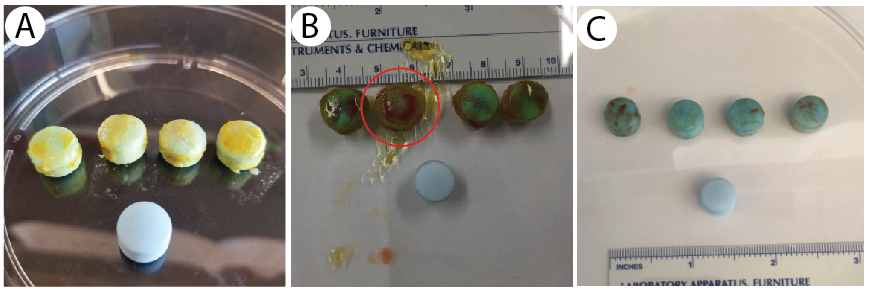
**Controlled delivery of bile acids to the colon**

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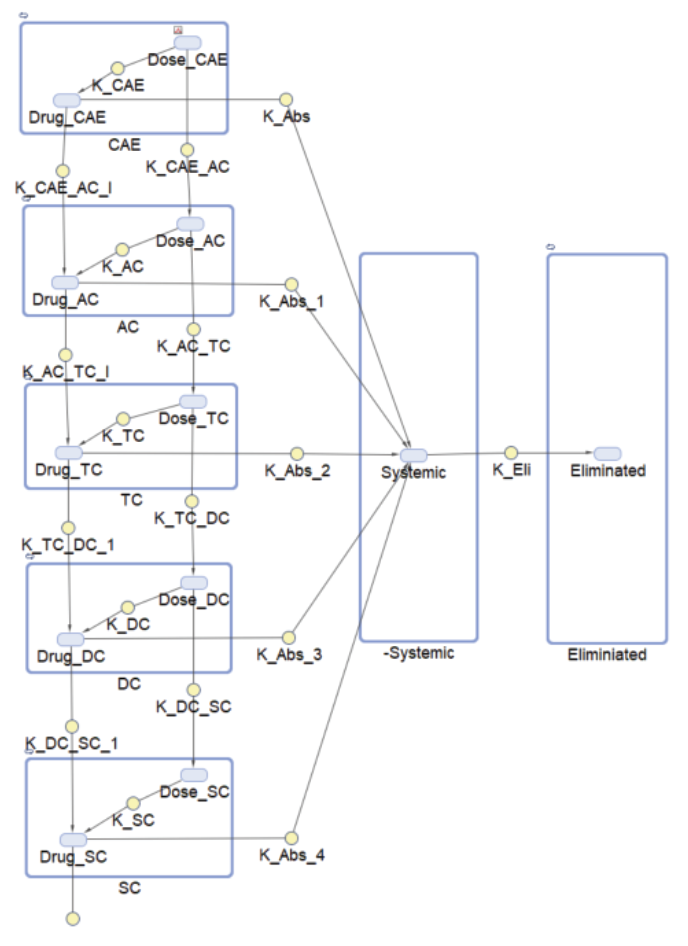
**Supplementary Materials**

Supplementary Table 1: Parameters used for pharmacokinetic simulation – see Supplementary Figure 2 for model.

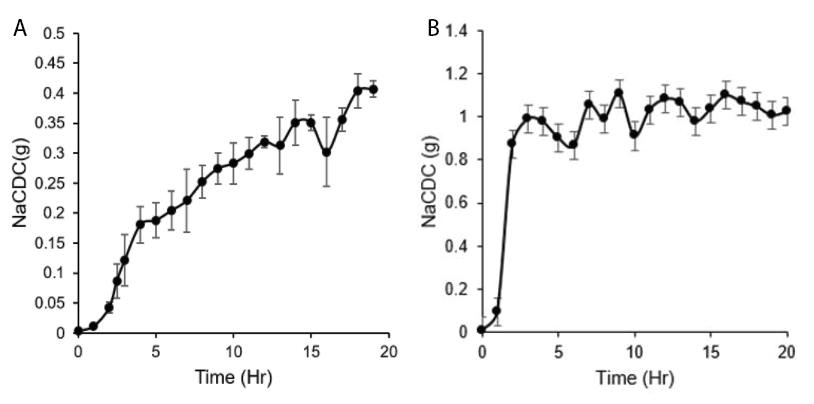
|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Colon volume and kinetics** | | | | |
| **Part** | **Volume [mL]** | **Half transit time [hour]** | **Rate [hour-1]**  **(=K)** | **Reference** |
| Caecum (CAE) | 50 | 1 | 0.693 | 1 2, 3 4 |
| Ascending colon (AC) | 203 | 2.5 | 0.277 |
| Transverse colon (TC) | 198 | 2.9 | 0.239 |
| Descending colon (DC) | 160 | 5.5 | 0.126 |
| Sigmoid (SC) | 250 | 12.1 | 0.057 |
| **Absorption of CDC** | | | | |
| Assuming first order kinetics and an average bile acid concentration of 2 mM: Kabs(0-5) = 0.323 h-1 | | | | 5 |
| **Distribution of CDC** | | | | |
| Vd = 25.81 L / Kg (1600 L / 62 Kg) Estimated pig weight: 40 Kg | | | | 6 |
| **Elimination of CDC** | | | | |
| Cl = 25 L / h 🡪 keli = 0.024218939 h-1 | | | | 6 |
| **Release kinetics** | | | | |
| Assuming first order kinetics  Capsule: t1/2 = 0.5 h (k(CAE, AC, TC, DC, SC) = 1.386 h-1); Bilayer pill: t1/2 = 2.5 hours (k(CAE, AC, TC, DC, SC = 0.277 h-1); Single layer pill: t1/2 = 6 hours (k(CAE, AC, TC, DC, SC) = 0.115 h-1) | | | | |



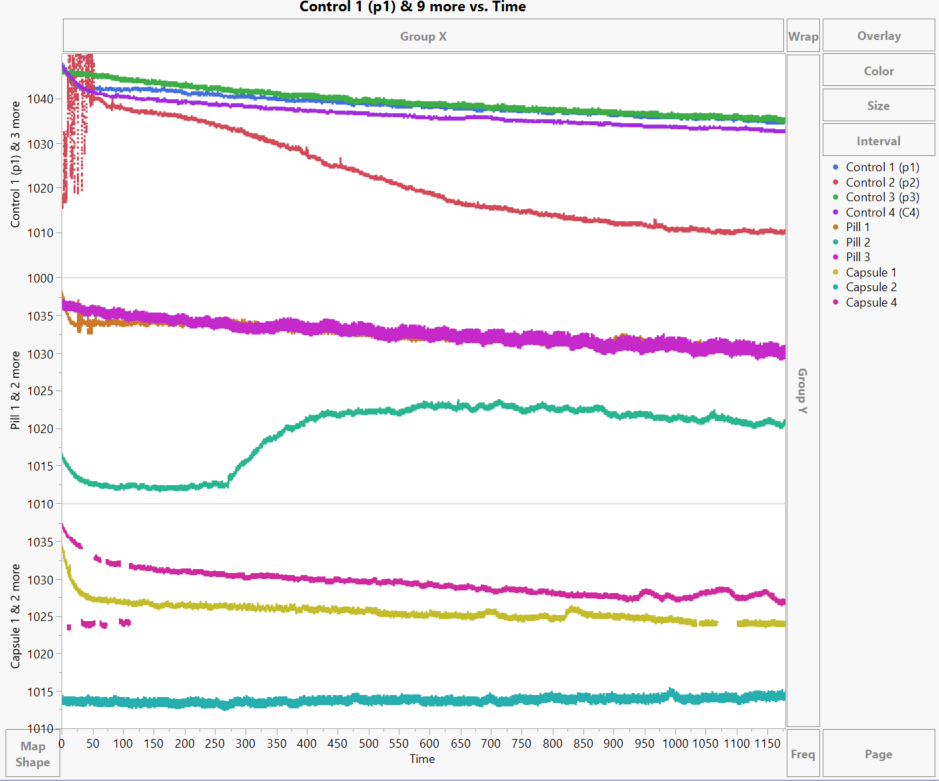
Supplementary Figure 1: Bilayered delivery systems retrieved from the small intestine of a terminal pig model. One (red circle) out of twelve delivery systems disintegrated after 4 hours.



Supplementary Figure 2: Five compartment pharmacokinetic model



Supplementary Figure 3: In vitro release pattern of A) the bilayer delivery system and B) the capsule formulation. Release was assessed in Simulated Intestinal Fluid (0.2M, SIF, pH 6.8) for one hour before the pH was adjusted to pH 7.4 (0.2M NaOH, 100 rpm).



Supplementary Figure 4: Primary data of rectal manometry patterns following rectal placement of uncoated release systems. Control 2 was excluded as pressure significantly dropped presumably due to a leakage. Pressure reading are depicted in mbar / time is depicted in seconds.

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