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# Probing the disintegration of tablets with different erosion mechanisms using radiolabelled charcoal

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## OBJECTIVES

The objectives of this study were to establish the suitability of radiolabelled charcoal as a marker for monitoring, using gamma scintigraphy, the *in vivo* erosion of two different types of controlled release matrix tablets: HPMC matrix tablets and waxy matrix tablets.

HPMC tablets swell on contact with water, forming a gel layer that acts as a barrier to drug diffusion. Once fully hydrated, this layer dissolves by a 'passive' erosion mechanism. Combination low-substituted hydroxypropyl cellulose (L-HPC)-wax matrix tablets on the other hand, exhibit an 'active' erosion mechanism, where erosion is dependent on the hydration and swelling of the disintegrant, L-HPC.

The marker used was $^{99m}$Tc-DTPA-labelled charcoal. Due to the insoluble nature of charcoal, it was hypothesised that it would also provide a good model for the behaviour of poorly water soluble drugs.

## METHODOLOGY

Three tablets were prepared by direct compression:

**A** 65:35 %(w/w) Glycerol behenate:L-HPC
**B** 20:69 %(w/w) HPMC:lactose; 10%(w/w) dicalcium phosphate; 1%(w/w) magnesium stearate
**C** 40:49 %(w/w) HPMC:lactose; 10%(w/w) dicalcium phosphate; 1%(w/w) magnesium stearate

The radiolabel was prepared by evaporation of a suspension of activated charcoal in an appropriate volume and activity of $^{99m}$Tc-DTPA saline solution. Radiolabelled charcoal (3 mg) was dispersed uniformly throughout the tablet blend prior to compression.

***In vitro* gravimetric analysis** was performed by removing tablets from a USP II dissolution at set intervals, drying at 50 °C for at least 36 hours, and weighing. Conditions: Distilled water, 37° C, 50 rpm.

***In vitro* scintigraphic dissolution** was carried out by placing a USP II apparatus in front of the gamma camera and acquiring sequential images. Conditions: Distilled water, 37° C, 50 rpm.

***In vivo* scintigraphic assessment** was undertaken in six healthy male volunteers, dosed 30 minutes after a light breakfast, with scintigraphic images acquired at regular intervals post-dose. Tablets **A**-**C** contained 4 MBq $^{99m}$Tc at time of dose.

## RESULTS

**WAX MATRIX TABLET (A)**

It was confirmed gravimetrically that the addition of charcoal did not have a significant effect on the erosion profile of the tablet ($f_2$ = 78). The *in vitro* scintigraphic erosion profile was comparable to the profile obtained from gravimetric studies.

Figure 1 shows an example scintigraphic image of a wax matrix tablet labelled with $^{99m}$Tc-DTPA-charcoal. Figure 2 shows the *in vivo* and *in vitro* scintigraphic erosion profiles for tablet **A** disintegrating in the stomach.

Figure 1 (above). Example image of a radiolabelled wax matrix tablet disintegrating in the stomach

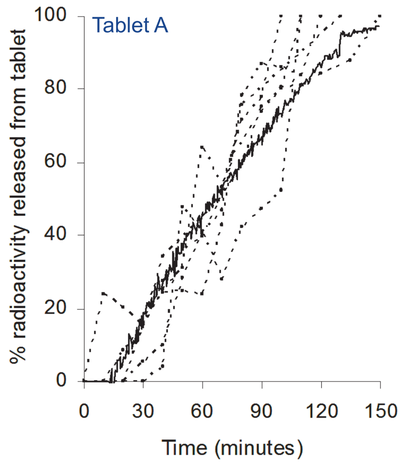


Figure 2 (right). Comparison of mean (n = 6) *in vitro* scintigraphic erosion profile (—) with individual *in vivo* erosion profiles for tablet **A**.

*In vivo,* erosion started in the stomach and completed in the SI for all 6 subjects. The times of onset and completion of erosion *in vivo* were 18.3±8.1 min (n=6) and 70.0±18.3 (n=6) respectively. The mean rate constant of erosion calculated for 5/6 subjects was 0.94±0.18% min$^{-1}$.

The onset of erosion *in vivo* was not significantly different ($p$ > 0.05, $t$-test) to that observed scintigraphically *in vitro* (17±4 min). Figure 2 shows the excellent *in vitro-in vivo* correlation for these tablets.

**HPMC MATRIX TABLETS (B & C)**

The HPMC tablets investigated in this study had both high (tablet **B**) and low (tablet **C**) water soluble component/polymer ratios.

It was confirmed gravimetrically that the addition of charcoal did not have a significant effect on the erosion profile of either tablet (tablet **B** $f_2$ = 50; tablet **C** $f_2$ = 70). Additionally, good correlation between scintigraphic and gravimetric erosion rates was found for tablets **B** and **C** *in vitro* ($f_2$ similarity factors of 51 and 62 respectively).

*In vivo*, tablet **B** displayed a higher erosion rate than tablet **C** (Figure 3). Tablet **B** showed non-uniform erosion (i.e. rapid erosion phase of at least 34% within 15 min) in 4 out of 5 subjects, whereas no such phases of rapid erosion were observed for tablet **C**. It can also be seen that there was a greater correlation between *in vivo* scintigraphic data and *in vitro* gravimetric data for tablet **C** than for tablet **B**.

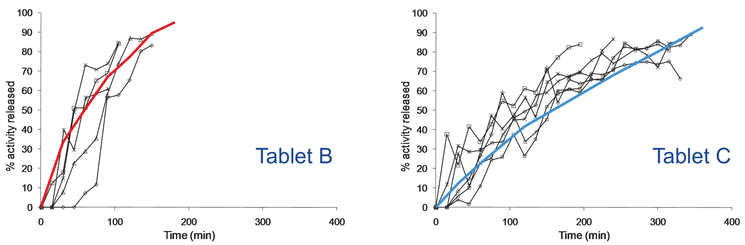


Figure 3. Comparison of mean scintigraphic *in vitro* (—) with individual *in vivo* erosion profiles for tablets B and C. *In vitro* conditions: USP II, distilled water, 37 ° C, 50 rpm.

The poor performance of tablet **B** is thought to be due to the low concentration of matrix-forming HPMC, which at 20% (w/w) is likely to be below the percolation threshold. The charcoal marker clearly demonstrated the rapid breakdown of the HPMC matrix *in vivo* for tablet **B**, while reflecting the slow erosion rate of formulation **C**, which has an HPMC content of 40% (w/w).

## CONCLUSIONS

In all cases, the dispersion of radiolabelled charcoal *in vivo* provided an accurate reflection of the erosion behaviour of the matrix system and could be expected to be representative of how a poorly water soluble drug would behave in such a system.