An Ingestible Capsule to Deliver Parenteral Pharmaceuticals into the Jejunal Wall

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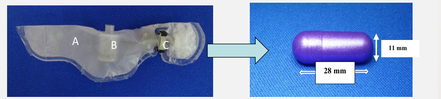
AIM OF THE RESEARCH: We developed a platform to painlessly deliver by mouth drugs that cannot be administered orally. This ingestible, capsule-like device deploys inside the small intestine and injects into its wall a biotherapeutic payload sealed inside a dissolvable microneedle.

RESULTS: We tested the delivery and examined the pharmacokinetics of several biopharmaceuticals, including recombinant human insulin, human immunoglobulin G, octreotide and teriparatide in anesthetized and conscious pigs and dogs. The bioavailability of these compounds delivered by the capsules was similar to that after subcutaneous delivery. For instance, the mean peak serum concentration of insulin after capsule delivery in 8 anesthetized pigs was 517 ± 109 pmol/l, versus 342 ± 50 pmol/l after subcutaneous injection in 9 other, sham-operated pigs. *In vivo* safety studies were conducted in 23 conscious beagles, which received between 2 and 18 capsules. All devices transited painlessly through the GI tract and were excreted within 96 h. The mean gastric residence time (GRT) of the capsules was 93 min, and subsequent intestinal deployment time (IDT) was 28 min. A pilot study in 10 fasting and 10 postprandial human volunteers examined the tolerability and safety of the capsule devoid of microneedle and payload. The mean GRT of the capsule was 217±36 min in the postprandial and 100±79 min in the fasting state, while the IDT were closely similar (100±40 vs. 97±30 min) in both groups. No subject perceived the device transit, deployment or excretion. **CONCLUSIONS**: The studies completed thus far in anesthetized or conscious animals have confirmed that to this ingestible device can deliver drugs in sufficient amounts. and rate to obtain therapeutic blood concentrations. Its oral administration was well tolerated by the human subjects. First-in-man studies are being planned to test the ability of this ingestible device deliver pharmaceuticals in healthy human volunteers and patients.

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AIM OF THE RESEARCH

To develop an ingestible drug delivery platform that injects medications into the small intestinal wall.



A. polyethylene/nylon film balloon; B. microsyringe; C reaction valve

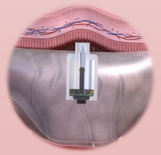
TECHNOLOGY



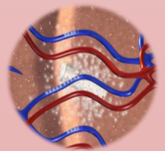
Ingested capsule remains intact in the stomach



Dissolution of capsule activates the syringe-like mechanism



Activation enables deployment of syringe and injection of payload



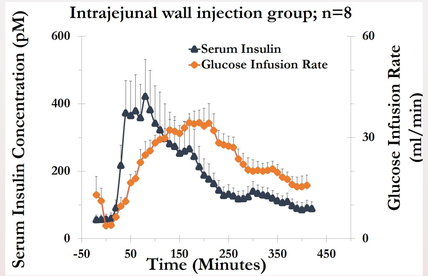
Rapid dissolution of drug enables microcirculation uptake

Pharmaceuticals Delivered

- Immunoglobulin G
- Teriparatide
- Octreotide
- Insulin



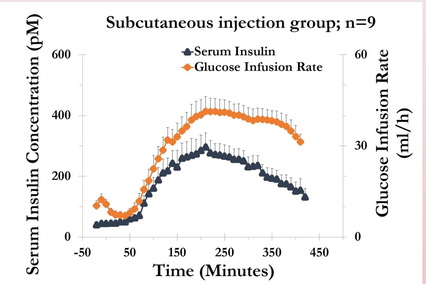
INTRAJEJUNAL AND ORAL DELIVERY OF PHARMACEUTICALS VIA INGESTIBLE CAPSULE IS AS EFFECTIVE AS SUBCUTANEOUS INJECTION

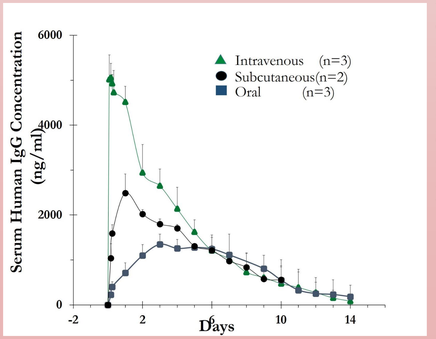


Model: Juvenile Pigs Under a 60-80 mg/dl Euglycemic Glucose Clamp administered 20 IU Recombinant Insulin

Mode of delivery: Intrajejunal or Subcutaneous

Measurements: Blood glucose by glucometer and Serum Insulin by ELISA





Model: Conscious Beagles dosed with 2.3 mg of Immunoglobulin G (IgG)

Mode of delivery: Intravenous (n=3), Subcutaneous (n=2) or Oral (n=3)

Measurements:

- Intestinal device and transit confirmed fluoroscopically
- Serum IgG by ELISA

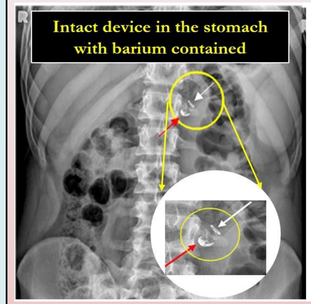
SAFETY AND TOLERABILITY OF THE INGESTIBLE CAPSULE

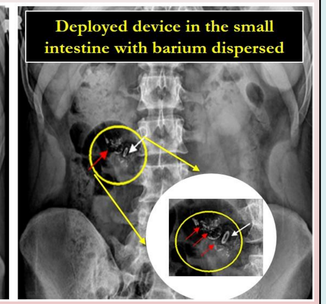
Model: Oral Administration of Ingestible Capsule in Humans

Measurements: Radiographic Tracking of Ingestible Capsule

The endpoints of the study were :

1) All clinical manifestations attributable to the capsule,
2) GET, between capsule ingestion and its radiographically confirmed entry into the proximal small intestine, and
3) IDT, between entry of the capsule in the proximal small intestine and its radiographically confirmed deployment.





	STUDY GROUPS			
	Fasting n=10		Postprandial n=10	
Times, min	GET	IDT	GET	IDT
Means ± SD	100±79	97±30	217±36*	100±40

CONCLUSION

This ingestible capsule can deliver drugs in sufficient amounts and rate to produce therapeutic blood concentrations. Its oral administration was well tolerated by human subjects. First-in-man studies are being planned to test its ability to deliver pharmaceuticals in healthy human volunteers