

VALIDATION OF SCINTIGRAPHIC QUANTIFICATION OF HYDROPHOBIC TABLET EROSION

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INTRODUCTION

Understanding tablet behaviour in the human body is a key component in improving current delivery systems. This communication describes a novel scintigraphic method for quantification of hydrophobic tablet erosion. These tablets consisted of materials used as barrier layer components in time-delayed delivery systems [1]. Initial *in vitro* studies involved comparing the erosion profiles obtained gravimetrically and scintigraphically, with the inclusion of radiolabelled charcoal in the tablets. A clinical study was then performed to investigate the erosion behaviour of these tablets *in vivo*.

EXPERIMENTAL METHODS

Investigational tablets

For all methods, the ratio of glyceryl behenate (GB): low-substituted hydroxypropylcellulose (L-HPC) was maintained at 65:35%(w/w) and the target tablet weight was 500 mg with dimensions of 13 mm x 4 mm. Tablets were prepared by three different methods: Direct Compression (DC), Melt Granulation (MG) and Direct Solidification (DS).

GB-coated cold-labelled or ^{99m}Tc-DTPA-labelled charcoal was added prior to compression for DC and MG tablets. Cold-labelled or ^{99m}Tc-DTPA-labelled charcoal was added to the melted GB prior to addition of L-HPC for DS tablets.

Gravimetric erosion studies

The ETs (with and without charcoal) were subjected to dissolution in a USP Apparatus II (50 rpm, 37 °C, 1000 mL distilled water). At set intervals, the ETs were removed and dried at 50 °C for at least 36 h. The eroded material was quantified by subtracting the weight of the dried tablet cores from the initial tablet weight.

Gamma scintigraphic erosion studies

Radiolabelled ETs were subjected to dissolution in front of the gamma camera under the conditions described above. Regions of interest were constructed around the tablet core and the counts were background and decay-corrected.

Clinical scintigraphic study

Six healthy male volunteers received one radiolabelled ET (4 MBq at time of dose) per study day. They were dosed with 240 mL water 30 min after a light snack (500 kJ). Imaging was performed with the subjects in a standing position. Anterior and posterior static acquisitions were collected.

RESULTS AND DISCUSSION

Figure 1 and Figure 2 show the erosion profiles of the tablets, obtained by gravimetric and scintigraphic methods respectively.

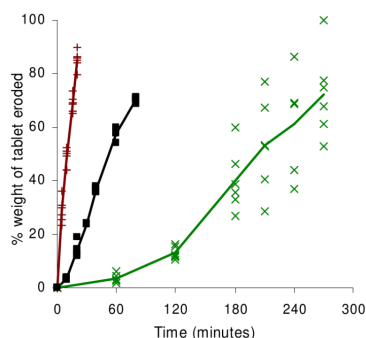


Figure 1: Gravimetric erosion profiles of ET-DC (+), ET-MG (■) and ET-DS (x) (n=6).

OBJECTIVES

1. To develop a suitable radiolabelling method for scintigraphic studies
2. To scintigraphically distinguish the effect of manufacturing process on the erosion characteristics of erodible tablets (ETs)
3. To validate the radiolabelling method by comparing with conventional gravimetric studies
4. To investigate the *in vitro-in vivo* correlation of the erosion behaviour of these tablets

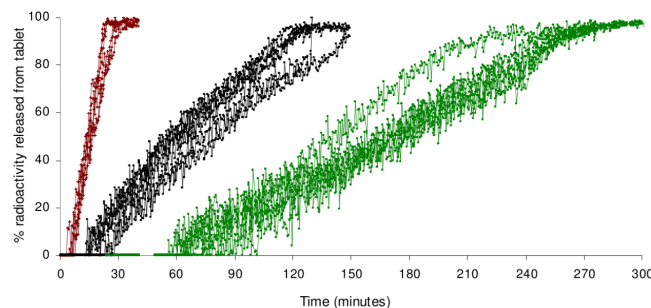


Figure 2: Scintigraphic erosion profiles of ET-DC (+), ET-MG (■) and ET-DS (x) (n=6).

Both methods clearly showed the effect of manufacturing method on the erosion profiles of the tablets. The rate of erosion decreased in the order: DC>MG>DS. The results obtained scintigraphically correlated well with those determined gravimetrically.

Scintigraphic images from the clinical study (Figure 3) enabled the visualisation and quantification of the tablet behaviour *in vivo* (Figure 4). In general, the *in vivo* behaviour of the tablets correlated well with the *in vitro* data. However, fragmentation of ET-DS was observed.

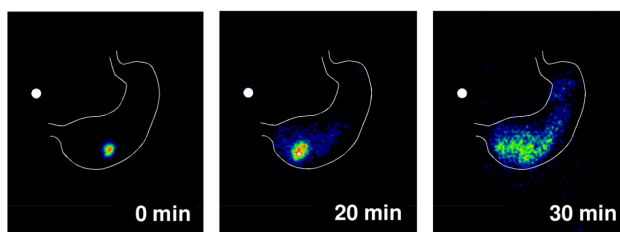


Figure 3: Sample images of ET-DC erosion *in vivo*.

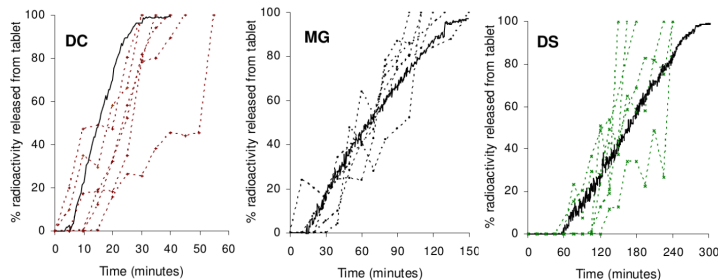


Figure 4: Comparison of mean (n=6) *in vitro* scintigraphic erosion profile (—) to individual *in vivo* erosion profiles.

CONCLUSION

Erosion behaviour of hydrophobic tablets was successfully characterised scintigraphically and validated against a conventional gravimetric method. Scintigraphic tracking of radiolabelled tablets was found to be a simple yet effective approach to evaluating the *in vivo* behaviour of these tablets. This method could be potentially be extended to investigating the behaviour of a wide range of formulations.

ACKNOWLEDGEMENTS

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REFERENCE

1. Ghimire, M. *et al.* (2007) *Eur J Pharm Biopharm.* 67(2):515-23.