ADVANCING HIGH TECH DRUG DELIVERY SYSTEMS FOR THE TREATMENT OF CROHN'S DISEASE

Douglas A. Miller, PhD[1] and Robert Niichel[1]

1. Veloce Corporation, Denver, Colorado, United States

Introduction High tech drug delivery systems, which allow for precise location targeting and efficient delivery mechanisms, can reduce the risk of side effects and increase dosage effectiveness in the treatment of Crohn's disease. We describe a revolutionary capsule technology which uses radiofrequency signaling to trigger an optimal release of the pharmaceutical contents to specified regions of the gastrointestinal tract.

System and method Data were observed in two groups of female Yorkshire-Cross swine. Intra-cecal ports were surgically placed in Group 2 swine. Conventional capsules for controls and SmartTab capsules were prepared containing 1000mg for the controls and ~500mg in the SmartTab. SmartTab capsules contained a lower dose due to the other ingredients and smaller payload volume. After baseline analysis was complete, all study animals were administered the SmartTab capsule (Group 1 administration via balling device, Group 2 administration via intra-cecal port) containing caffeine, barium sulfate, citric acid, and sodium bicarbonate. SmartTab capsules were activated by a radiofrequency triggering event, immediately following administration in Group 2 swine and 30 minutes following administration in Group 1 swine. Blood samples were taken at 0.25, 0.50, 1, 2, 3, and 6 hours after dosing and capsule activation was confirmed using a C-Scan.

16.2 **Table 2: Body Weights**

Group 1: Smart Tab Oral Administration		
Study Timepoint (Study Day)	**Animal Number**	**Body Weight (Kg)**
Pre-Surgical (Day -20)	1501	14.3
	1502	14.5
Pre-Baseline Dose (Day -13)	1501	15.8
	1502	15.9
Pre-SmartTab Dose (Day 1)	1501	18.2
	1502	17.6

Group 2: Smart Tab IC Port Administration		
Study Timepoint (Study Day)	**Animal Number**	**Body Weight (Kg)**
Pre-Surgical (Day -20)	2501	14.4
	2502	13.8
Pre-Baseline Dose (Day -13)	2501	15.3
	2502	15.7
Pre-SmartTab Dose (Day 1)	2501	17.1
	2501	17.5

Group	Animal Number	Study Timepoint (Study Day)		
		Pre-Surgical (Day -20)	Pre-Baseline Dose (Day -13)	Pre-SmartTab Dose (Day 1)
Group 1: Smart Tab Oral Administration	1501	14.3	15.8	18.2
	1502	14.5	15.9	17.6
	Average	14.4	15.9	17.9
Group 2: Smart Tab IC Port Administration	2501	14.4	15.3	17.1
	2502	13.8	15.7	17.5
	Average	14.1	15.5	17.3

Results Pharmacokinetic analysis revealed increased caffeine concentrations in the targeted areas. Absorption was significantly higher and more consistent in the cecum targeted administration of the SmartTab compared to the control. Although, caffeine concentrations in the stomach regions were fairly similar amongst both the experimental and control groups.

In the C-Scan images below the capsule can be seen in its pre-activation and post-activation state, indicating that the drug payload has been released.

Study Day 1 (Pre-SmartTab Capsule Activation): Right lateral view for Animal 1502   Study Day 1 (Post-SmartTab Capsule Activation): Right lateral view for Animal 1502
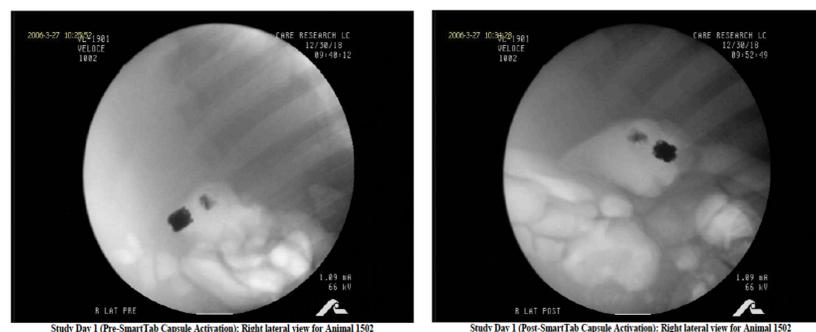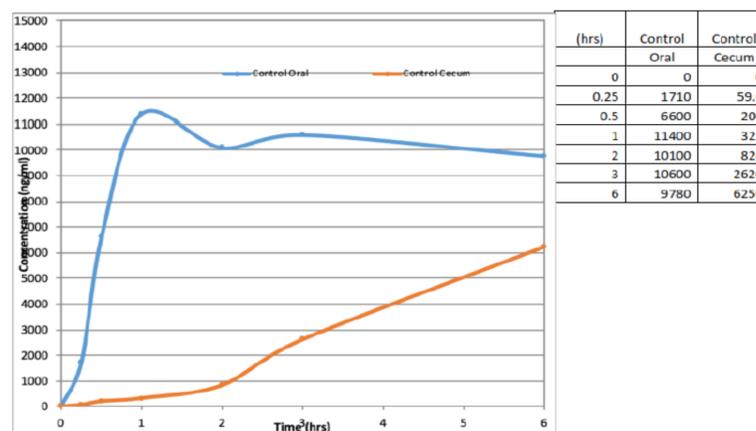
Table I below demonstrates the pharmacokinetic profile for the control capsules administered both orally and intra-cecal. Note in particular the profile for the cecal introduction and its similarity to the SmartTab profiles in the following tables.

Table I-Control Capsules with Oral and Cecum Port Administration

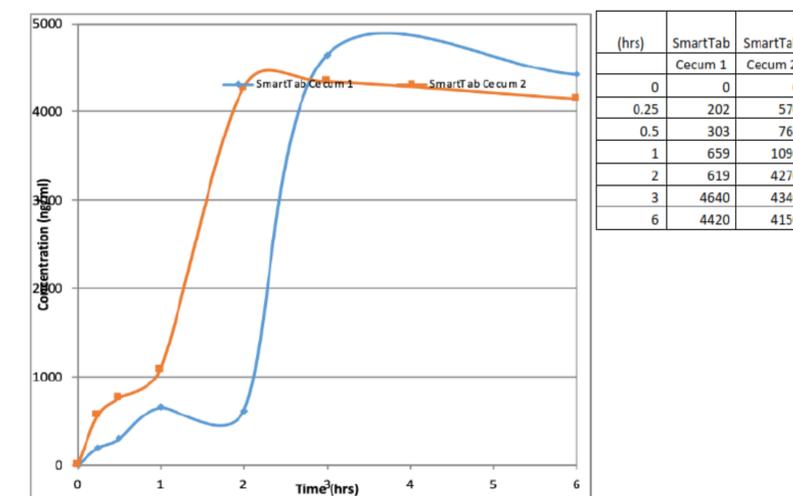| (hrs)	Control Oral	Control Cecum
0	0	0
0.25	1710	59.6
0.5	6600	200
1	11400	322
2	10100	826
3	10600	2620
6	9780	6250

In Table II it can be seen that the SmartTab oral administration had similar pharmacokinetic profiles. Total concentrations for SmartTab were lower due to the lower active pharmaceutical ingredient (API) capacity of the capsule.

Table II-SmartTab Capsule Oral Administration

(hrs)	SmartTab Oral 1	SmartTab Oral 2
0	0	0
0.25	161	301
0.5	165	448
1	224	917
2	312	1830
3	874	2630
6	1160	3450
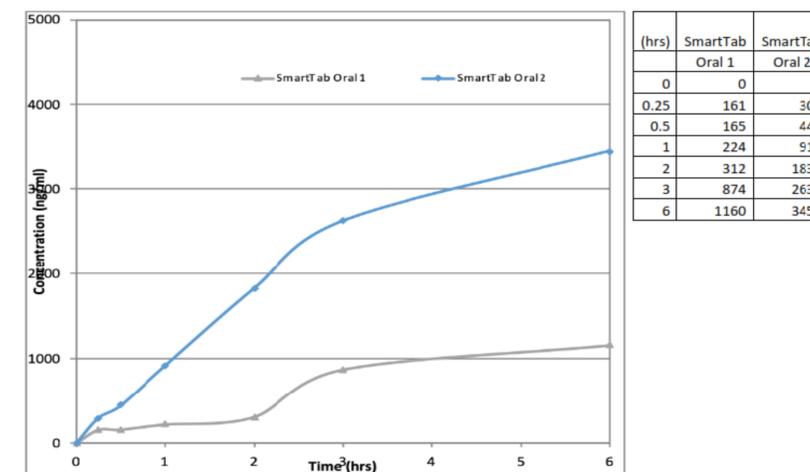
However, for the cecum targeted region the absorption was higher and more consistent than the control capsule. These results provided initial validation that the Target-tab is effective in delivering an active ingredient to a targeted site.

Table III-SmartTab Capsule Cecum Port Administration

(hrs)	SmartTab Cecum 1	SmartTab Cecum 2
0	0	0
0.25	202	570
0.5	303	768
1	659	1090
2	619	4270
3	4640	4340
6	4420	4150

Conclusions In this study it was shown that, the SmartTab capsule can successfully administer, via radio frequency signaling, active ingredients to the chosen target site. With pre-installed onboard sensors, enabling the devices to send real-time data to physicians and personalize treatments using AI algorithms, this technique holds the potential to generate further advancement in high-tech drug delivery systems. Preparations are currently in order to reapply this technology in the form of an injection capsule.