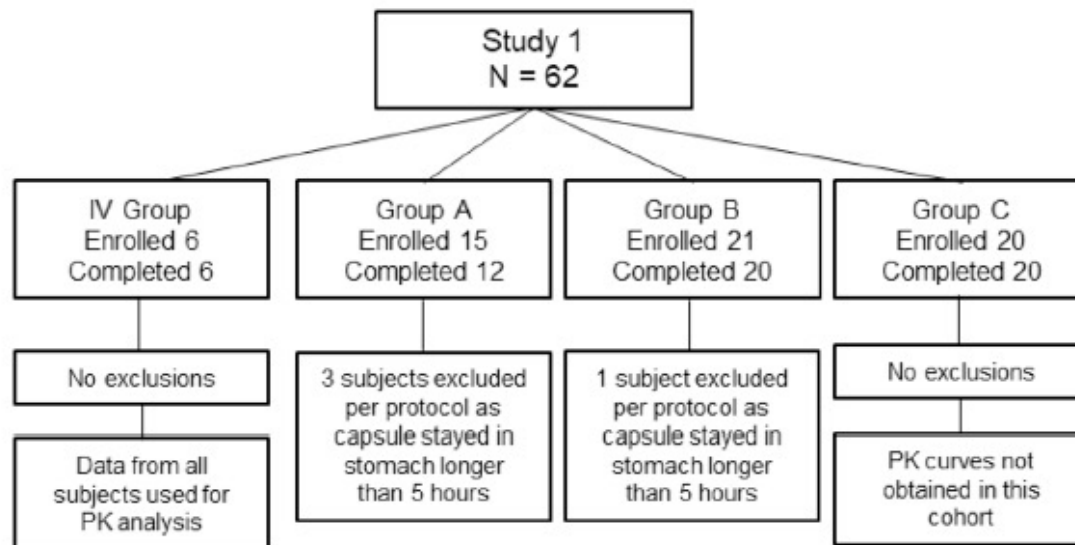


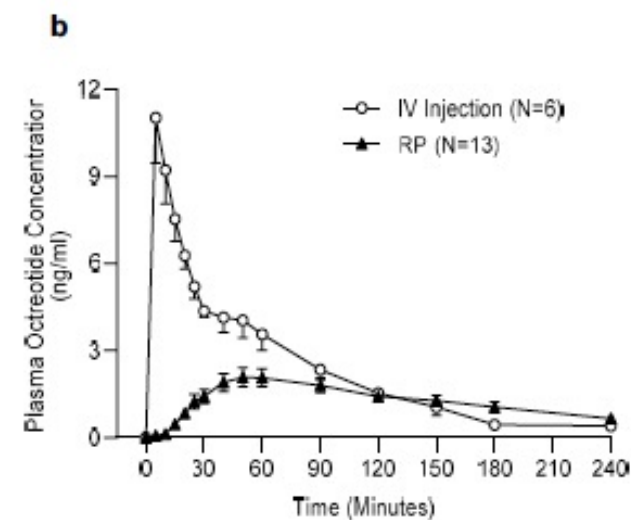
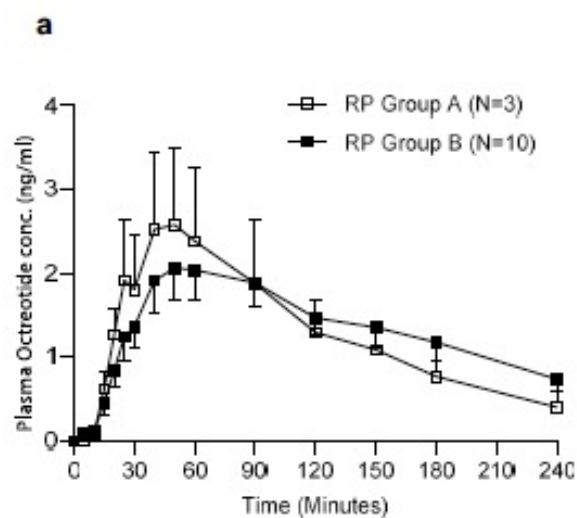
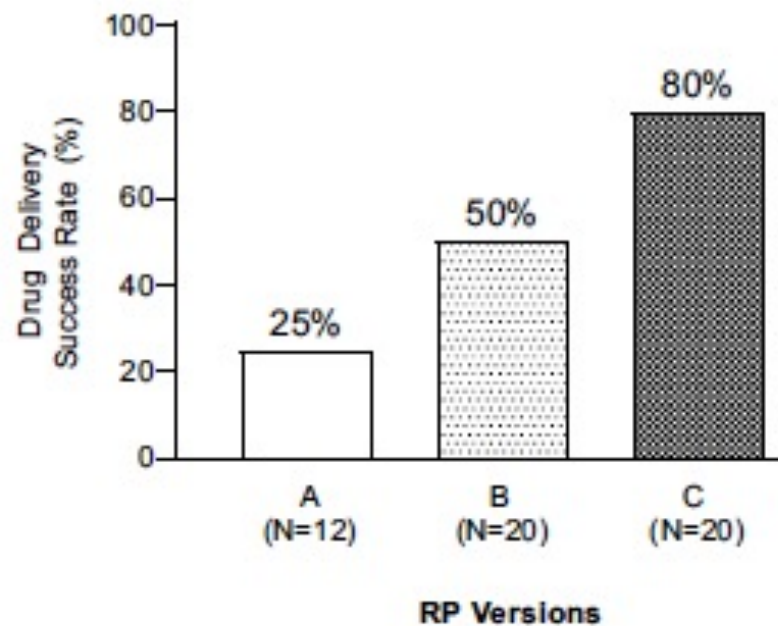
A robotic pill for oral delivery of biotherapeutics: safety, tolerability, and performance in healthy subjects

Arvinder K. Dhalla¹ · Ziad Al-Shamsie¹ · Simret Beraki¹ · Anvesh Dasari¹ · Leonard C. Fung¹ · Laura Fusaro¹ · Anusha Garapaty¹ · Betsy Gutierrez¹ · Delia Gratta¹ · Mir Hashim¹ · Kyle Horlen¹ · Padma Karamchedu¹ · Radhika Korupolu¹ · Eric Liang¹ · Chang Ong¹ · Zachary Owyang¹ · Vasudha Salgotra¹ · Shilpy Sharma¹ · Baber Syed¹ · Mansoor Syed¹ · April T. Vo¹ · Radia Abdul-Wahab¹ · Asad Wasi¹ · Alyson Yamaguchi¹ · Shane Yen¹ · Mir Imran¹

Accepted: 3 February 2021 / Published online: 19 February 2021
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100 µg Octreotide





PK parameters for Octreotide administered via IV injection and RP

Group	C _{max} (ng/mL)	T _{max} (min)	AUC _{last/Dose} ((min*ng/mL)/(μg/kg))	Bioavailability (% F)
IV Sandostatin (N=6)	11.1 ± 1.6	5	389 ± 22	NA
RP (N=13)	2.4 ± 0.3	50	226 ± 30	65 ± 9

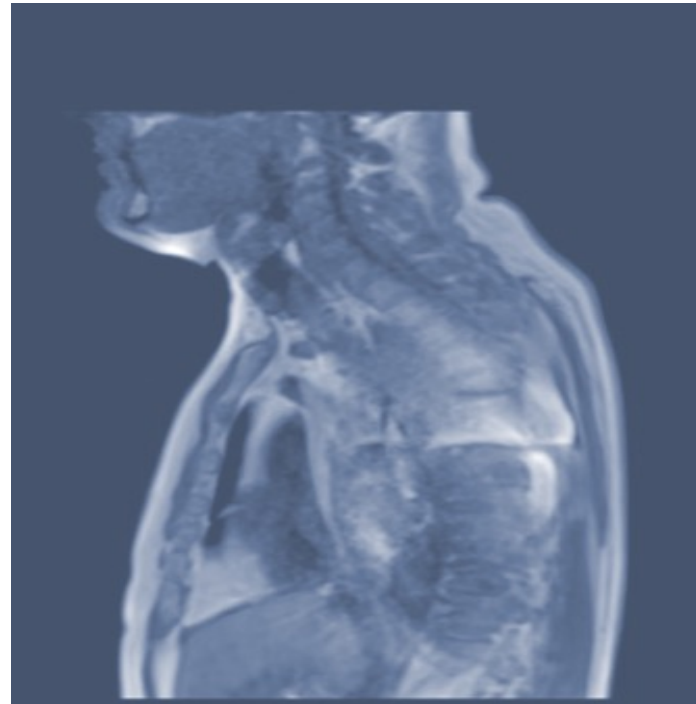
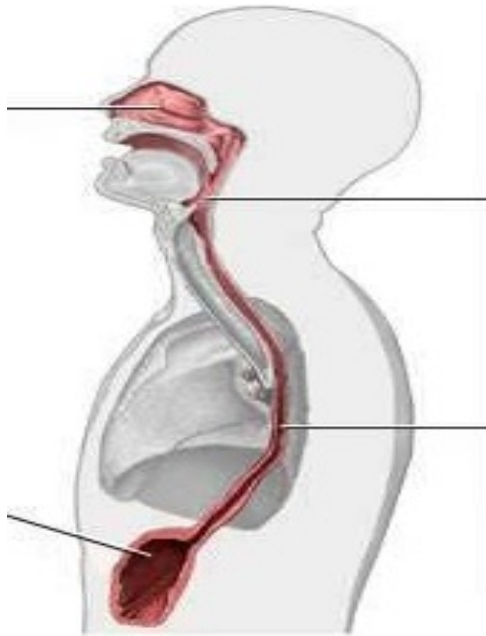
(Micro)needles

Questions:

- Reliability
- Applicable doses
- Technical realisation: sterile products, complex production
- Environmental compatibility
- Safety

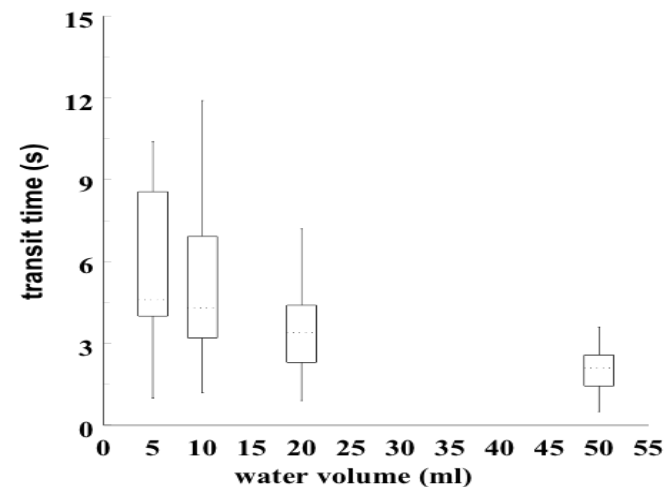


Topical drug delivery to the esophagus: **EsoCap**



Local Treatment – Problems

- Esophageal passage times are generally short (< 30 s)
- Esophageal clearance is high (peristaltic movements)
- Esophageal transit times of tablets and capsules are very short and depend on the co-swallowed water volume

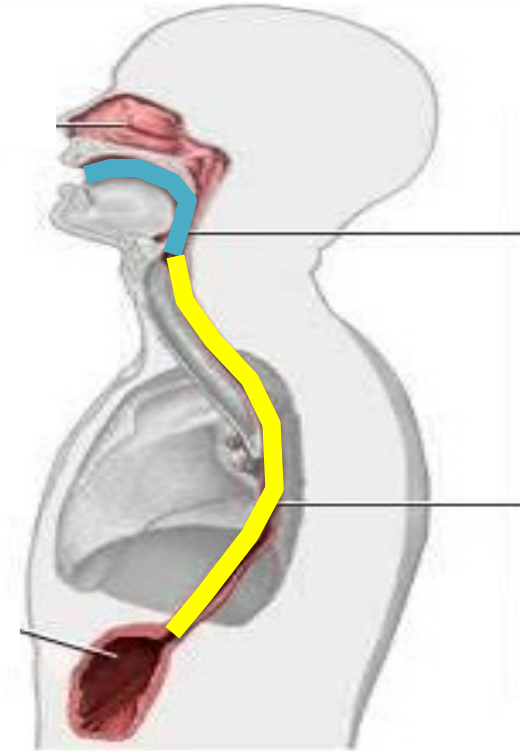
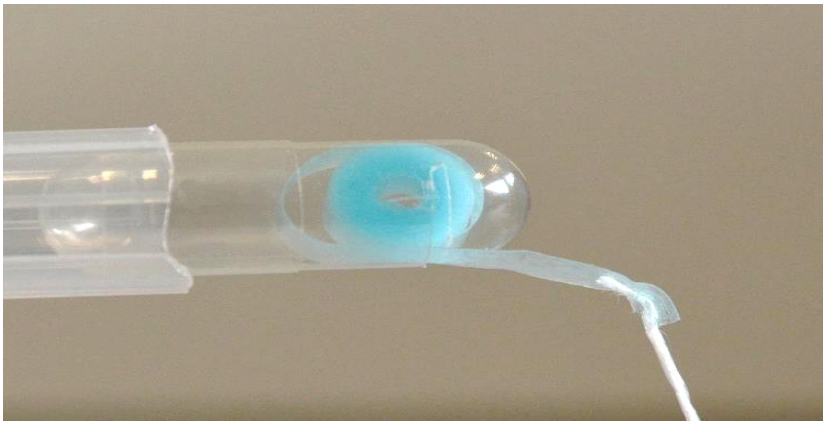


Osmanoglu et al. Neurogastroenterol Motil. 2004

EsoCap – Basic Idea

 Retainer (15 cm)
 Wafer (24 cm)

- Applying a mucoadhesive film onto the esophagus
- Swallowing of a capsule containing a mucoadhesive wafer that rolls off during esophageal transit.



EsoCap – Proof of principle



Journal of Controlled Release 327 (2020) 1–7



Contents lists available at [ScienceDirect](https://www.sciencedirect.com)

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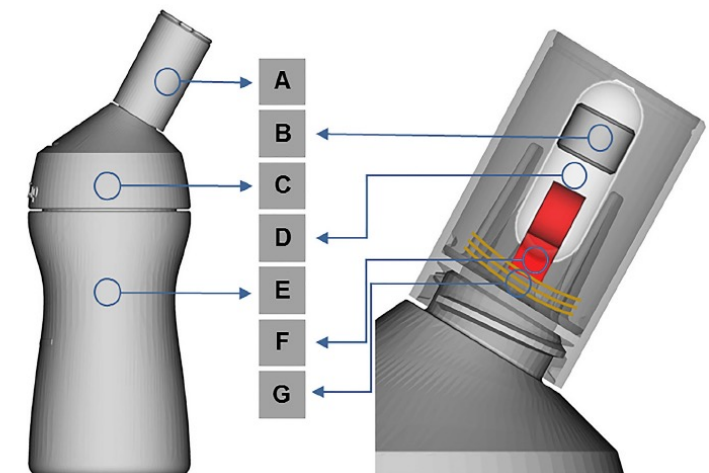
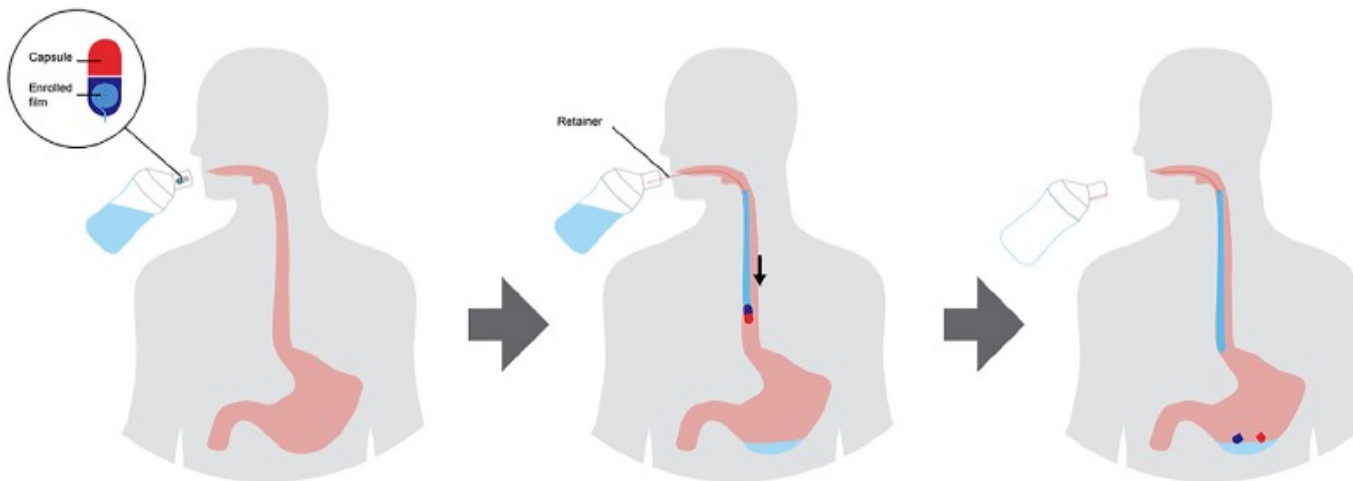
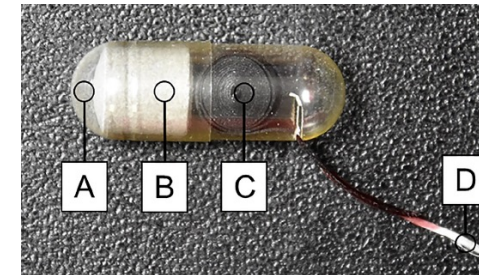
journal homepage: www.elsevier.com/locate/jconrel

The EsoCap-system – An innovative platform to drug targeting in the esophagus

Julius Krause^a, Christoph Rosenbaum^a, Michael Grimm^a, Adrian Rump^a, Rebecca Keßler^b, Norbert Hosten^b, Werner Weitschies^{a,*}

^a University of Greifswald, Institute of Pharmacy, Department of Biopharmaceutics and Pharmaceutical Technology, Center of Drug Absorption and Transport, Felix-Hausdorff-Str. 3, 17487 Greifswald, Germany

^b Department of Diagnostic Radiology and Neuroradiology, University Hospital Greifswald, Ferdinand-Sauerbruch-Straße, 17475 Greifswald, Germany



EsoCap – Proof of principle



Journal of Controlled Release 327 (2020) 1–7



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The EsoCap-system – An innovative platform to drug targeting in the esophagus

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^a University of Greifswald, Institute of Pharmacy, Department of Biopharmaceutics and Pharmaceutical Technology, Center of Drug Absorption and Transport, Felix-Hausdorff-Str. 3, 17487 Greifswald, Germany

^b Department of Diagnostic Radiology and Neuroradiology, University Hospital Greifswald, Ferdinand-Sauerbruch-Straße, 17475 Greifswald, Germany



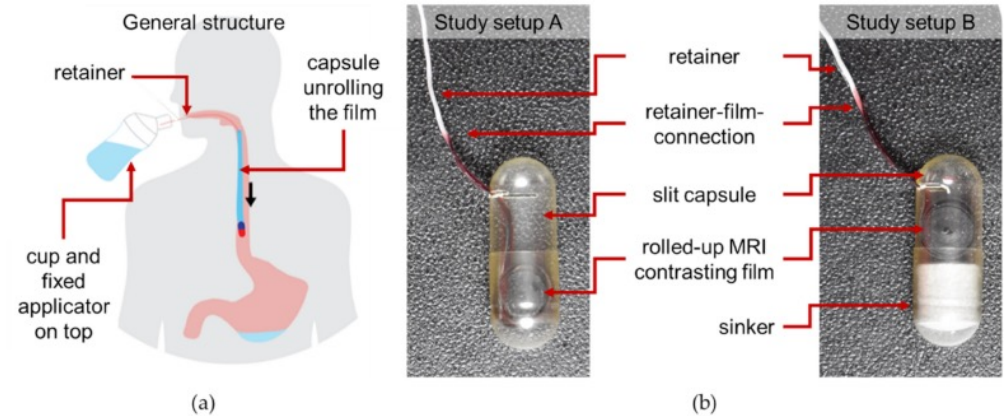
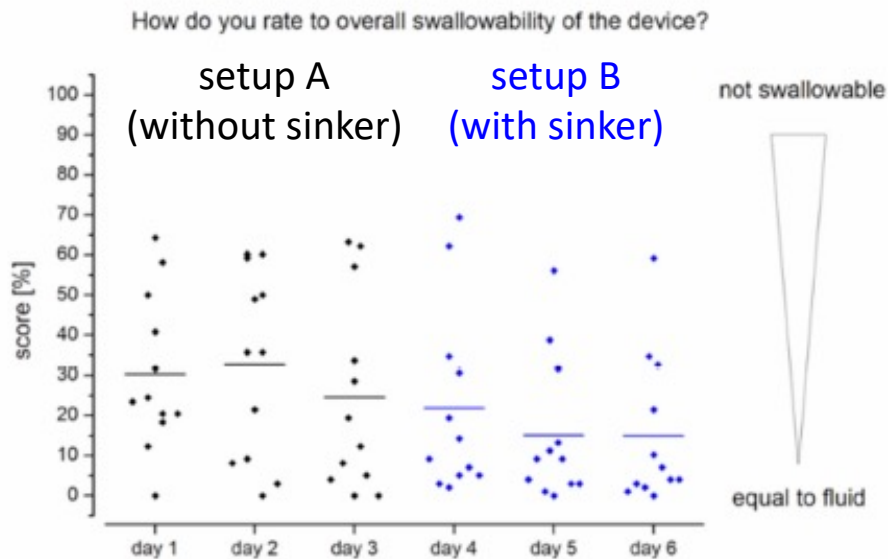
EsoCap – Functionality



Article

Functionality and Acceptance of the EsoCap System—A Novel Film-Based Drug Delivery Technology: Results of an In Vivo Study

Christoph Rosenbaum ¹, Michael Grimm ¹ , Julius Krause ¹, Adrian Rump ¹, Rebecca Kessler ², Norbert Hosten ² and Werner Weitschies ^{1,*}



EsoCap: ACESO Study



A randomized, placebo-controlled, double-blind trial evaluating the efficacy, tolerability and safety of ESO-101 in adult patients with active EoE (eosinophilic esophagitis).



Capsule with film containing 0.8 mg mometasone, dissolving retainer and sinker



Assembled Study Medication

Conclusion

Some exciting projects are on their way in the field of Gastric Retention as well as Oral Protein Delivery. However, whether the holy grails have already been discovered is still an open question.