MAGNETIC MOMENT IMAGING - A PILOT STUDY IN FED AND FASTED VOLUNTEERS

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INTRODUCTION

Magnetic moment imaging (MMI) relies on the detection of a magnetic signal to track movement of a dosage form through the gastrointestinal (GI) tract. An amount of ferromagnetic material is incorporated into the dosage form and magnetised. The resultant magnetic moment, a parameter dependent on magnetic signal strength and distance, is detected and analysed to locate the dosage form within the body. An intact dosage form provides a permanent moment while disintegration results in complete loss of moment. This property is used to determine the site of tablet disintegration.

This study has pioneered the use of the Magnetic Tracking System (MTS-1000) (Figure 1) in investigating the behaviour of magnetic tablets *in-vivo*. It is portable, relatively inexpensive and does not require a magnetically-shielded room.

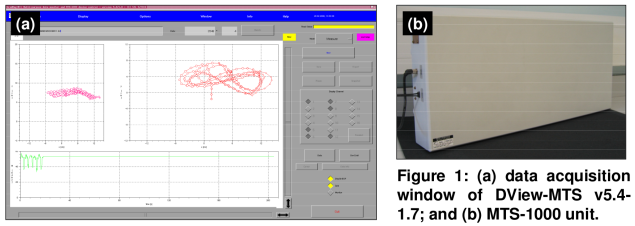

Figure 1: (a) data acquisition window of DView-MTS v5.4-1.7; and (b) MTS-1000 unit.

OBJECTIVES

To assess the feasibility of using the MTS-1000 to:

- measure the gastric emptying time of an enteric-coated tablet
- investigate tablet movement and behaviour in the stomach in fed and fasted states

MATERIALS AND METHODS

Formulation of enteric-coated magnetic tablets

Placebo magnetic tablets (MTs) containing microcrystalline cellulose, sodium starch glycolate, magnesium stearate and food grade iron oxide (E172) were prepared by direct compression. A base coat of polyvinyl pyrrolidone was applied prior to coating with Eudragit L100 using a Caleva Minicoater / Drier. The coated tablets containing 1g iron oxide were magnetised to 0.013 Tesla using a permanent magnet array.

Clinical study

Design Single-centre, analyst-blind, randomised, two-way crossover study.

Subjects 8 healthy male volunteers (mean age 40.3 ± 16.9, range 23 to 65 years).

Dosing Subjects were dosed with one MT per study day either fasted or 15 minutes after consuming a light breakfast (770kJ). The tablet was swallowed with 240mL water.

Scanning Schedule Scans of 60s duration (scan rate 100Hz) were taken in the upright position immediately after dosing and every 15 minutes post-dose. Imaging was stopped after the magnetic signal was lost. Data was analysed using Axum Mathcad v5.0.

RESULTS AND DISCUSSION

MT behaviour in GI tract

Tracking of tablet movement in the stomach was possible in both the fed and fasted states. Spatial positioning of the tablet within the GI tract was visualised on the x, y and z planes. Figure 2 is an example of tablet movements collated over the duration of a study day. Gastric emptying (GE) occurred between 1.25h and 1.5h.

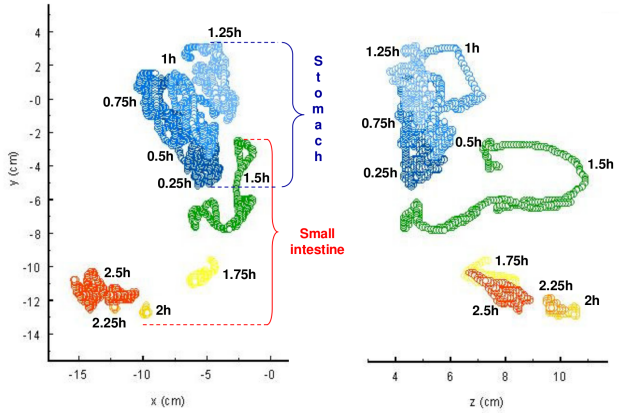

Figure 2: Movement of MT in GI tract (Subject 004, fed).

It was possible to discriminate the stomach and small intestinal regions as the tablet travelled through the GI tract. The tablet displayed significant tumbling in the stomach. The 1.5h acquisition showed the tablet travelling within the proximal small intestine. The movement of the tablet within the small intestine after that was much more restricted. Analysis of the tablet velocity during each acquisition confirmed the greater degree of tumbling movement in the stomach (Figure 3).

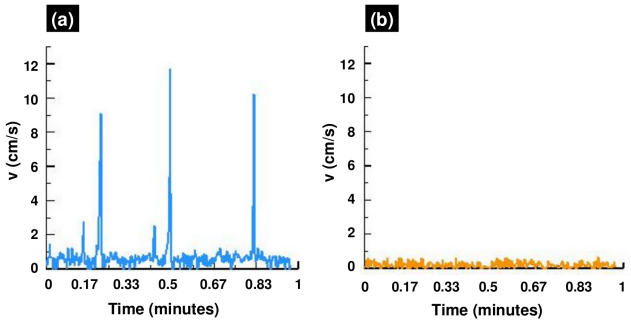

Figure 3: MT velocity measurements in the (a) stomach - 1.25h; and (b) small intestine - 2.25h (Subject 004, fed).

In Figure 4a, the tablet displayed a relatively stable magnetic moment within the stomach, reflecting its intact state. After gastric emptying (Figure 4b), the moment gradually decreased as the enteric coat deteriorated and absorption of water resulted in swelling of the tablet, weakening the magnetic signal. This was confirmed by *in-vitro* experiments. Complete disintegration was marked by the inability of the MTS-1000 to detect the tablet's moment.

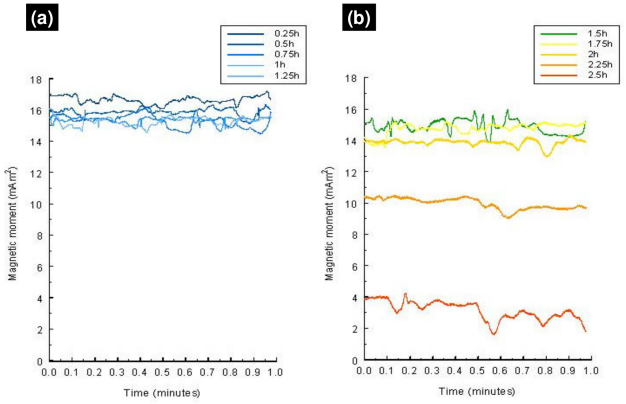

Figure 4: Magnetic moments of MT (a) within the stomach; and (b) post-gastric emptying (Subject 004, fed).

Food effects

Poor integrity of the enteric coat may have caused premature disintegration of the tablet within the stomach. Hence GE was not detected for certain subjects resulting in the varying n values in Table 1. It was unclear whether a true food effect had occurred in the emptying of the MT although the mean gastric emptying time in the fed state was slightly longer than that of the fasted. The tablet disintegration times post-GE were 1.4±0.7h (n=4) and 1.9±0.5h (n=6) in the fed and fasted states respectively.

Parameter	Fed		Fasted	
	Mean (S.D.)	n	Mean (S.D.)	n
GE (h)	2.1 (0.6)	4	1.6 (1.4)	6
Tablet disintegration time post-dose (h)	3.9 (1.0)	7	3.2 (1.6)	7

Table 1: Effect of food on gastric emptying and tablet disintegration times.

CONCLUSION

MMI using the MTS-1000 is a promising alternative to current imaging techniques to study upper GI transit and behaviour of dosage forms.