Investigation of pH and temperature profiles in the GI tract of fasted human subjects by Intellicap® system

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ABSTRACT SUMMARY
The electronic drug delivery device Intellicap® was given to 20 healthy human subjects in order to study the pH and temperature profiles present under conditions mimicking the administration of a solid oral dosage form in the fasted state. The results revealed high variability of transit times in stomach and small intestine and related of pH profiles. Even in the stomach, significant pH fluctuations were observable owing to water intake and reflux of duodenal contents. In the small intestine, pH values slightly increased from pH 6 to pH 7-8. Temperature measurements indicated a drop from 37°C down to 20-25°C depending on water temperature and volume.

INTRODUCTION
Regional differences within the human gastrointestinal (GI) tract are known to alter the drug release from solid oral dosage forms. In particular, the drug delivery behavior of enteric coated or modified release dosage forms are affected by transit times as well as pH values in stomach, small intestine and colon. Therefore, the characterization of the transit conditions in the human GI tract is required for a thorough comprehension of the in vivo processes.

Recently, Medimetrics (Netherlands) introduced Intellicap®, which is an electronic drug delivery system.¹ This ingestible capsule is able to deliver the drug at a certain place by a pumping system based on different triggers such as pH or localization in the GI tract. Besides, Intellicap® is a helpful diagnostic tool for the in vivo investigation of dosage form transit due to its capability of real-time pH and temperature monitoring.

In this paper we present the results of two studies investigating the pH and temperature profiles in stomach and small intestine of fasted healthy human subjects by Intellicap® system.

EXPERIMENTAL METHODS
The two studies were both conducted in ten healthy human subjects. Intellicap® (Medimetrics, Netherlands) was ingested together with a glass of water (room temperature) after an overnight fasting period. Temperature data (relative accuracy: +/- 0.1°C) and pH values (relative accuracy: +/- 0.3 pH units) were recorded via wireless communication. Four hours after administration, subjects received lunch.

As illustrated in Figure 1, gastric emptying time (GET), small bowel transit time (SBTT) and colonic arrival time (CAT) were determined by consideration of significant pH changes (> 0.9 pH units).

RESULTS AND DISCUSSION
Figure 2 indicates the high interindividual variability of pH values and transit times in stomach and small intestine. In the fasted stomach, low pH values of 1-2 were observed. However, short episodes of higher pH values...
were registered that are most likely caused either by water intake as well as reflux of duodenal contents containing alkaline hydrogencarbonate. This is in accordance with studies by Hausken et al., who described the retropulsion of duodenal contents back into the stomach under fasting conditions. Data from magnetic marker monitoring (MMM) studies support this hypothesis due to the fact that the retrograde movement of solid dosage forms through the pylorus is rather unlikely.

In contrast to the stomach, the pH profiles in the small intestine are relatively uniform if the localization of the tablet is considered by normalizing the SBTT (Figure 3).

Moreover, the data revealed high variability of the SBTT (67-508 min) in comparison to the gastric residence time, which was significantly shorter (7-202 min). In Figure 4, box plots for GET, SBTT and CAT are depicted.

Regarding the temperature, a decrease to values of 20-25°C was observed at the time point when the capsule was ingested. Using a novel dissolution test setup called “dynamic open flow through test apparatus” we could recently demonstrate that this can have serious consequences for the dissolution behavior of immediate release dosage forms (manuscript submitted).

CONCLUSION

By use of Intellicap® system, pH and temperature profiles in the upper human GI tract can be studied. The results revealed high variability of pH values in stomach and small intestine, which were caused by water intake, retropulsion of duodenal contents back into stomach and different transit times. Both, pH profiles and transit times are highly relevant for drug release behavior of solid oral dosage forms and need further investigation.

REFERENCES

