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Targeted drug release to distinct GI regions using pH measurement data from the IntelliCap® system and simultaneous imaging

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PURPOSE

The IntelliCap® system is a CE-certified medical device which is capable of achieving controlled release of drugs to specific GI target sites in a fast, cost-effective and convenient manner. The system consists of a single-use, swallowable electronic device that is capsule-shaped (11 mm x 27 mm) which measures pH and temperature data wirelessly in real-time throughout GI transit, a control PC, a start-up unit and a portable unit which is worn by the subject.

This clinical study was designed to allow tracking of the capsule through the GI tract using gamma scintigraphy in conjunction with the recorded pH data. Additionally, visualisation of the radiopharmaceutical release from the capsule provided clear indication of drug payload release.

Figure 1. The IntelliCap® system.

METHODS

Five healthy male volunteers were enrolled into this pilot clinical study. The subjects received an IntelliCap® capsule containing a 175 mg/mL solution of the marker drug, quinine hydrochloride dihydrate, radiolabelled with approximately 4 MBq ^{99m}Tc-DTPA (at time of dose) in the fasted state on two occasions.

The IntelliCap® capsule was actuated to release 35 mg of drug over a period of 15 min as follows:

Period A Approximately 100 min post-gastric emptying, targeting the **distal small intestine (dSI)**
Period B Upon ileocaecal valve passage determined by pH measurement and scintigraphic confirmation of **ascending colon (AC)** arrival

Scintigraphic images were taken every 15 min until complete radiolabel release was noted. Blood samples for pharmacokinetic (PK) analysis were taken at specified intervals to 24 h post-dose and centifuged to obtain the plasma fractions which were frozen at -20 ° C until analysed by LC-MS for detection of quinine. pH and temperature data were also recorded by the IntelliCap® system.

RESULTS

Of the five subjects who were enrolled, four completed Period A and three completed Period B. During Period A, one subject withdrew consent due to cannulating issues and prior to dosing on Period B, one subject was excluded due to failing a drug screen.

Scintigraphic images of key events occurring in the gastrointestinal transit of an IntelliCap® capsule in Subject 003 are shown in Figure 2. These are images representative of those acquired throughout the study.

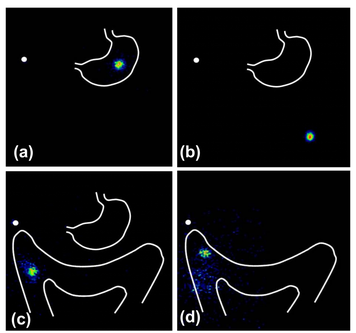

Figure 2. Anterior scintigraphic images of key events in the GI transit of the IntelliCap® capsule in Subject 003 at various times post-dose:

(a) 0 min (IntelliCap™ capsule located in stomach)
(b) 30 min (confirmation of capsule gastric emptying)
(c) 345 min (onset of radiolabel release in the AC)
(d) 630 min (imaging complete)

When released in the dSI, the mean quinine C_{max} was higher than when released in the AC (329±141 ng/mL and 158±84 ng/mL, respectively). A similar reduction in $AUC_{0\text{-}24}$ was also observed: 230209±106770 ng/mL.min (dSI) and 142195±88447 ng/mL.min (AC). These data (Figure 3) are consistent with successful drug release targeting to the dSI and AC, as absorption of quinine diminishes distally along the GI tract [1].

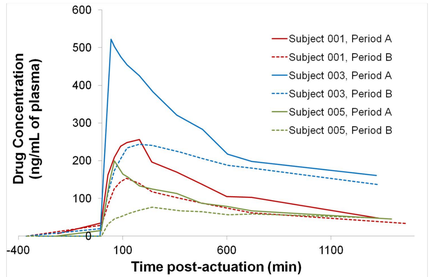

Figure 3. PK profiles for Subjects 001, 003 and 005.

Table 1 details the comparative GI transit and drug release parameters obtained from scintigraphic imaging and pH data.

Table 1. GI transit and drug release parameters.

	Gastric emptying time (min post-dose)		Drug release (min post-dose)	
Period A	*Scintigraphy*	*pH*	*Radiolabel release*	*Capsule actuation*
	69.0±59.2	70±60	175.2±63.7	169±62
Period B	*Scintigraphy*	*pH*	*Radiolabel release*	*Capsule actuation*
	27.5±8.7	28±7	337.5±0.3	330±0

CONCLUSION

This clinical study confirmed good correlation of capsule localisation within the GI tract as determined by scintigraphic and pH data. Targeting drug release to the dSI and AC was successful in all attempts. Lower bioavailability of quinine was observed, as expected, when released in the AC compared to the dSI.

REFERENCE

[1] J.M. Hebden, C.G. Wilson, R.C. Spiller, P.J. Gilchrist, E. Blackshaw, M.E. Frier and A.C. Perkins. “Regional differences in quinine absorption from the undisturbed human colon assessed using a timed release delivery system.” *Pharm. Res.* **16** (1999) 1087-1092.