Development of flow through cell method for in-situ visualization of dissolution processes in solid dosage forms

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Introduction:

X-ray µCT is an increasingly popular tool to determine the density distribution and morphology of granules in the pharmaceutical dosage forms.

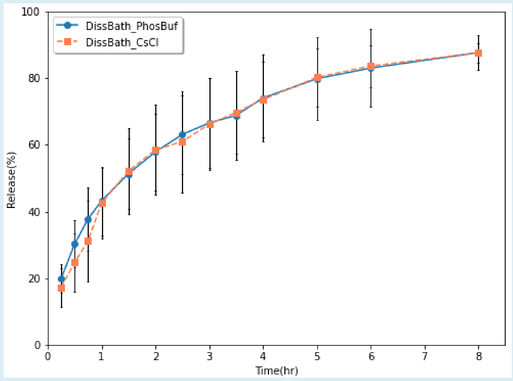
The focus of this project is to monitor the dissolution process of a 3D printed tablet by conducting in-situ experiments using dynamic X-ray µCT (4D-µCT). In-situ monitoring of the dissolution process in combination with the visualization of the internal structure at microscale will help to get a better understanding of drug release mechanisms from different processing techniques.

Objectives:

- Develop a flow-through cell method to mimic the in vivo dissolution process.
- Identify a suitable contrasting agent that doesn't affect the drug release process.
- Investigate the correlation between drug release calculated from in-vitro dissolution test and the results from 4D-µCT.

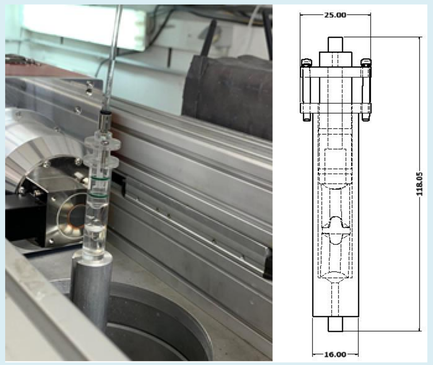
CsCl as a contrast agent:

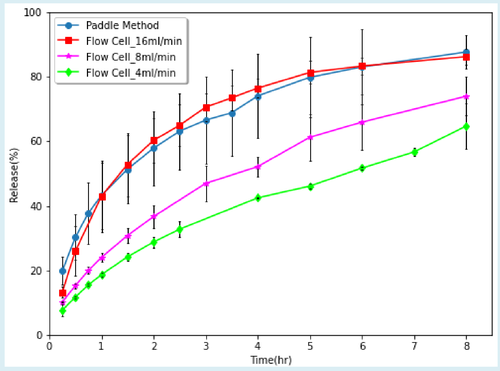
To investigate the impact of CsCl brine on the dissolution rate of API from the tablets, in-vitro dissolution test (paddle method) was performed: one using CsCl as dissolution medium and the other in a phosphate buffer.



Design and validation of flow cell:

a) A custom flow-through cell was designed and developed. This system was used at the EMCT rotating gantry µCT scanner of UGCT [1] to obtain these results.

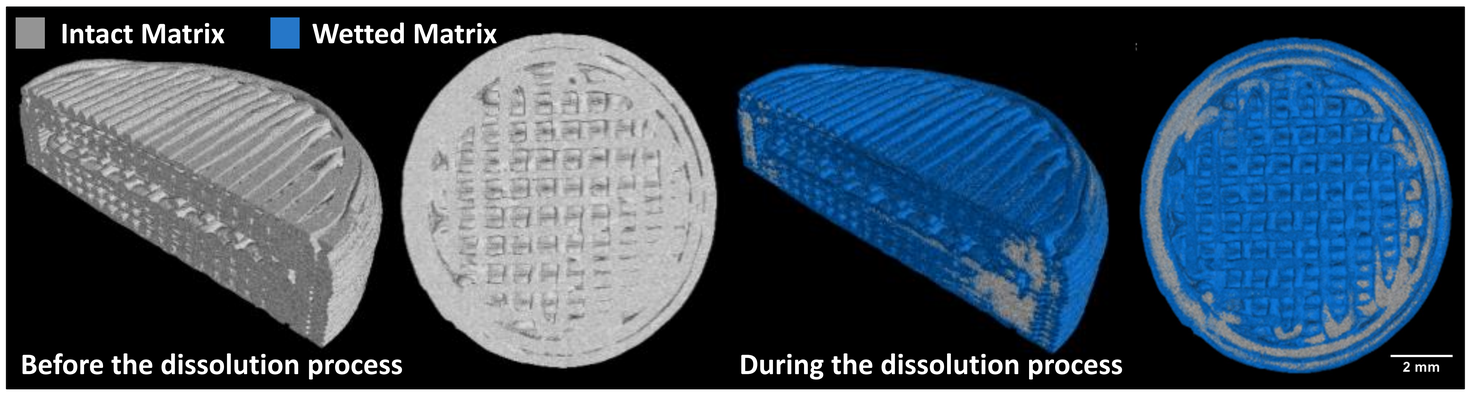




b) Different flow rates were used, and the flow rate of 16 ml/min shows an analogous release profile to the in-vitro dissolution test.

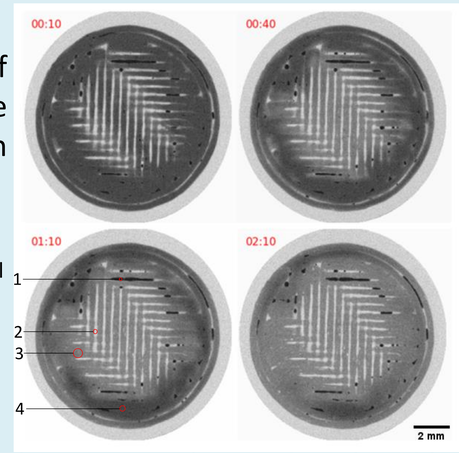
µCT results:

X-ray µCT scans were acquired at the dry state and different time steps of the dissolution, with a temporal resolution of 2 minutes for a full rotation, and a spatial resolution of 9.95 µm.

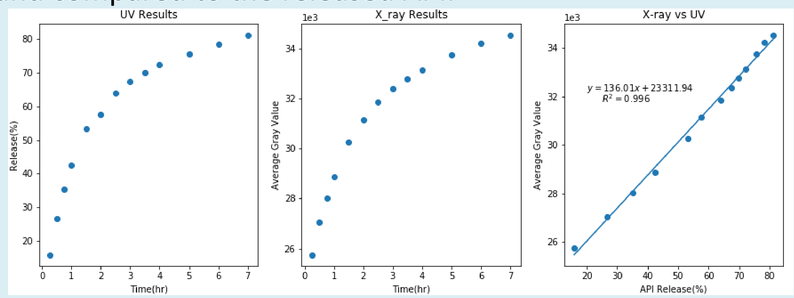


Cross sectional view of sample at different time steps of dissolution process.

Black (1): Pores filled with air
Light gray (2): Pores filled with CsCl brine
Gray (3): Wetted Matrix
Dark gray (4): Intact matrix



Every time step, 5 ml of solution was taken and analyzed by UV spectrometer to measure released API. Based on X-ray images, average gray value of tablet materials (segmented in the dry sample) was determined for different time steps and compared to the released API.



Conclusion:

The results illustrate the feasibility of the developed method. The advantage of the proposed method is that it doesn't need further sample preparation which may affect the internal structure.

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References:

[1] Dierick, Manuel, et al. "Recent micro-CT scanner developments at UGCT." Nucl Instrum Methods Phys Res Sect B Beam Interact Mater At. 2014 Apr 1;324:35–40

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