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# Surface Dissolution Imaging: Quantification of the Drug Release and Swelling of Carbamazepine-Polymer Tablets

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## PURPOSE

The Pion SDi2 (Surface Dissolution imaging) instrument combines high resolution UV/vis imaging with a USP IV type flow through cell to study drug product performance. The scope of the project was to characterise and compare the extent of swelling of four polymer tablets containing no active pharmaceutical ingredient (API) and eight corresponding polymer tablets containing carbamazepine (CBZ), and obtain and compare the drug release profiles of the eight CBZ-polymer tablets, under gastric and intestinal conditions.

## METHOD

Four polymer tablets (HPC-HFP, HPC-MFP, methocel K4M and methocel K100M) and eight corresponding carbamazepine (CBZ) containing tablets (tablets containing high quantities of CBZ (64%); high HFP, high MFP, high K4M, high K100M, as well as tablets containing low quantities of CBZ (10%); low HFP, low MFP, low K4M and low K100M), (Nisso Chemical Europe GmbH, Düsseldorf, Germany) were studied using the Pion SDi2. The USP IV type flow-through dissolution cell was used in an open loop configuration to accommodate the tablets during dissolution. The dissolution media was introduced to the flow cell at a rate of 5 mL $min^{-1}$ for a total of six hours; the system maintained gastric conditions (0.1 M HCl, pH 1.2) for the initial two hours followed by intestinal pH conditions (0.05 M monobasic potassium phosphate, pH 6.5) for the remaining four hours.

Absorbance of UV light by dissolved drug was measured by illuminating the flow cell with a 300 nm LED, while swelling phenomena were monitored using a 520 nm LED (Fig. 1). The 4.2 Mpixel detector chip recorded absorbance per pixel per frame, at a rate of 1 frame per second per wavelength, to build up a two dimensional video at each wavelength.

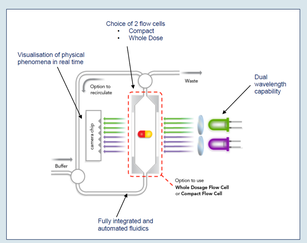



**Figure 1.** Pion SDi2 schematic.

Images were converted from greyscale to false colour and videos were extracted (Fig. 2). In each experiment involving CBZ-polymer tablets, a measurement zone was placed in a region above the tablet and the concentration of dissolved drug passing through this zone was measured in real-time in order to calculate the drug release with the use of a previously determined extinction coefficient, 7213 $M^{-1}$ $cm^{-1}$.

In addition, a cross measurement zone was placed across the center of the tablet to measure tablet swelling over time; the tablet edge threshold was considered to be absorbance greater than 1000 mAU. The tablet width and height were monitored in real time at 520 nm, for all twelve sample tablets.

## RESULTS

**Drug Release**

All eight CBZ containing tablets showed a transient burst of drug release upon transition from gastric conditions to intestinal conditions (Fig. 3-4). Total API release from the polymer was incomplete for all tablets at the end of the six hour experimental duration.

All of the "high" CBZ polymer tablets exhibited a higher drug release profile, when compared to their "low" CBZ polymer counterparts. The highest drug release profile was produced by the high MFP tablet, followed by high K4M, high K100M, and then high HFP. Low MFP, HFP, K4M and K100M all displayed relatively similar average concentrations over the duration of the experiments.

High MFP exhibited the highest $C_{max}$ of all of the tablets, reaching a peak concentration of 0.0156 mg/mL at 108 minutes, whereas low K100M exhibited the lowest average concentrations, with a $C_{max}$ of 0.0035 mg/mL at 120 minutes.

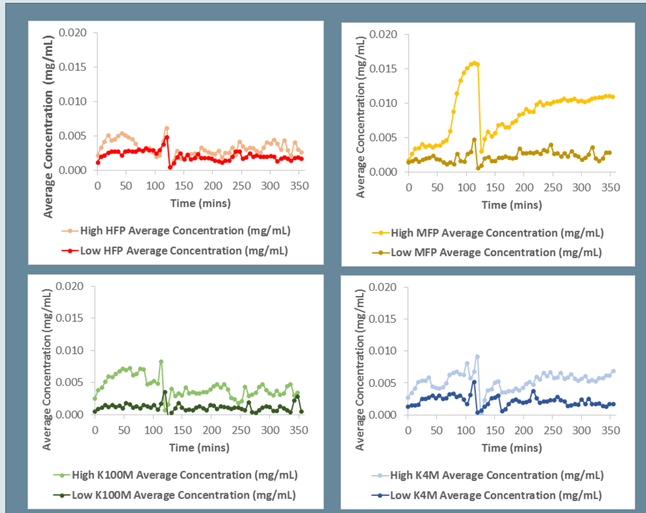
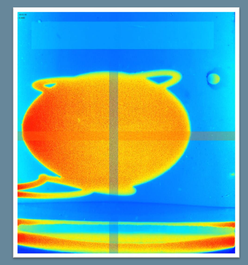



**Figure 3**. (left) Average concentration comparative drug releases profiles of carbamazepine-containing HFP-, MFP-, K4M- and K100M-based tablets.

**Figure 4.** (below) Video of high K4M tablet drug release and swelling, at 300nm.



| Sample | Δ Height (mm) | Δ Width (mm) |
|---|---|---|
| High HFP | 1.67 | 1.39 |
| High MFP | 0.45 | 0.25 |
| High K4M | 2.96 | 3.08 |
| High K100M | 2.50 | 2.82 |
| Low HFP | 1.68 | 1.28 |
| Low MFP | 1.76 | 0.73 |
| Low K4M | 2.37 | 3.03 |
| Low K100M | 2.90 | 2.90 |
| HFP | 2.78 | 3.13 |
| MFP | 2.14 | 2.17 |
| K4M | 2.85 | 2.45 |
| K100M | 3.42 | 4.05 |

**Table 1.** Change in dimensions of all 12 tablets over experimental duration.

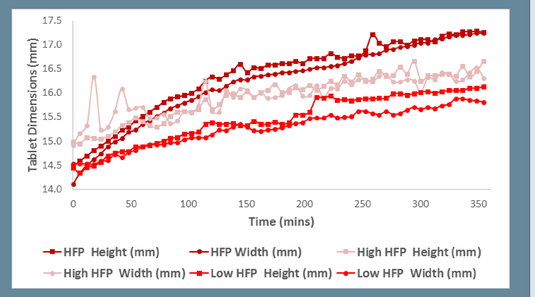
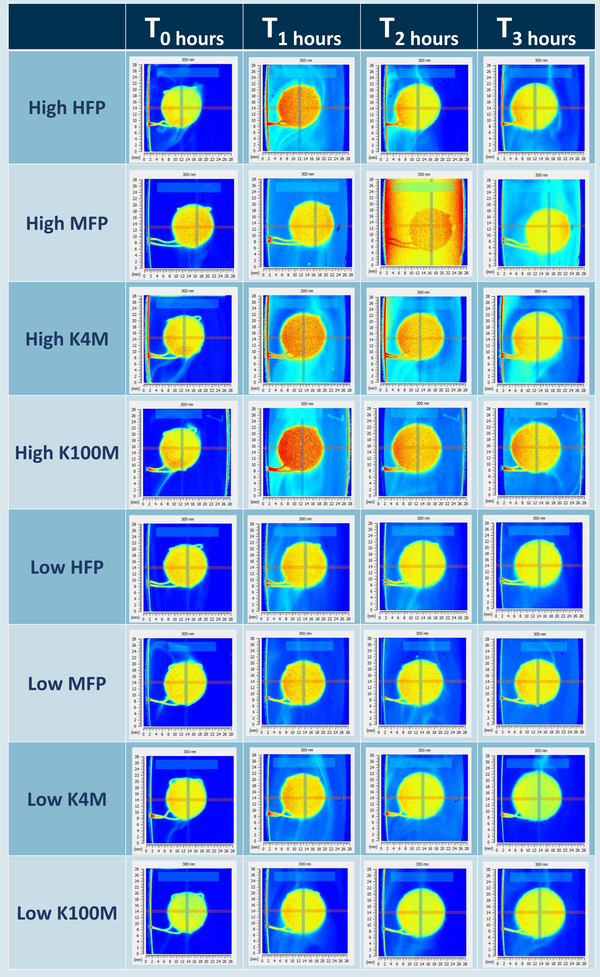



**Figure 5.** Comparative swelling profiles of HFP- based tablets.

**Figure 2.** (Right)Images taken at 300 nm, at 0, 1, 2 and 3 hours, to obtain the drug release profiles of eight CBZ-polymer tablets exposed to gastric conditions for 1 hour and intestinal conditions for the subsequent 5 hours.




**Swelling**

The K4M- and K100M-based tablets showed the largest increase in size due to swelling, in comparison to the MFP- and HFP-based tablets (Table 1).

HFP, K4M and K100M samples all exhibited the same trend with regards to swelling; the API free polymer swelled the most significantly, followed by the high CBZ polymer, and the low CBZ polymer tablet swelled the least (Fig. 5). MFP showed a slightly different trend; the API free tablet had the most significant swelling, followed by the low API containing tablet, and the high API containing tablet showed the least swelling.

## CONCLUSION

The drug release and swelling profiles of four API-free polymer tablets and eight corresponding CBZ containing tablets were analysed using the Pion SDi2.The highest drug release was exhibited by the high CBZ (64%) polymer tablets, and conversely the low CBZ (10%) polymers tablets showed the lowest extent of drug release.
Analysis of the tablets at a visible wavelength visually illustrated that methocel polymer based tablets (K4M and K100M) swelled more significantly than HPC polymer based tablets (MFP and HFP). The CZB containing tablets exhibited different swelling behaviour compared to the CBZ-free tablets. Therefore the presence of API and the API drug load influences the behaviour of the polymer and should be considered in addition to polymer behaviour alone .

## ACKNOWLEDGEMENTS

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## REFERENCES

1. J. Østergaard, F. Ye, J. Rantanen, A. Yaghmur, S. W. Larsen, C. Larsen and H. Jensen, *J. Pharm. Sci.*, 2011, **100**, 3405-3410

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