POSTER 72

Multi-modal Dissolution Testing System for Pharmaceutical Tablets

H. Jesney[1,2], I. Khadra[2], J. Mann[3], R. Barker[3] and D. Markl[1,2]

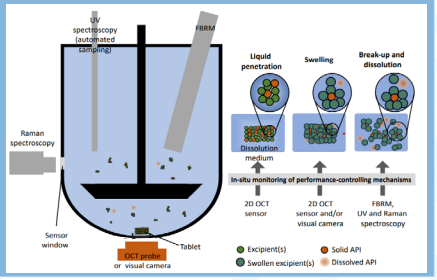
1 Centre for Continuous Manufacturing & Advanced Crystallisation, University of Strathclyde, Glasgow, UK.
2 Strathclyde Institute of Pharmacy & Biomedical Sciences, University of Strathclyde, Glasgow, UK.
3 Oral Product Development, Pharmaceutical Technology & Development, Operations, AstraZeneca, Macclesfield, UK.

Introduction and Aims

The fundamental processes that underpin **disintegration and dissolution** are highly complex and poorly understood [1]. As disintegration and dissolution play key roles in **drug release**, it is essential to gain a **better understanding** of:

- these processes
- the **synergistic mechanisms** that contribute to them
- how they relate to each other
- the factors that influence them

This project aims to develop a novel multimodal sensor system that is capable of resolving the key processes, as well as how these processes are linked to microstructure, formulation and raw material attributes.



Methods

Optical coherence tomography (OCT) has been integrated with a bathless direct heating vessel and stirrer to create a system that mimics a standard USPII dissolution system. Off-line UV-Vis is used to analyse dissolution samples.

What is Optical Coherence Tomography?

- High resolution imaging technique that captures 2D and 3D cross-sectional images at high speed (up to 200 2D images per second)
- Image contrast results from variations in the refractive index at the interface of different materials

Interesting fact!
The particle (A2) in Figure 1 is actually an image artefact but presents an interesting opportunity to measure the size of disintegrating particles.

What is being measured and why?

Liquid penetration and tablet swelling to establish the relationship between drug release and these mechanisms for any formulation undergoing testing.

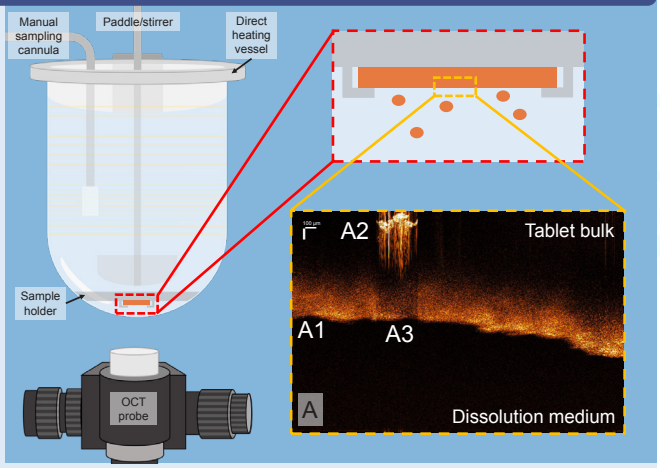


Figure 1 – A simplified diagram of the experimental set-up and areas of interest. **A** is an OCT B-scan of a tablet undergoing dissolution testing in the novel set-up. A**1** is interface between the tablet surface and the dissolution medium. **A2** is a disintegrating particle falling to the bottom of the vessel. **A3** is a section of the tablet that **A2** is blocking the light to, leading to an incomplete image of the surface.

Results and Discussion

Why is a Sample Holder Needed?

- Stop sample movement under stirring conditions
- Accurate and consistent sample placement
- Hold the tablet off the bottom of the vessel

Figure 2 – A 3D rendering of the sample holder that is held in place at the bottom of the vessel by magnets (see Figure 1).

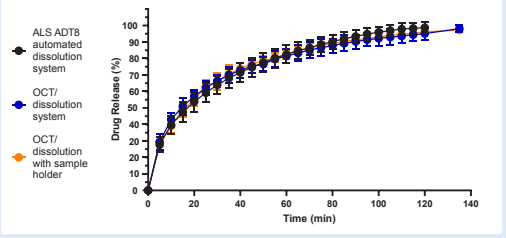


Figure 3 – System validation data. Percent drug release for 200 mg (20 % w/w paracetamol) tablets in pH 5.8 phosphate buffered saline, in three experimental set-ups. $N = 3$. Error bars represent standard deviation.

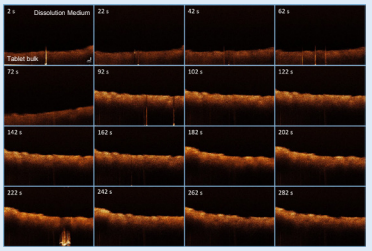


Figure 4 - Time series OCT images of 200 mg tablet (20 % Paracetamol, 79 % MCC and 1 % MgSt). OCT/Dissolution system with tablet in holder. pH 5.8 phosphate buffer. Scale bar in first image (2 s) true for all images

Conclusion

Optical coherence tomography has been successfully integrated with a bathless direct heating vessel as the first step in the development of a unique analytical system. Integration of additional analytical probes will enable greater information to be gained and will aid in the overall goal of furthering the understanding disintegration and dissolution.

Future Work

1. Integration of other analytical probes including FBRM, pH monitoring, UV-Vis auto-sampling and in-situ Raman spectroscopy.
2. Analysis of a variety of formulations, with a focus on those that have issues relating to disintegration and dissolution.

Acknowledgements
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References
[1] Markl, D., & Zeitler, J. A. (2017). A Review of Disintegration Mechanisms and Measurement Techniques. Pharmaceutical research, 34(5), 890–917. https://doi.org/10.1007/s11095-017-2129-z