Online UV Imaging of API-excipient mixtures during dissolution

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Introduction

The Sirius SDI has been shown to provide real-time information of the dissolution process at the surface of drug compacts (1, 2). Here, the release mechanism of Carvedilol (CAR), a BCS class II drug, with either HPMC or Eudragit EPO was investigated.

Materials and Methods

Compacts of Carvedilol (CAR), HPMC (Benecel E3, Ashland) and Eudragit EPO (EPO) (Evonik) and mixtures thereof were and exposed to simulated gastric fluid (SGF, pH 1.2) in a flow cell suitable for UV imaging. Dissolution assays for CAR only compacts were also performed using SGF buffer containing 1% and 5% of HPMC or EPO, respectively.

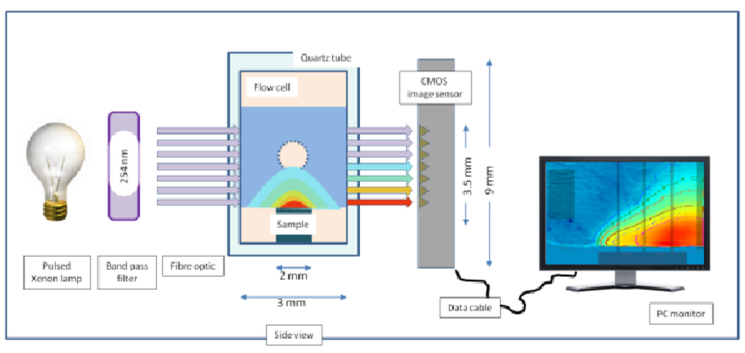

Figure 1. Schematic side view of the SDI system.

Results

To assess dissolution of polymer only compacts only, analysis was performed using a visible wavelength range. HPMC showed swelling behaviour, whereas EPO did not (Figure 3).

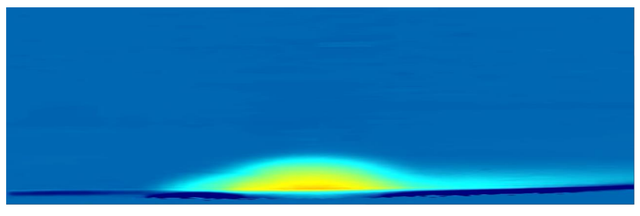

Figure 3b: HPMC at 550nm.

Figure 3a: Eudragit EPO at 550nm.

Physical mixtures of CAR with HPMC showed a steady release of the drug, whereas mixtures with EPO showed drug release in small ‘bursts’ (Figure 4). The presence of polymer increased the amount of drug released.

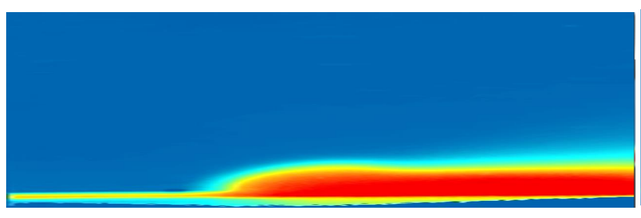

Figure 4a: Physical mixture CAR-HPMC at 280nm.

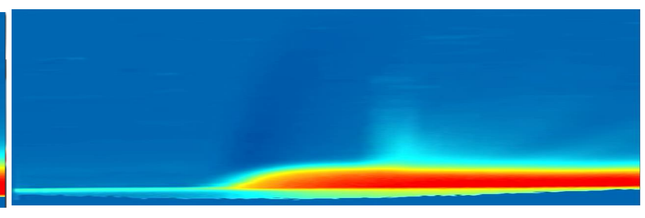

Figure 4b: Physical mixture CAR-EPO at 280nm.

Physical mixtures at 280nm

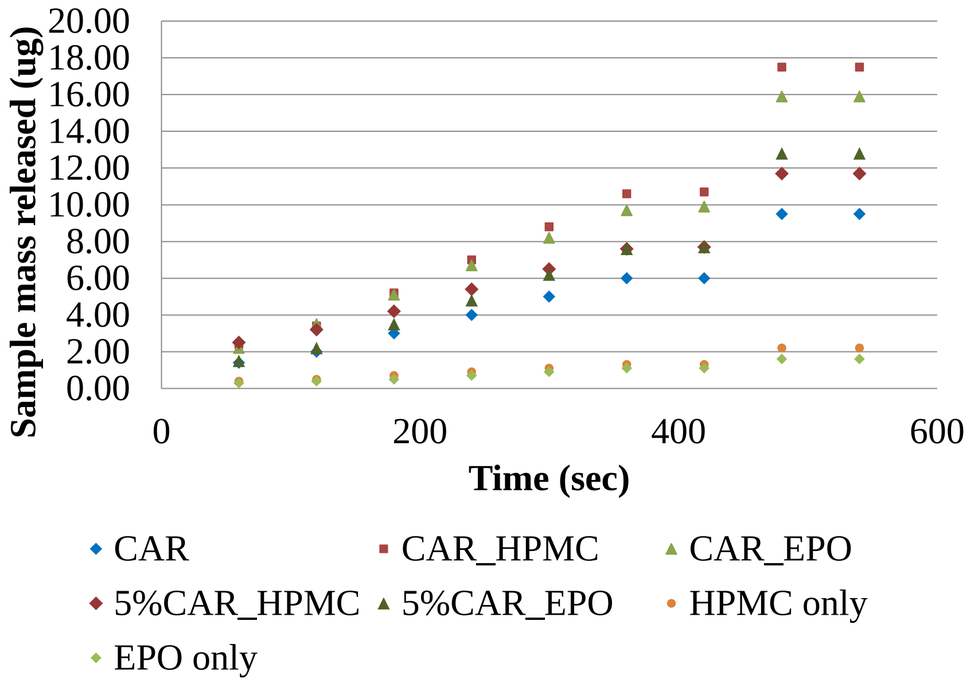

Figure 5: Physical mixture sample mass released at 280nm.

Buffer modifications

Buffer containing 1% EPO, improved the diffusion behaviour of CAR over media only and other buffers containing excipients. However, an increase to 5% EPO resulted in a diffusion inhibiting effect. This may be due to the higher viscosity of the dissolution medium.

Buffer modifications - 280nm

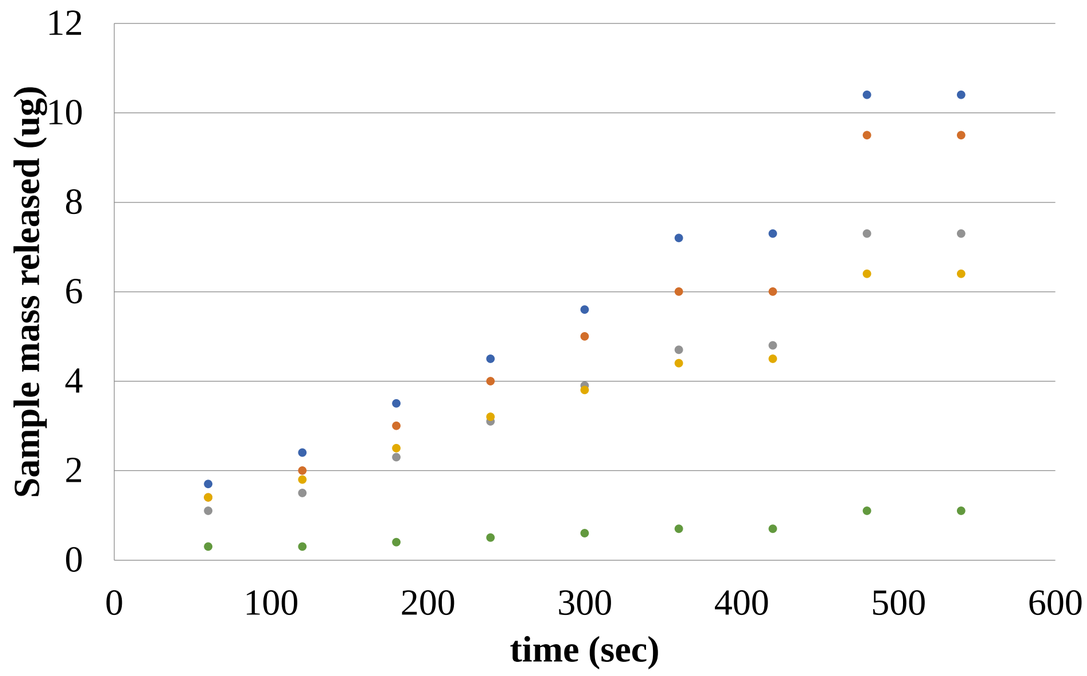

Figure 6: Buffer modifications, sample mass released at 280nm.

Discussion and Conclusion

UV imaging was used to characterise dissolution behaviour of CAR in the presence of excipients, showing ‘bursts’ of CAR released from physical mixtures with Eudragit EPO during the dissolution assay, whereas HPMC showed a steady swelling/erosion release behaviour.
In experiments with excipient modified SGF buffers, only 1% EPO showed an increase in drug dissolution. The altered viscosities/densities of modified buffers, may decrease the concentration gradient in the buffer system and therefore reducing dissolution rates. It may also indicate that the interaction between the polymer and drug requires a non-hydrated polymer, or a higher polymer concentration at the drug surface in concurrence with a low viscosity buffer to drive dissolution via a concentration gradient.

Future Work

Further characterisation of compact surface are required to determine the impact of polymers on release behaviour of CAR. Rheological assessment of modified dissolution buffers. Analysis of processed formulations including Raman monitoring of potential phase transitions during the dissolution assay.

Acknowledgements:
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References:

1. Ostergaard, J., Wu, J., Naelapää, K. Boetker, J. P, Jensen H., Rantanen, J. 2014; Journ Pharm Sci., 103, 1149-1156.
2. Matthews D., Stockton B., Butcher G., Mole J., Sirius Analytical Application Note; Faster dissolution methods for the early-stage screening of pharmaceutical salts.