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

Thursday, 3 June 2021 14:40 (1 hour)

In the pharmaceutical industry, different methods have been developed to analyze the internal structure of solid dosage forms such as mercury porosimetry, and gas adsorption (1,2). These methods are destructive and unable to study the dynamic property of a sample during dissolution. Hence there is a growing demand for developing non-destructive techniques to visualize and characterize the internal structure of dosage form during the dissolution process. X-ray tomography is one such technique that has been used to monitor structural change during the dissolution process, mostly by halting the process and drying the sample before the imaging (3). However, these processing steps could change the internal structure.

In this work, dynamic X-ray  $\mu$ CT imaging was used to monitor and analyze the dissolution of a 3D printed tablet. A flow-through cell was developed to mimic the in-vivo dissolution process, and enables us to visualize the internal structure of pharmaceutical tablets during the process. To increase the attenuation contrast between water and the tablet, CsCl was used as the contrast agent. Finally, we investigated the correlation between drug release calculated from in-vitro dissolution and the results from 4D- $\mu$ CT.

Conventional dissolution tests were performed to investigate the impact of CsCl brine on the dissolution rate of active pharmaceutical ingredient (API) from the tablets: one using CsCl brine (PH=6.6) as dissolution medium and the other in a phosphate buffer (PH=6.8). The dissolution profiles of tablets in different mediums were compared. The result shows that the effect of CsCl brine on the dissolution profile is negligible.

The Environmental Micro-CT (EMCT) scanner of the Ghent University Centre for X-ray Tomography was used for imaging (4). The tablets were scanned with a temporal resolution of 2 minutes for a full rotation, and a spatial resolution of 20  $\mu$ m. X-ray  $\mu$ CT scans were acquired at dry state, at the time that medium filled the flow cell, and several time steps ranging from 0.25 to 7 hours of the dissolution. Immediately after each scan, 5 ml of solution was taken and analyzed by UV spectrophotometer at 222 nm ( $\lambda_{max}$  MPT in CsCl brine) to measure the concentration of released API. All scans were reconstructed using filtered backprojection as implemented in Octopus Reconstruction. Octopus Analysis was used for the 3D analysis of the reconstructed scans. From segmenting the wetted region, the volume of penetrated water was determined.

The API release shows a linear relation to water penetration to the tablet (which is reflected by an increase in local X-ray attenuation coefficient due to the penetration of the brine into the dosage form), suggesting that the slope of this line can be used to convert the image data to the amount of API released from the tablet. This study demonstrates the potential of X-ray  $\mu$ CT to examine the internal structures of pharmaceutical tablets during the dissolution process. The advantage of the proposed method is that the dynamic property of dosage form during the dissolution process can be assessed without further sample preparation.

### Time Block Preference

Time Block B (14:00-17:00 CET)

### References

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3. Li H, Yin X, Ji J, Sun L, Shao Q, York P, et al. Microstructural investigation to the controlled release kinetics of monolith osmotic pump tablets via synchrotron radiation X-ray microtomography. *Int J Pharm.* 2012 May 10;427(2):270-5.
4. Dierick M, Van Loo D, Masschaele B, Van den Bulcke J, Van Acker J, Cnudde V, 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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