Linking digital manufacturing to a digital tablet: Simulating tablet disintegration using discrete element and pore-scale modelling

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Introduction: Industry challenges

Most tablets are designed to break up into smaller fragments when they come in contact with a physiological fluid in order to accelerate the dissolution of the drug. This break up is typically caused by the swelling of individual particles in a tablet that leads to the interruption of the interparticulate bonds. These steps are referred to as the tablet disintegration processes, which are critical steps to dissolve and enable the absorption of the drug substance The disintegration process of a tablet can thus only be understood and optimised by considering the interconnection of every step involved in the disintegration and dissolution processes. This can be realised by developing models of the disintegration process by consider each mechanism, thereby realise the digital design of future oral medicines.

Materials & Methods

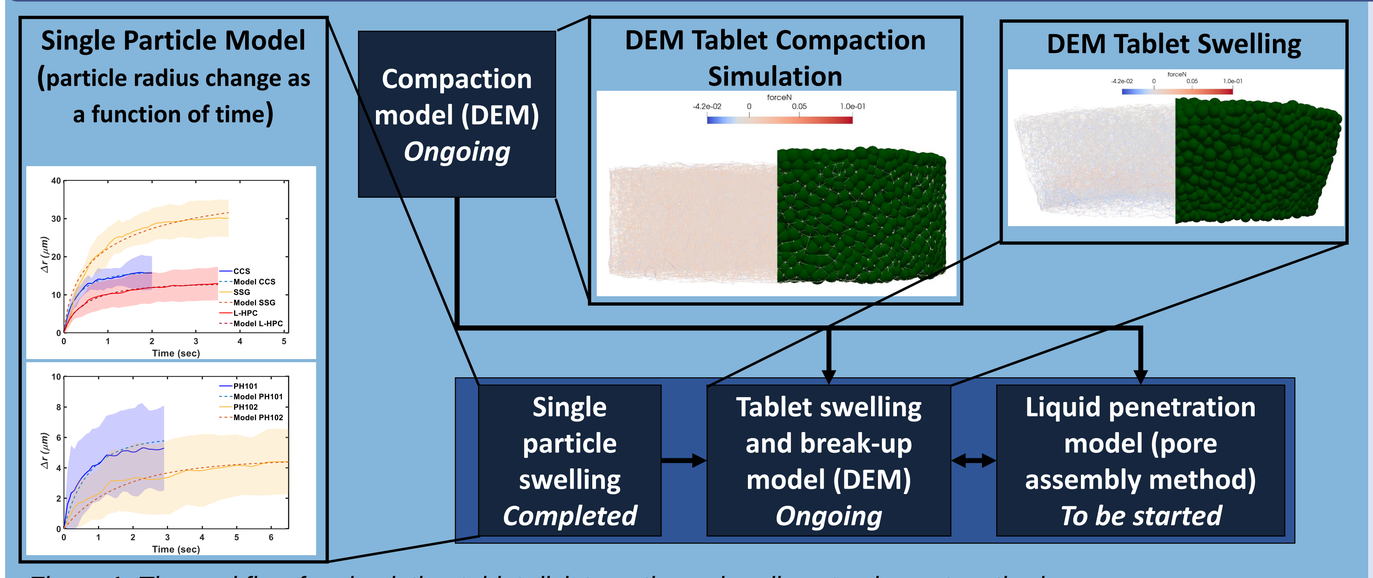


Figure 1: The workflow for simulating tablet disintegration using discrete element method.

- The swelling of many individual particles was measured for various pharmaceutical materials to calibrate a single particle swelling model [1] and quantify swelling characteristics such as the diffusion coefficient and maximum absorption ratio [2].
- The compaction of three microcrystalline (MCC) PH101 tablets with three different porosities (ε_0) (10, 15 and 22%) and MCC PH101 croscarmellose sodium (CCS) at three different CCS concentrations (c_{CCS}) (2, 5 and 8%) was modelled using discrete element modelling (DEM). DEM was calibrated through an optimisation procedures on the 15% porosity tablets against measured compression profiles.
- The swelling of the tablets were modelled by combing the single particles model and experimental liquid penetration data obtained from a THz imaging setup [3].

Results and Discussion

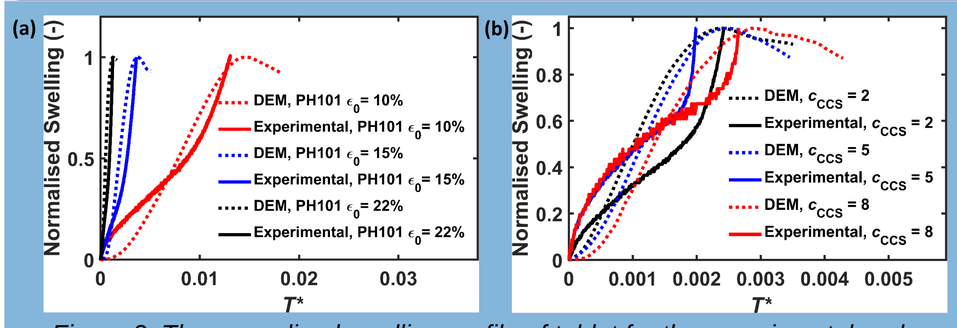


Figure 2: The normalised swelling profile of tablet for the experimental and modelling results (a) PH101 tablets (b) PH101 CCS tablets.

Figure 3: The pore size ratio (PS/PS_0) as a function of tablet height focusing on pores < 30 μm during swelling at 1 s and 3 s. The black vertical line in each plot indicated the liquid penetration position at that particular time point. PS is the pore size at time t and PS_0 is the pore size at t =0 s.

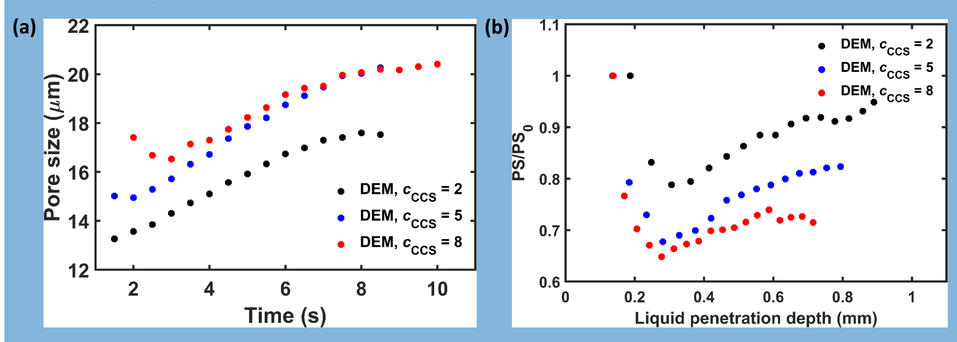
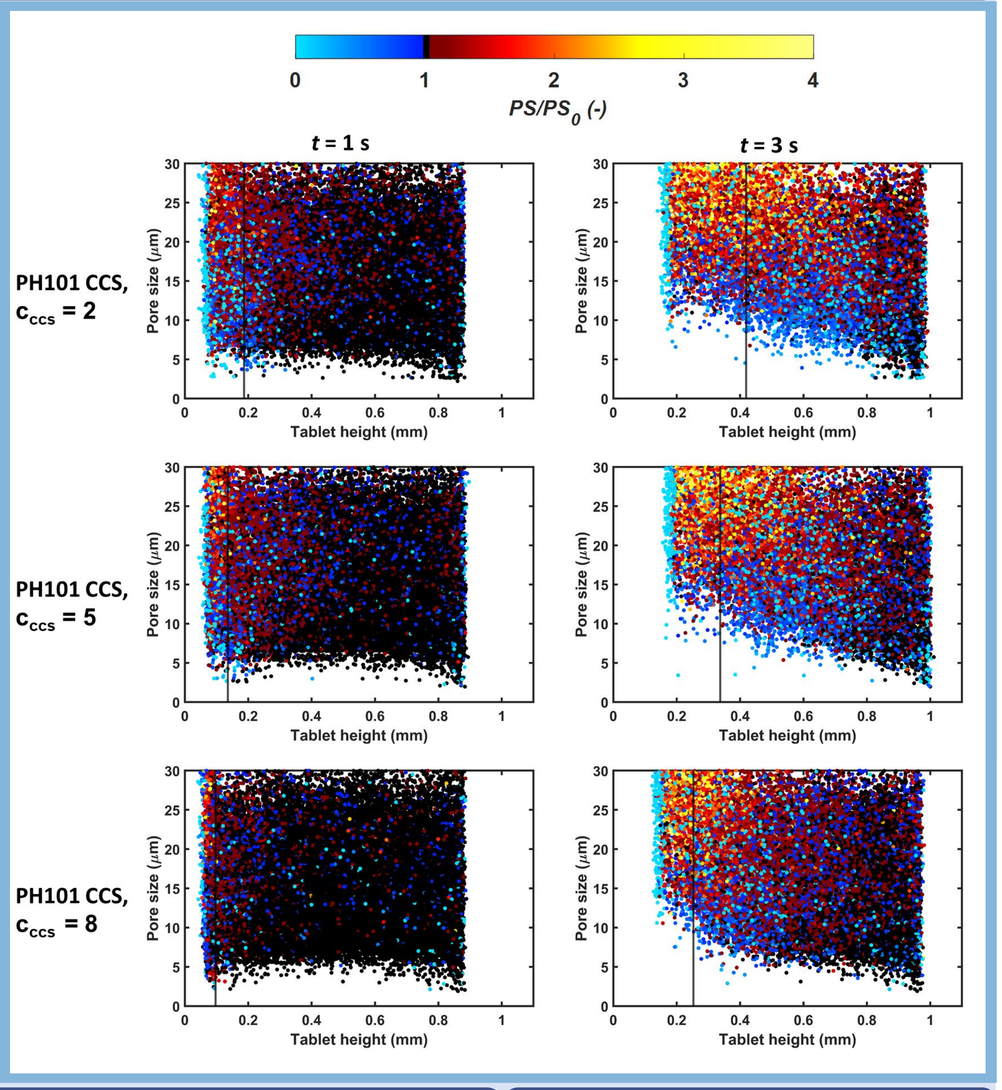


Figure 4: Pore size analysis of the wetted volume for PH101/CCS tablets. (a) The average pore size of the tablets at different time points during swelling. (b) The pore size ratio (PS/PS_0) of the pores placed up to 0.2 mm behind the liquid front as a function of the liquid penetration depth.



- The model captures the difference in swelling behaviour of various tablets well.
- The model reflects the difference in swelling time between the tablets with lower CCS content, c_{CCS} = 2 and 5%, and the tablet with highest CCS content, c_{CCS} = 8%, as both experimental and model shows a slow down of tablet swelling with highest c_{CCS}.
- **Key Observation & New Knowledge**: The pores in a tablet close in both the wetted and dry volume. This pore closure hinders the liquid from accessing other particles and slows down the overall swelling, in particular for tablets with high swelling ability.

Outcomes and Impact

- A discrete element model (DEM) was coupled to the single particle model to describe the swelling of a tablet.
- Reduced drug product development times by utilising a digital design approach and reduced material waste (sustainable manufacturing) by replacing physical experiments with digital experiments using the models from this activity.
- Optimised dissolution behaviour of tablets by having a scientific sound understanding of the link between the swelling of a single particle and the swelling of a tablet.

References

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2. Soundaranathan, M et al, 2020, Int. J. Pharm., 590, 119903.
3. Al-Sharabi, M et al, 2021, Chem. Eng. Res. Des., 165, 386-397.

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