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Capsule disintegration and enteric coatings for novel SPED devices used in oral drug delivery

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Not only the patients prefer oral medication due to its comfort, but also pharmaceutical companies favor it owing to the greater chemical stability of oral dosage forms. Unlike the most small molecule drugs, biopharmaceuticals are challenging when it comes to the oral route. They are sensitive to the acidic environment in the stomach and they are not readily absorbed into the bloodstream through the gastrointestinal tract [1]. In order to overcome these challenges, several devices have been investigated for oral delivery of biopharmaceuticals such as insulin [2]. We have conceptualized a new type of devices named Self-configurable Proximity Enabling Devices (SPED) [3]. The idea is that these devices will unfold in the gut, align to the intestinal wall and release biopharmaceuticals in the close proximity of the epithelium (Figure 1). In our first study, the foil was placed in a gelatin capsule and then surgically placed and guided to the rat intestine. As the capsule dissolved, the foil unfolded and released the embedded insulin formulation. Hereby, we have been able to achieve delivery of insulin (although, with a low oral bioavailability) in the blood stream of rats. However, this is not a preferred method of administration since, in an ideal condition, the whole gelatin capsule should be orally administered, then bypass stomach and move to the intestine to perform as intended. Therefore, there is a need for an established method to make enteric capsules for our devices.

There are established methods and enteric polymer formulations for making coated capsules used in the industry and research; however, they cannot easily be used for our SPED devices on account of a constant internal pressure from SPED to the gelatin capsule. The rolled-up foil is made of polydimethylsiloxane (PDMS) elastomer that wants to return to its initial shape (a flat foil) and this stress puts a certain pressure from inside to the gelatin capsule. This pressure makes it highly difficult for an enteric coated capsule to stay intact inside the stomach when the enteric polymer and gelatin capsule become a bit soft. This means that by using established polymer formulations and methods, our SPED device opens at a non-desired site, the stomach, rather than in the intestine (Figure 2). It is noteworthy to mention that the enteric coating thickness (the amount of deposited enteric polymer) on the gelatin capsules also plays an important role in capsule disintegration. After considering several enteric polymers, formulation and thickness, sufficient resistance could be achieved in the gastric environment (for two hours) and our SPED device could be released in the intestinal environment after 20 minutes (Figure 3). This gives our rolled-up foil sufficient time to bypass the stomach through gastric emptying and reach the intestine to efficiently oral deliver biopharmaceuticals.

[1] P. Tyagi et al., J. Controlled Release. 287 (2018) 167-176
[2] A. Abramson et al., Science. 363 (2019) 611–615
[3] J. R. Jorgensen et al., J. Controlled Release. 329 (2021) 948-954

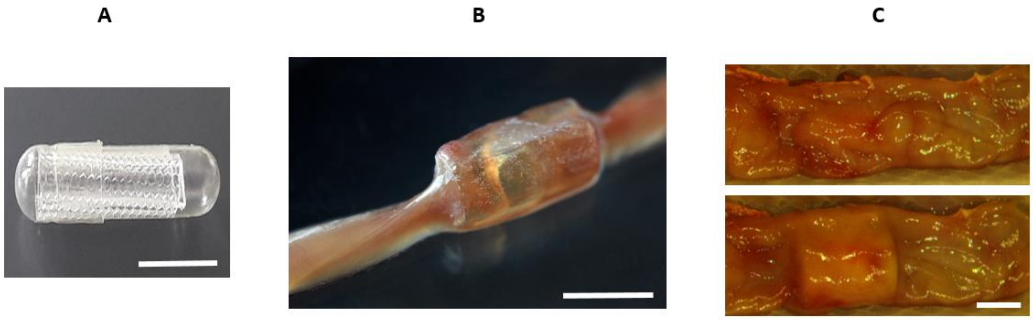

Figure 1. The concept of rolled-up foil. A) Rolled up foil in a gelatin capsule. B) Unrolled foil inside the rat intestine. C) Rolled up foil in a gelatin capsule placed in a piece of the pig intestine (upper image), the gelatin capsule disintegrated and the foil unrolled in the pig intestine (bottom image). The scale bar is 0.5 cm.

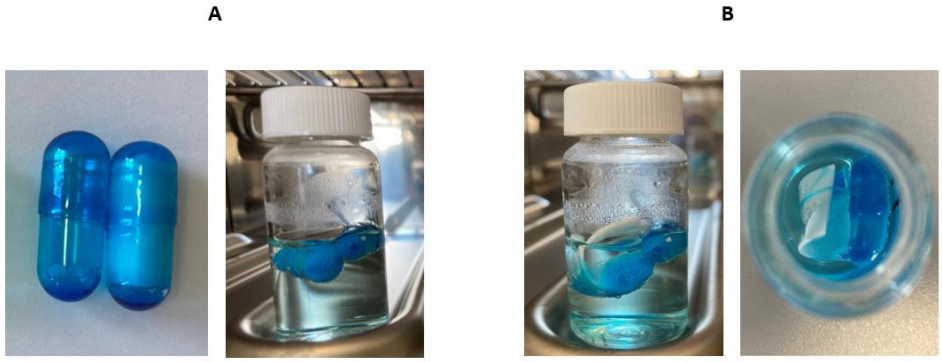

Figure 2. Regular enteric coated capsule could not tolerate the internal pressure from PDMS foil in simulated gastric media. A) Capsule with and without foil were enteric coated according to the previous published paper and was placed in simulated gastric medium (pH: 2) at 37º C. B) The capsule containing foil was opened up after 42 min in simulated gastric medium.

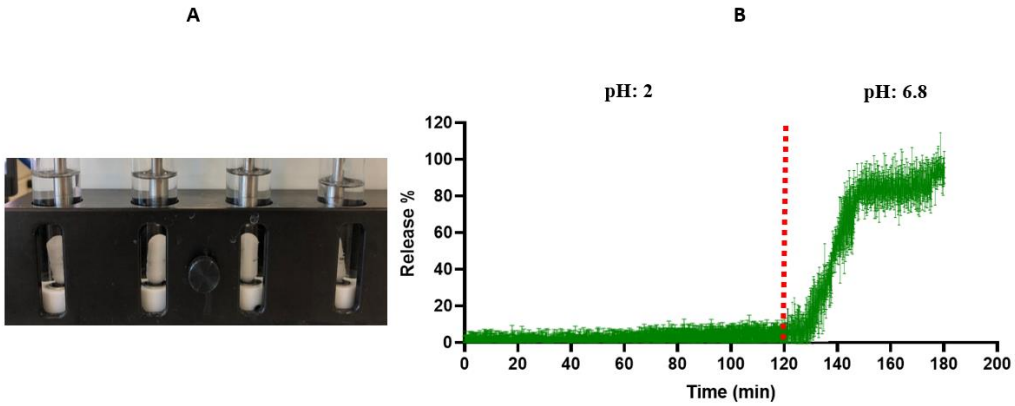

Figure 3. The desirable coated capsules containing rolled up foils. A) Depicts coated capsules in a simulated gastric medium in a µ-DISS Profiler to investigate drug release. B) The model drug (paracetamol) was not released from enteric capsules containing foils in simulated gastric medium (pH: 2) for 2 hours and the capsule and foils opened up by changing the solution with simulated intestinal medium (pH: 6.8).