Use of the *InteliSite*® Capsule to Study Ranitidine Absorption from Various Sites Within the Human Intestinal Tract

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Purpose. The purpose of this study was to evaluate the extent of ranitidine absorption from an externally activated drug-delivery system in two distinct regions of the intestine (jejunum and ileum) in healthy human volunteers. This investigation also was designed to evaluate the utility of the *InteliSite*® capsule for studying regional intestinal drug absorption in humans.

Methods. The intestinal absorption of ranitidine from the jejunum and ileum was compared in eight, healthy volunteers in this open-label, two-way crossover study. In two of the eight volunteers, absorption from the colon also was studied. Subjects swallowed the capsule containing ranitidine solution (121 mg) and 100 μCi of ^{99m}Tc-DTPA. The endcap of the capsule contained 20 μCi of ^{111}In-DTPA. At the desired intestinal site, the capsule was activated by the application of an external RF magnetic signal (6.78 MHz operating frequency) and the ranitidine solution was released. Blood samples were collected from a forearm vein for 12 hours after capsule activation.

Results. The capsule released the ranitidine solution when activated in the jejunum, ileum and colon (visualized by the gamma camera). There was no difference in the extent of ranitidine absorption or ranitidine pharmacokinetics when the capsule was activated in the jejunum or ileum.

Conclusions. This study demonstrates the utility of a novel, externally activated drug-delivery system to assess site-specific intestinal drug absorption in humans. Results indicate that use of the *InteliSite*® capsule method to evaluate site-specific intestinal ranitidine absorption in humans yields data similar to that obtained previously by means of oral intubation studies.

KEY WORDS: site-specific absorption; ranitidine; intestinal absorption; *InteliSite*® capsule.

PURPOSE AND RATIONALE

Evaluation of regional drug absorption in the gastrointestinal tract of humans usually is accomplished with a nasoenteric/oroenteric intubation technique. This technique has been used to study the site-specific intestinal absorption of drugs such as talinolol (1), oxprenolol (2), ranitidine (3), nefazodone (4), gepirone (5) and dietary components such as glucose (6), starch (7,8), carbohydrates (9,10), zinc (11), and iron (12). After drug administration at a specific intestinal site in subjects, the tube may be retained during the plasma collection and drug washout periods and then allowed to progress to the next intestinal site for drug administration. Thus, subjects may need to remain intubated for prolonged periods of time if the drug exhibits a long half-life and if multiple sites of administration are being investigated. Apart from the discomfort to volunteers, there is concern that the enteric tube affects gastrointestinal motility and gastric emptying. Further, the volume of fluid administered to flush the dose through the tube (≥ 10 ml) may alter absorption characteristics. As an alternative to intubation studies, an externally activated drug-delivery capsule has been developed to evaluate regional intestinal absorption of drugs under non-invasive conditions. This device is registered as the *InteliSite*® capsule. This study was performed to evaluate the utility of this capsule system in investigating site-specific intestinal drug absorption in humans.

The H_2-receptor antagonist, ranitidine, was chosen as the model drug for this study. The plasma concentration-time profiles for ranitidine after oral dosing are characterized by distinct double peaks. Several possible mechanisms for this double-peaking phenomenon have been proposed including delayed gastric emptying of a portion of the oral dose (13). Enterohepatic recirculation is not the cause of the double peaks in rats (14) although the presence of bile enhanced ranitidine absorption *in vivo* in rats. Another possible explanation for the double-peaking phenomenon is the presence of 'absorption windows' for ranitidine in the intestine. *In situ* intestinal perfusions in rats indicated that ranitidine was absorbed from the entire small intestine but the extent of ranitidine absorption was greatest in the terminal ileum (15). Intestinal absorption of ranitidine in different segments of the human intestine indicated that ranitidine absorption rates were the highest in the regions of the duodenal jejunal junction and in the distal jejunum/ileum (16). The present study was undertaken to further characterize ranitidine absorption from two intestinal sites, the jejunum and ileum, in eight healthy human volunteers. The *InteliSite*® capsule was employed to release ranitidine at specific sites in the intestinal tract. Ranitidine plasma concentration-time profiles achieved with the *InteliSite*® capsule were compared to data obtained from a previous intubation study (3).

MATERIALS AND METHODS

The *InteliSite*® Capsule

The *InteliSite*® capsule (Innovative Devices LLC., Raleigh, NC) is an inert, non-disintegrating, drug-delivery system that can be externally activated to release contents from the reservoir compartment after the capsule has been swallowed. The capsule characteristics are listed in Table I. The *InteliSite*® capsule diameter approximates the size of a "000" capsule and is similar in size to other orally administered products (e.g., Micro-K®, Procardia XL® and the Heidelberg pH monitoring capsule). The activating mechanism of the *InteliSite*® capsule is based upon the use of shape memory alloy wires that are formed at high temperature into a particular shape and then cooled to room temperature. When heated above a certain transition temperature (i.e., 40–43°C), the alloy wires return to their

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Table I. The *InteliSite*® Capsule System Characteristics

Size	3.5 cm (length) × 1 cm (diameter)
Capacity	0.8 ml of liquid (drug solution)
Weight	~ 2.5 gm
Operating frequency	6.78 MHz
Operating distance	10 cm
Activating temperature	40–43°C
Activation time	120 seconds
Operating power	120 watts

original shape. The required temperature is generated by a magnetic field via an external transmitting coil and a set of resistors within the *InteliSite*® capsule. The change in shape causes the inner sleeve of the capsule to rotate with respect to the outer sleeve, aligning the slots in the capsule and permitting release of the solution/suspension from the reservoir compartment. The magnetic field strength generated by the activator coil is four to five orders of magnitude less than that used with MRI. The capsule is tracked within the gastrointestinal tract by means of a gamma camera which is capable of detecting radio-tracer(s) placed within the capsule.

Study Procedures

This randomized, open-label, crossover study in healthy volunteers was conducted at the General Clinical Research Center of the University of North Carolina at Chapel Hill. The study followed the tenets of the Declaration of Helsinki (1964) and was approved by the University of North Carolina Committee on the Protection of Rights of Human Subjects and the University of North Carolina Hospitals Committee on the Use of Ionizing Radiation in Humans. After giving informed consent and meeting all inclusion criteria, eight subjects, 19–37 years in age (mean age 28.3 ± 5.8 years) underwent study procedures in which the *InteliSite*® capsule was activated in the jejunum or ileum (Period I) followed in 7–20 days by Period II in which the capsule was activated in the other site. The order of activation was randomized. Two of the eight subjects participated in an additional treatment period in which the *InteliSite*® capsule was activated in the colon. All subjects were within 10% of their calculated ideal body weights (weight range 62–79 kg). Individuals who had participated in any radiological or scintigraphic procedures within three months of the study, or who were occupationally exposed to any form of ionizing radiation were excluded from the study. Individuals who had undergone any gastrointestinal surgery, including an appendectomy, also were ineligible for the study. As part of the initial screening procedures, volunteers were asked to swallow an empty '000' gelatin capsule, in order to exclude subjects who might have difficulty swallowing the *InteliSite*® capsule. Individuals with any implanted device (e.g., pacemaker) that may be sensitive to radiofrequencies were excluded from participation.

Subjects were fasted for at least eight hours prior to administration of the capsule during each treatment period. On Day 1 of each treatment period, the *InteliSite*® capsule containing 121 mg ranitidine (0.6 ml of drug solution) mixed with 100μl (<100μCi) of ^{99m}Tc-DTPA (technicium diethylene triamine penta acetic acid) was administered orally along with 250 ml apple juice to the volunteers. Twenty μl (<20μCi) ^{111}In-DTPA was placed in a separate small compartment in the end of the capsule. ^{111}In served as a marker for the position of the capsule. The technetium (measured at a different keV) indicated if leakage of the capsule's contents occurred prior to activation. An external marker (^{60}Co) was placed at the umbilicus and intravenous fluid administration tubing filled with dilute ^{99m}Tc-DTPA was taped along both anterior-inferior rib-cage margins and vertically along the flanks to assist with localization of the capsule anatomically. By drawing a horizontal line at the umbilical marker and a vertical line passing through the umbilical marker and the xyphoid marker by the apex of the rib markers, four abdominal quadrants could be identified on the images. The subjects were positioned under or in front of a gamma scintillation camera equipped with a medium energy parallel hole collimator. The pulse analyzer was adjusted to detect ^{99m}Tc (8% window) at 140 keVs and ^{111}In (15% window) at 247 keV. Subjects were provided standard, caffeine-free low-fat meals at 5 and 11 hours after oral administration of the *InteliSite*® capsule. Once the position of the *InteliSite*® capsule at a particular site was confirmed, the release of ranitidine from the capsule was triggered by directed exposure of an external magnetic signal applied to the capsule for a maximum of 2 minutes at a distance of approximately 10 cm from the location of the *InteliSite*® capsule. The approximate three-dimensional location of the capsule within the volunteer was estimated by imaging the subject in frontal and lateral planes. The release of drug solution containing ^{99m}Tc-DTPA could be visualized on the gamma camera image. No more than two attempts to activate the capsule were made. Blood samples (5 ml) were obtained 10 minutes prior to swallowing the capsule, immediately prior to activation, and at 0.25, 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 8, 10 and 12 hours *after capsule activation.* Subjects were imaged continuously and images were captured and stored every 20 seconds *after oral administration* of the capsule until the capsule reached the desired site of release. During the time that the capsule remained in the fundus of the stomach, imaging was intermittently stopped for up to 30 minutes. Passage through the pylorus was indicated by movement to the right of midline followed by very rapid progression around the C-loop to the left upper quadrant (Ligament of Treitz area); activation at that point constituted jejunal release. With continuous imaging, the capsule was observed to follow a meandering course in the left upper quadrant after passing the Ligament of Treitz, occasionally entering briefly into the left lower quadrant or right upper quadrant. When the capsule remained in the right upper or left lower quadrant for more than 10 minutes, it was assumed to be in the mid small bowel and to have entered the ileum. Activation at that point constituted ileal release. Subsequently, the capsule usually followed a meandering path in the left lower quadrant, often descending into the pelvis, and then entered the far lateral right lower quadrant where the rate of movement became much slower. Activation at that point (presumed to be the cecum) constituted colonic release. Subsequent images showing a course consistent with movement through the ascending and transverse colon confirmed colonic localization. Visualization of loops of 20 second images often helped clarify the location of the capsule. Once the capsule had been activated, images were recorded for eight hours at the approximate time of blood samples. After that, images were recorded no less frequently than once every eight hours until the *InteliSite*®

capsule had been defecated. The retrieved capsule was examined for signs of proper activation.

Scintigraphic Analysis

Scintigraphs containing time averaged data from the previous 60 sec of gamma camera images were marked to delineate specific regions in the intestine. These scintigraphs were then digitally scanned to obtain radioactivity count data in the three regions of the gastrointestinal tract (i.e., jejunum, ileum and colon). External markers at the umbilicus and rib margins of the subject allowed for the anatomical alignment of intestinal regions in different scintigraphs for a specific treatment. The ^{99m}Tc counts were adjusted for radioactive decay and background prior to plotting counts in specific regions of the intestine vs. time after swallowing the capsule.

Sample Analysis

Blood samples were collected in lithium heparin tubes and centrifuged for ten minutes at 3000 rpm. The plasma was transferred to screw-capped polypropylene tubes and stored at −20°C until analysis. Ranitidine concentrations in plasma were determined by a previously published analytical method (17).

Pharmacokinetic and Statistical Analyses

Plasma concentrations were analyzed by model independent methods using WinNonlin (Scientific Consulting Inc., Apex, NC) to estimate the following pharmacokinetic parameters: AUC (area under the curve from time 0 to infinity), C_{max} (maximum plasma concentration), T_{max} (time of maximum plasma concentration), MRT (mean residence time) and K (first-order terminal elimination rate constant). Pharmacokinetic parameters (except T_{max}) were log-transformed to ensure normal distribution. Parameters were compared between treatments by Analysis of Variance using the PROC MIXED procedure in SAS (PC version 6.10) with a significance level of $p < 0.05$. Differences in T_{max} between treatments were analyzed by the non-parametric Wilcoxon Rank Sum test (significance level of $p < 0.05$). The C_{max} and the T_{max} of first and subsequent ranitidine peaks for the three treatments were compared.

RESULTS

As determined by gamma-scintigraphy images of ^{99m}Tc-DTPA, there was no leakage of drug from the capsule prior to activation during all eighteen treatments of the study. All capsules opened when activated during each treatment, as determined by gamma-camera imaging of ^{99m}Tc-DTPA and examination of the retrieved capsules (one capsule was not retrieved after it was defecated). None of the subjects had difficulty swallowing the capsule and the capsule was in the stomach within minutes of swallowing. The gastric emptying time of the *InteliSite*® capsule was 2.6 ± 0.8 (mean ± SD) hours. In all treatments, the capsule was defecated within 36 hours of swallowing. The highest variability in the transit time of the capsule was observed in the lower ileum and the colon. There were no adverse events during the study.

Figure 1 illustrates the gamma camera images of the *InteliSite*® capsule in a subject prior to and immediately after capsule activation in the jejunum, respectively. Capsule activation was confirmed by dispersion of the tracer as the drug solution (containing ^{99m}Tc-DTPA) left the capsule.

Representative ranitidine plasma concentration-time profiles in a single subject after activation of the capsule and release of ranitidine from the jejunum, ileum and colon are shown in Figure 2. Absorption from the ileum and jejunum was greater than the colon, consistent with data from previous intubation studies (3). Ranitidine concentrations in plasma were detectable in only one of the two subjects in which the capsule was activated in the colon.

The mean (± SD) ranitidine plasma concentration-time profiles after capsule activation and release of ranitidine in the jejunum ($n = 8$), ileum ($n = 8$) and colon ($n = 1$) are shown in Figure 3; the calculated pharmacokinetic parameters for the treatments are tabulated in Table II. There were no consistent differences in the plasma concentration time-profiles of ranitidine after activation of the capsule in the jejunum and ileum. No statistically significant differences in any of the pharmacokinetic parameters were observed between the two sites of capsule activation ($p > 0.05$). No significant sequence effect (order of treatments) or period effect (carryover effect from previous treatment) based on analysis of AUC data was observed. The calculated ranitidine AUC in each subject (Figure 4) confirmed the lack of a consistent trend in the extent of ranitidine absorption when the capsule was activated in the jejunum vs. the ileum. Greater inter-subject variability was noted in the AUC data when the capsule was activated in the ileum (compared to the jejunum).

Data from this study were compared to results from a previous intubation study (Table III) where ranitidine (150mg) was administered into the jejunum and colon (3). To facilitate comparison, the pharmacokinetic parameters (AUC and C_{max}) from the present study (121 mg ranitidine dose) were adjusted to a 150 mg dose of ranitidine. The ranitidine AUC was lower and less variable with the use of the *InteliSite*® capsule. However, no statistically significant differences were detected between any of the pharmacokinetic parameters (including AUC) when ranitidine was administered via the two different methods in the jejunum of subjects. Ranitidine pharmacokinetic parameters after administration in the colon via the two different methods could not be evaluated statistically due to the small sample size, although values appeared comparable.

Following capsule activation, timed scintigraphs allowed for the tracking of radioactivity (^{99m}Tc counts per minute corrected for radioactive decay) in the different regions of the intestine until the capsule was defecated. A timed comparison of radioactivity in the jejunum, ileum and colon, with ranitidine plasma concentrations for a representative subject following capsule activation in the jejunum and ileum, is provided in Figure 5. Radioactivity in the jejunum and ileum usually was observed at times corresponding to the initial ascent in the ranitidine plasma concentration-time profile. Intestinal absorption of ranitidine occurred predominantly when radioactivity was present in the jejunum or ileum. In all treatments, significant radioactivity in the colon was observed only at times after ranitidine plasma concentrations had peaked. These results indicate that little absorption of the drug occurred after the ^{99m}Tc (released from the capsule with the ranitidine solution) reached the colon, corroborating poor absorption of ranitidine from this site.

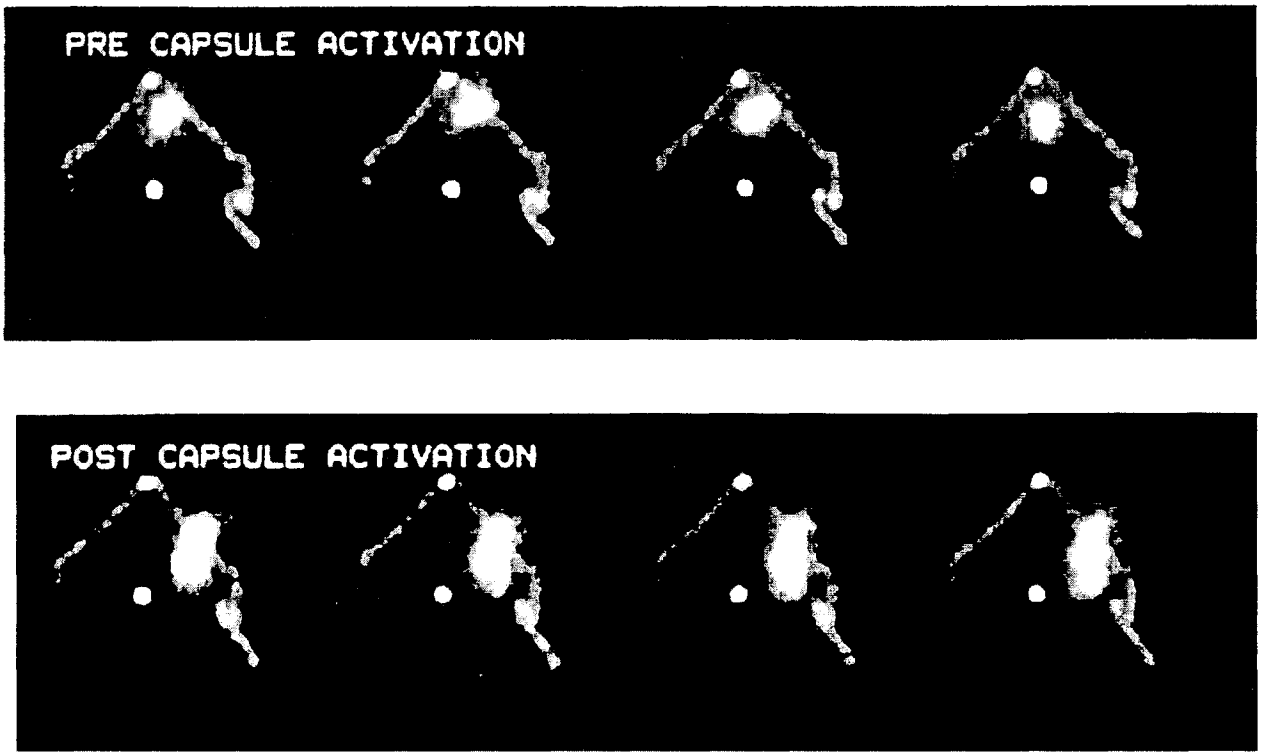

Fig. 1. Pre-Activation Image: Gamma camera image of the capsule in a volunteer prior to release of the drug. The low-intensity inverted 'V' at the top of the image represents tubing that was filled with a trace amount of ^{99m}Tc-DTPA, and taped along the lower periphery of the subject's rib-cage. ^{60}Co markers placed at the xyphoid process of the sternum and at the umbilicus can be observed as the two smaller high-intensity spots at the top and middle of the image, respectively. The high-intensity large spot represents the position of the *InteliSite*® capsule. Post-activation Image: Gamma camera image of the capsule in the same volunteer immediately after (within 1 minute) capsule-activation in the jejunum. The highly focused spot of high intensity shown in the previous image spreads out as the drug diffuses out of the capsule.

DISCUSSION

This study demonstrates the utility of a novel, externally activated, drug-delivery system to assess site-specific intestinal absorption of drugs in humans. It was assumed that the release of ^{99m}Tc-DTPA from the capsule mirrored the release and movement of ranitidine solution from the capsue. ^{111}In was incorporated in the end-cap of the capsule as a marker for the non-disintegrating delivery system. If fluids from the intestinal tract seeped into the endcap and the electronics component of the capsule, ^{111}In-DTPA would have leaked out of the capsule. This was not observed during this study. In future studies with the *InteliSite*® capsule, only a single isotope (mixed with the drug solution in the capsule reservoir) would be necessary to track the capsule. The ingestion of a solution of the second isotope along with the capsule would provide contrast in the gastrointestinal tract for more precise localization of the capsule.

One risk involved in using this non-disintegrating delivery system is the potential for mechanical obstruction of the gastrointestinal tract by the capsule. This did not occur in any of the eighteen study treatments. Patients with a history of abdominal surgery were excluded from the present study.

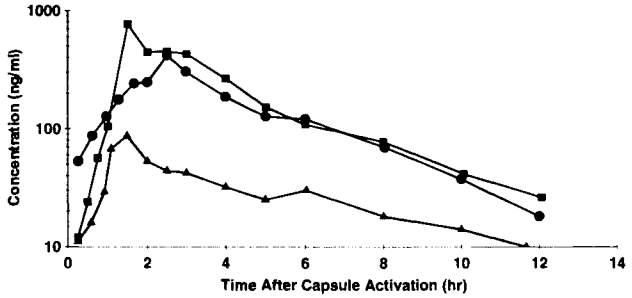

Fig. 2. Ranitidine plasma concentration-time profile after capsule activation at three sites [jejunum (●), ileum (■), colon (▲)] in a representative subject.

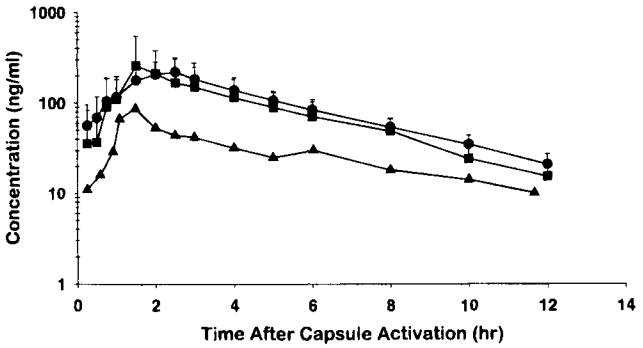

Fig. 3. Mean (± SD) plasma ranitidine concentration-time profiles after capsule activation in the jejunum (n = 8; ●), ileum (n = 8; ■) and colon (n = 1, ▲).

Table II. Ranitidine Pharmacokinetic Parameters[a]

	Jejunum [n = 8]	Ileum [n = 8]	Colon[b] [n = 1]
AUC (ng.hr/ml)	1198 (280)	1054 (652)	380
CL/F (L/hr)	108 (34)	178 (135)	318
MRT (hr)	5.30 (0.79)	5.42 (1.16)	6.22
K(1/hr)	0.232 (0.042)	0.235 (0.039)	0.188
C_{max} (ng/ml)	253.5 (90.5)	283.8 (258.7)	87
T_{max} (hr)	2.38 (0.51)	2.32 (1.42)	1.48

[a] Mean (SD). No statistically significant differences in any of the pharmacokinetic parameters were observed between the capsule activations ($p > 0.05$) in the jejunum and ileum. No significant sequence effect (order of treatments) or period effect (carryover effect from previous treatment) based on analysis of AUC data was observed in this study.

[b] The *InteliSite*® capsule was activated in the colon of two subjects. However, ranitidine concentrations were only detected in one treatment.

Table III. Ranitidine Pharmacokinetic Parameters After Jejunal or Colonic Administration via the *InteliSite*® Capsule or Naso-enteric Intubation[a]

	InteliSite® capsule		Intubation[e]	
	Jejunum[b] (n = 8)	Colon (n = 1)[d]	Jejunum[b] (n = 8)	Colon (n = 8)
AUC (ng.hr/ml)	1485 (347)[c]	471	2061 (600)	331 (122)
CL/F (L/hr)	108 (34)	318	78 (20)	541 (252)
MRT (hr)	5.30 (0.79)	6.22	4.49 (0.72)	5.33 (0.61)
K (1/hr)	0.23 (0.04)	0.19	0.31 (0.05)	0.23 (0.03)
C_{max} (ng/ml)	314.3 (112.2)[c]	108	472.3 (190.0)	52.6 (18.2)
T_{max} (hr)	2.38 (0.51)	1.48	2.94 (0.73)	2.69 (0.90)

[a] Mean (SD).

[b] There were no statistically significant differences between ranitidine pharmacokinetic parameters when administered via the *InteliSite*® capsule *vs.* intubation in the jejunum.

[c] Adjusted for a dose of 150 mg ranitidine base (actual dose = 121 mg).

[d] The *InteliSite*® capsule was activated in the colon of two subjects. However, ranitidine concentrations were only detected in one treatment.

[e] Data from Williams *et al.*, *Pharm. Res.* 9(9); 1190–1194, 1992.

Subjects swallowed the capsule along with 250 ml apple juice. Ranitidine absorption from the intestinal tract is influenced by food, and the apple juice provided identical caloric input to the subjects (who were fasted at least eight hours prior to swallowing the capsule). Also, previous studies with radiolabeled tablets indicated that apple juice aligns phases of the Migrating Motor Complex (MMC) in humans (18).

After the capsule was swallowed, it remained in the stomach until the large contractile wave of the MMC propelled it through the pyloric sphincter. The relatively slow mobility of the capsule in the stomach and the considerable time of gastric residence makes this a site that is easily amenable to the use of the *InteliSite*® capsule in studying drug absorption. After gastric emptying, the capsule rapidly passed through the duodenum. The rapid movement of the capsule through the relatively short (approximately 25 cm) length of the duodenum makes this a difficult site for capsule activation unless a tether was attached to the capsule. Due to the lack of anatomical landmarks to separate the jejunum and the ileum, activation of the capsule in these regions requires expertise. Familiarity with gastrointestinal anatomy, coupled with careful examination of multiple images of the capsule's transit through the intestine, allows for the identification of these sites. Prolonged residence time of the capsule in the ascending, transverse and descending segments of the colon makes these relatively easy sites for capsule activation. However, when the capsule is located within the pelvic girdle, it is possible that the distance from the capsule to the external activating antenna may exceed the recommended range of reliable capsule activation (i.e., 10 cm).

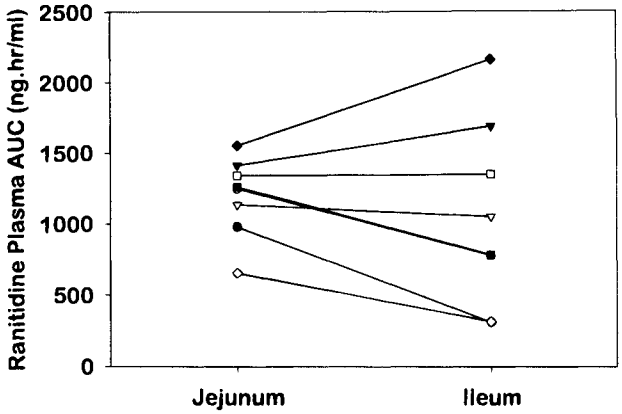

Fig. 4. Ranitidine AUC after capsule activation in the jejunum or ileum in each subject. Symbols denote individual subjects [Subject 201 (●), 202 (○), 203 (▼), 204 (▽), 205 (■), 206 (□), 301 (♦), 302 (◇)].

Ranitidine pharmacokinetic parameters were not significantly different when the capsule was activated in the jejunum compared to the ileum. This is in contrast to *in situ* rat data which indicate that ranitidine is better absorbed from the ileum as compared to the jejunum (15). Also, in contrast to rat (14) and human (3) data from other pharmacokinetic studies after oral administration of ranitidine, the incidence of secondary peaks in the plasma concentration-time profiles was less pronounced in the present study. Using previously published criteria for the definition of double peaks (14), only three of eight subjects exhibited double peaks after ileal activation in this study. Although small shoulders were observed on the upswing of some ranitidine plasma concentration-time profiles (e.g., Figure 5, left panel), no double peaks were observed with any of the jejunal activations. The reason for the lower incidence of secondary peaks observed in this study is unclear.

Comparison of the two methods for studying site-specific intestinal absorption of drugs in humans is imperative. The presence of the nasogastric/oroenteric tube may affect gastric and intestinal motility. Read and colleagues have reported that gastric emptying was significantly retarded in twelve intubated subjects compared to ten control subjects (19). Also, colonic filling was considerably accelerated in intubated subjects. If the bioavailability and absorption characteristics (including C_{max} and T_{max}) of a drug are significantly affected by gastric emptying and intestinal transit time, data from intubation studies may be misleading (20,21). The volume of fluid ($\geq$ 10 ml) used to flush the dosing solution in intubation studies may alter the absorption conditions. Volunteer comfort and compliance

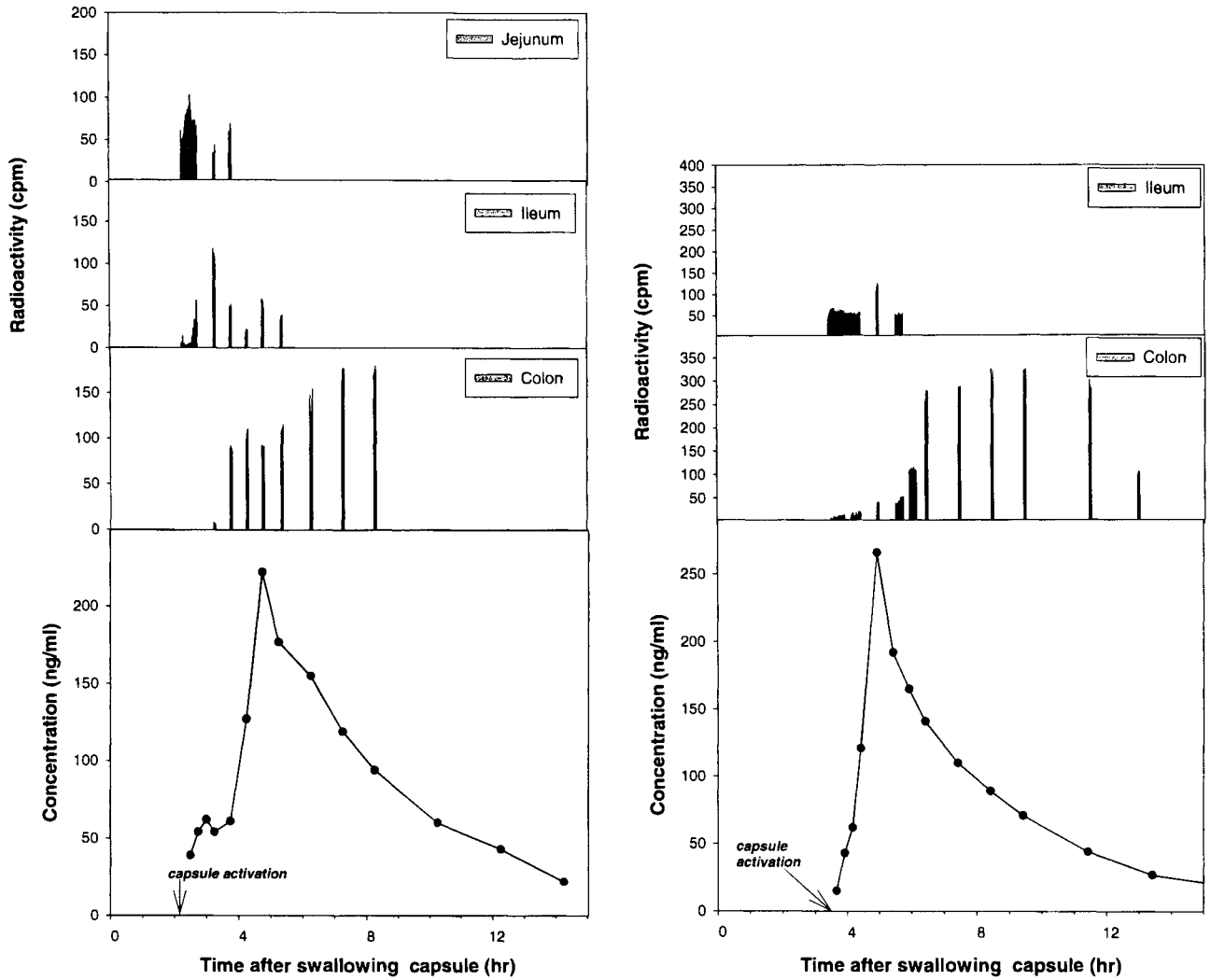

Fig. 5. Comparison of radioactivity in the jejunum, ileum and colon with ranitidine plasma concentrations (●) in a representative subject after capsule activation in the (left panel) jejunum and (right panel) ileum.

are additional considerations. For drugs with long half-lives, subjects are required to remain intubated for several days if absorption is evaluated from more than one specific gastrointestinal site (to allow for adequate periods of sampling and washout at each site). Although the *InteliSite*® capsule alleviates all of the above concerns, other factors must be considered. Subjects ingesting the *InteliSite*® capsule should be within 10% of their ideal body weight. This is to ensure efficient activation of the capsule with use of the magnetic field generator (capsule must be within 10 cm of the transmitter for activation). The *InteliSite*® capsule used in this study also can only accommodate up to 0.8 ml of drug solution in the capsule reservoir. However, *InteliSite*® capsules now are available which permit the placement of dry powders within the capsule.

CONCLUSIONS

This investigation demonstrates the clinical utility of an externally-activated drug-delivery system as an alternative to intubation studies for the clinical evaluation of site-specific intestinal absorption of drugs. The *InteliSite*® capsule released ranitidine when activated in all treatments. There were no differences in the extent of ranitidine absorption or ranitidine pharmacokinetic parameters after activation of the capsule in the jejunum and ileum. Ranitidine was poorly absorbed from the colon, consistent with previous results from intubation studies. There were no statistically significant differences between pharmacokinetic parameters when ranitidine was administered in the jejunum via the *InteliSite*® capsule or via naso-enteric intubation.

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