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Modelling the swelling of pharmaceutical tablets from single particle understanding using DEM

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Introduction and Aims

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 caused by the swelling of individual particles in a tablet that leads to the interruption of the interparticulate bonds. This study focused on modelling the swelling of a tablet using discrete element modelling (DEM) paired with a single particle swelling model [1,2] and experimental liquid penetration depth data measured by a flow through cell [3] coupled with a commercial terahertz (THz) system (TeraPulse 4000, Teraview Ltd., UK).

Materials & Methods

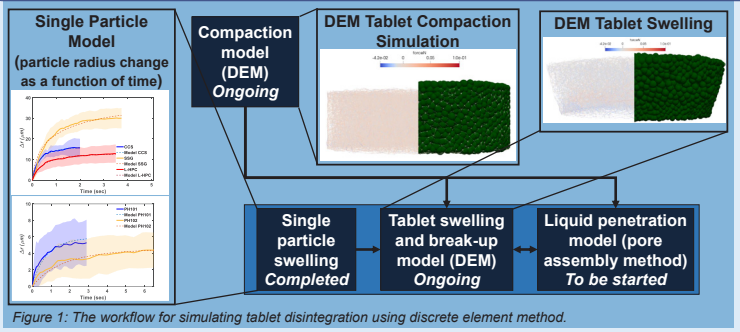


Figure 1: The workflow for simulating tablet disintegration using discrete element method.

- 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 (D) and maximum absorption ratio (Q^{max}) for different materials.
- The compaction of three MCC PH101 tablets with three different porosities (10, 15 and 20%) was modelled using DEM. DEM was calibrated through an optimisation procedures on the 15% porosity tablets against measured compression profiles.
- The swelling of the PH101 tablets were modelled by combing the single particles model and experimental liquid penetration data obtained from THz imaging setup [3].

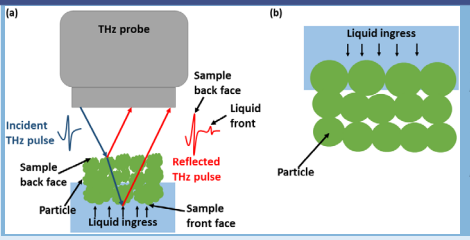


Figure 2: A schematic showing the liquid penetration into a compacted tablet a) Investigating using THz probe. b) In Discrete element method.

Difference between DEM and experimental tablet and normalisation:

- In our DEM, phenomena such as deformation, mechanical interlocking and fragmentation were not considered.
- DEM used spherical particles as the single particle swelling model assumes a sphere.
- The swelling profiles were normalised to account for the difference between DEM and the experimental data.
- The thickness (H_0) of the DEM tablet was reduced to 1 mm from 2 mm to reduce the computation time. To account for the size change, the time was normalised: $T^* = \frac{t \cdot D}{H_0^2}$.

Results and Discussion

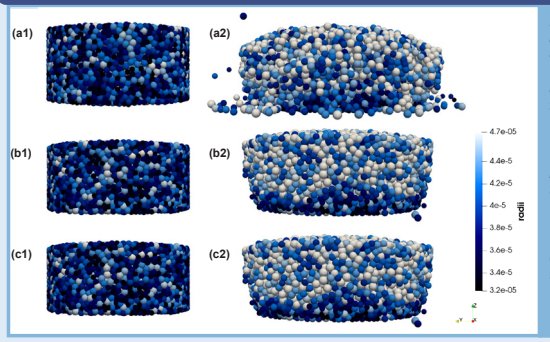


Figure 3: Images of tablet at different time points during swelling

a) PH101 20% porosity tablet,
1) t = 0 s
2) t = 4.25 s.

b) PH101 15% porosity tablet,
1) t = 0 s
2) t = 12 s.

c) PH101 10% porosity tablet,
1) t = 0 s
2) t = 25 s.

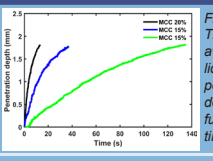


Figure 5: The average liquid penetration depth as a function of time.

Figure 6: Pore size distribution in PH101 tablet during swelling at time points a) 20% porosity tablet and b) 15% porosity tablet.

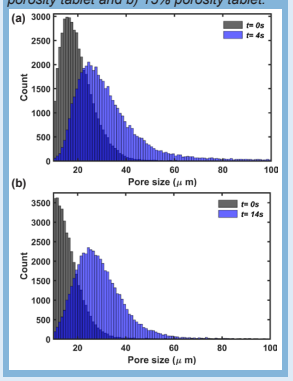
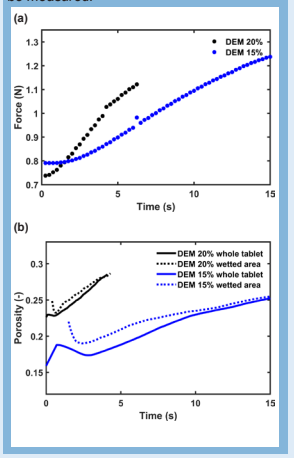


Figure 7: a) Total interparticuler forces for PH101 tablet during swelling. b) Porosity change during swelling of the whole tablet. and porosity change during swelling of only the wetted region of the tablet. The delay in due to the wetted region being to small to be measured.



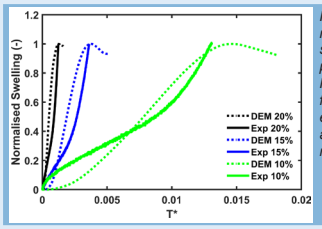


Figure 4: The normalised swelling profile of PH101 tablet for the experimental and modelling results.

- The tablet with 20% porosity swells the fastest both in DEM and experiments, followed by 15% and 10%.
- Experimental and DEM swelling data are in very good agreement.
- The pores inside the tablet opens up when the tablet began to break-up, as seen in Fig 6.

Conclusion

- Both measured and simulated swelling profiles show that tablets reach their maximum capacity at approximately the same time. The model captures the difference in swelling behaviour of various tablets well.
- Porosity decreases for the wetted area, which indicates that the pores are closing.

Future Work

- Simulate the swelling of MCC PH101 and croscarmellose sodium mixture tablets by including the liquid penetration data and single particle model.
- Include a pore unit assembly method for modelling the liquid flow in the tablet.

Acknowledgements
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