In-Vitro Characterisation of Radiolabelled Erodible Tablets

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INTRODUCTION

Granules consisting of glyceryl behenate (GB) and low-substituted hydroxypropyl-cellullose (L-HPC, grade LH-21) prepared by the melt granulation method have been previously been established as a barrier layer component in a press-coated tablet [1]. Additionally, it has been documented that the drug release profile from GB matrix tablets depended on the method of tablet preparation [2].

The aims of the current study were to investigate the effect of manufacturing process on the erosion characteristics of erodible tablets (ETs) and to suitably radiolabel ETs in view of a clinical study using gamma scintigraphy.

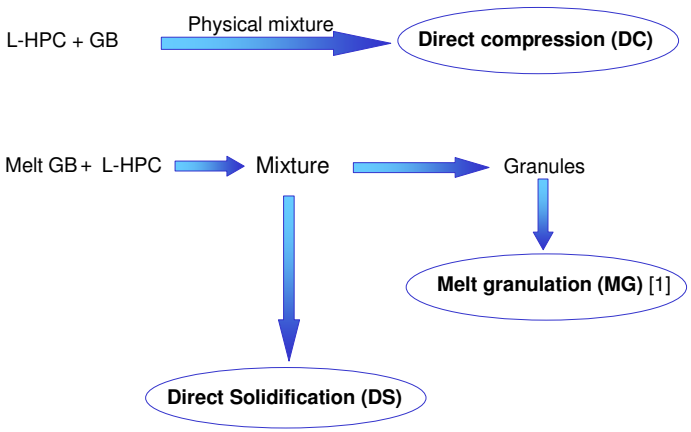
EXPERIMENTAL METHODS

RADIOLABELLING OF CHARCOAL

0.5ml of technetium-99m-diethylenetriaminepentaacetic acid (^{99m}Tc-DTPA) solution was added to activated charcoal stirred and evaporated to dryness using hot air dryer. *In-vitro* adsorption test showed this label remained associated with charcoal for up to 24 hours in media ranging from pH 1.2 to 6.8 (Data not shown).

PREPARATION OF ERODIBLE TABLETS

For all methods, the ratio of GB:L-HPC was maintained at 65:35%(w/w) and the target tablet weight was 500mg with dimensions of 13mm x 4mm. Tablets were prepared by three different methods as shown below.



GB coated cold-labelled or radiolabelled charcoal was added prior to compression for tablets prepared by direct compression and melt granulation method. Cold-labelled or radiolabelled charcoal was added into melted GB prior to addition of L-HPC for tablet prepared by direct solidification method.

GRAVIMETRIC EROSION STUDIES

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

GAMMA SCINTIGRAPHIC EROSION STUDIES

ETs radiolabelled with ^{99m}Tc-charcoal underwent dissolution in front of the gamma camera with dissolution conditions described above. Regions of interest were constructed around the tablet core and the counts were background and decay-corrected.

RESULTS AND DISCUSSION

GRAVIMETRIC EROSION STUDIES

Fig 1 shows the erosion profiles of ET-DC, ET-MG and ET-DS. Swelling and disintegration properties of L-HPC particles were responsible for the erosion characteristics of the ET [3]. L-HPC particles distributed within the ET was uncoated by GB in ET-DC, while most of L-HPC particles were completely coated in ET-DS. For ET-MG, the L-HPC particles was distributed within the granules as well as surface of the granules prior to compression, leading to occurrence of higher level of partially coated L-HPC particles in MG than in DS. Higher variability in erosion profiles was observed in ET-DS possibly due to the non-uniform distribution of L-HPC particles within the tablet during the solidification process. No difference in the erosion profiles of tablets was found with or without charcoal (Fig 1).

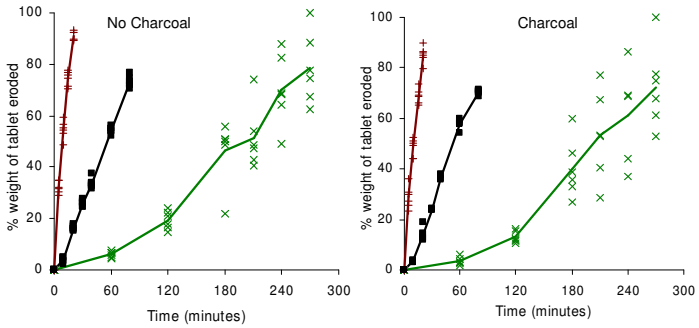


Fig 1. Gravimetric erosion profiles of ET-DC (+), ET-MG (■) and ET-DS (x) (n=6 for all).

GAMMA SCINTIGRAPHIC EROSION STUDY

Fig 2 illustrates *in-vitro* erosion of radiolabelled tablets. The dispersed remains strongly associated with the charcoal label after erosion from the tablet. This is indicated by accumulation of activity at the surface of dissolution vessel.

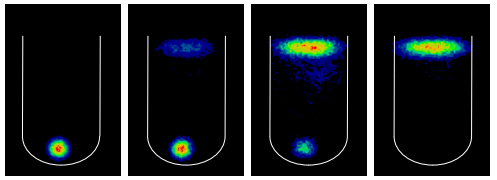


Fig 2. Summed dynamic images showing erosion of ^{99m}Tc labelled ET-DC tablet (Left to Right 0-10 min, 10-20 min, 20-30 min, 30-40 min). Outline of dissolution vessel is for presentation only and is not to scale.

The erosion profiles of ^{99m}Tc-charcoal-labelled ETs are shown in Fig 3. A clear lag time prior to onset of erosion was found in all formulations. The rate of erosion was found in deceasing order of tablet prepared by DC>MG>DS and correlated with results obtained from gravimetric method.

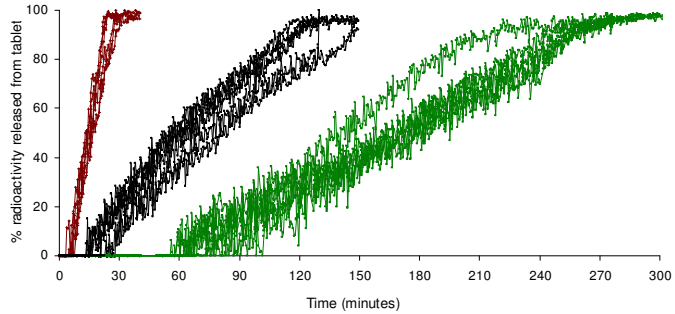


Fig 3. Scintigraphic erosion profiles of ET-DC (+), ET-MG (■) and ET-DS (x) (n=6 for all).

CONCLUSIONS

The current study showed that that manufacturing process affects the ET erosion rates. The tablet radiolabelling process and quantification of erosion rates by scintigraphic methods were also validated.

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