

Introduction

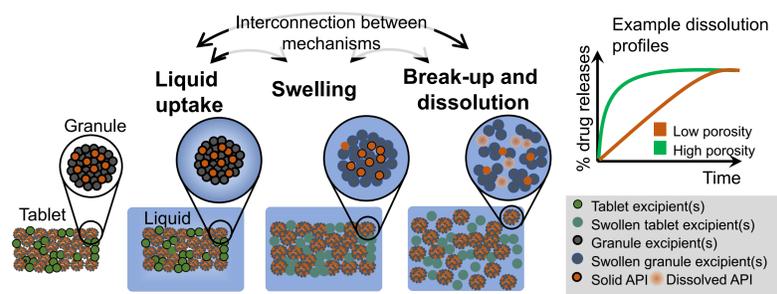


Figure 1: The mechanisms involved in the disintegration and dissolution of granulated tablets, including liquid uptake, swelling, and dissolution.

- How a pharmaceutical granule and tablet disintegrates and dissolves when it comes in contact with a physiological fluid is a crucial for the performance of the medicine.
- These critical performance characteristics are controlled by the chemical and physical properties of the drug substance and excipients as well as the manufacturing processes used to transform the powder into a granule.
- The microstructure created during manufacturing in combination with the wetting and swelling properties of the raw materials are decisive for reliable drug release.
- This study applied a range of measurement techniques to observe performance-controlling mechanisms of particles and granules when they come in contact with liquid.

Single Particle Swelling [1]

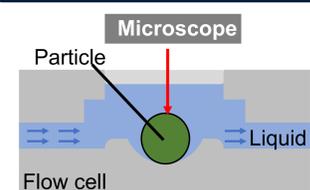


Figure 2: The swelling of individual particles is measured using a custom flow cell for microcrystalline cellulose (MCC) PH101 and PH102, croscarmellose sodium (CCS), sodium starch glycolate (SSG) and low-substituted hydroxypropyl cellulose (L-HPC).

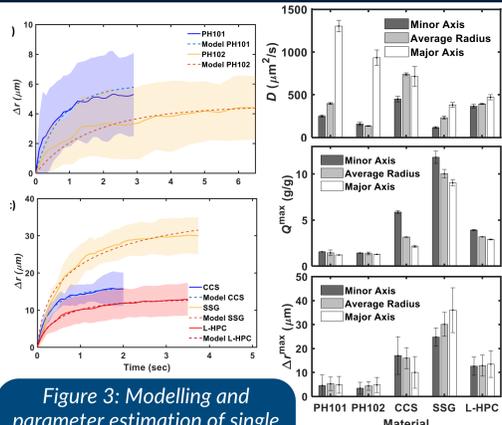


Figure 3: Modelling and parameter estimation of single particle swelling.

Granule Preparation & Analysis

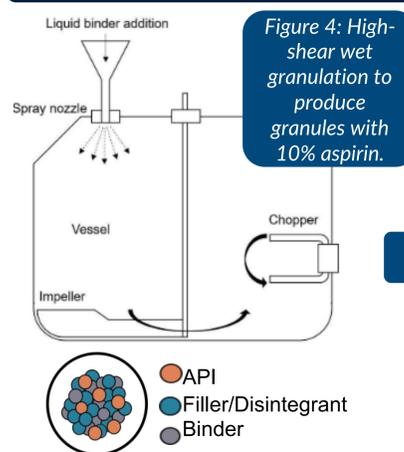
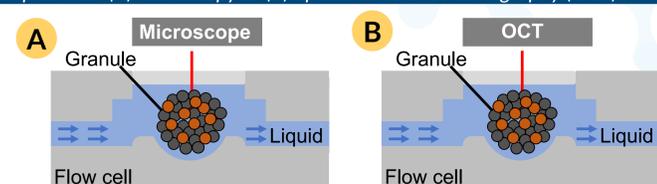


Figure 4: High-shear wet granulation to produce granules with 10% aspirin.

Table 1: Materials used to manufacture granules

Material	Function	Concentration (%)
Aspirin	API	10
MCC	Filler, disintegrant, partial lubricant	80 – 90
SSG	Superdisintegrant	2-7
Water/PEG	Liquid binder	-

Figure 5: Measurement of granule swelling and liquid uptake using the flow cell coupled with (A) microscopy or (B) optical coherence tomography (OCT).

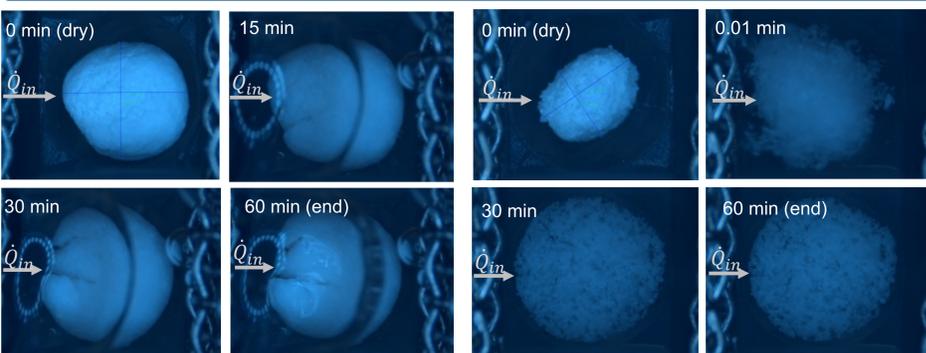


Granule Liquid Uptake & Swelling

Table 2: Assessment of the swelling performance of granules

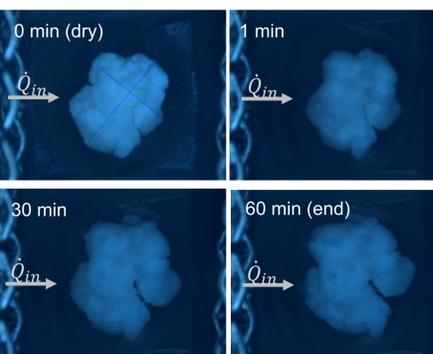
Material	Size, x (mm)	Porosity, ε (%)	L/S	Flow Rate, Q (mL min ⁻¹)
MCC	1.9 – 2.5	-	1	10
MCC/SSG	1.8 – 1.9	-	1	10
Aspirin/MCC	1.9 – 2.5	30 – 62	0.8 – 1.2	10
Aspirin/MCC/SSG	1.9 – 2.5	-	1	10

Figure 6: Swelling of granules with different components.



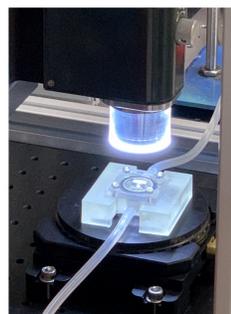
MCC
Surface erosion and slow crack propagation over time. No excessive granule movement, challenges with bubble formation.

MCC/SSG
Sudden expansion and swelling over time with inclusion of superdisintegrant. Slow loosening of microstructure and strain recovery observed.



Aspirin/MCC
Erosion and crack propagation observed with slow swelling.

Aspirin/MCC/SSG
Gradual swelling, with controlled crack propagation and erosion.



Optical Coherence Tomography (OCT) is a non-destructive, contactless, and fast method to resolve sub-surface structures. OCT generates 1D, 2D and 3D depth profiles within seconds. The acquisition rate of 1D profiles can be as high as 230 kHz (230 cross-sectional images per second).

Using a lens with 18 mm focal length, bursts of images were collected upon liquid addition to analyse granule disintegration in 2D.

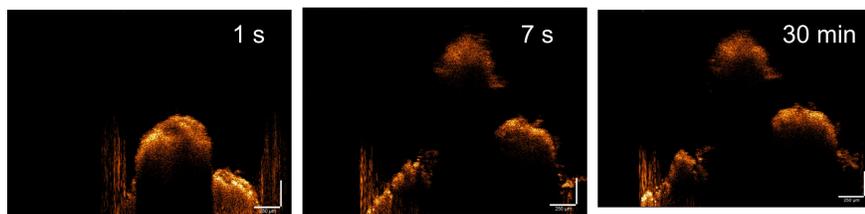
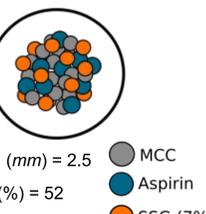
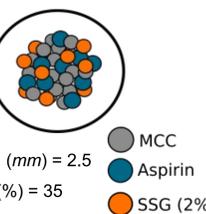
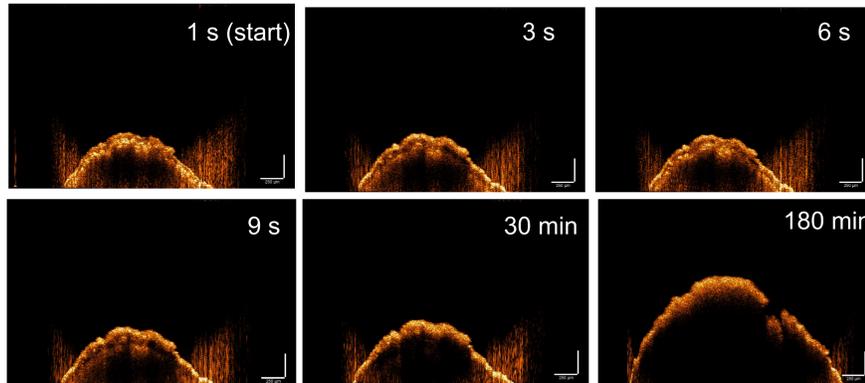
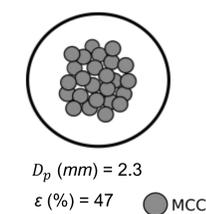
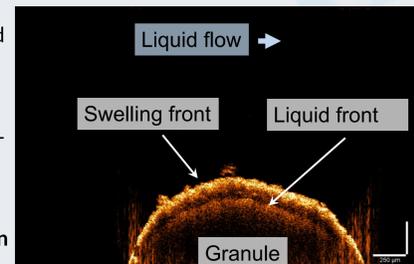
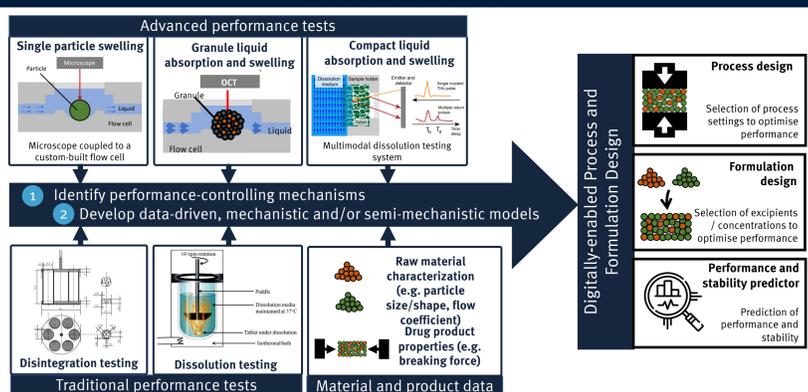


Figure 7: Investigation of granule disintegration using OCT.

Conclusions



References

- Sundaranathan et al. Quantification of swelling characteristics of pharmaceutical particles. *Int J Pharm*, 2020.

Abbreviations

API – active pharmaceutical ingredient;
 CCS – croscarmellose sodium;
 L-HPC – low-substituted hydroxypropyl cellulose;
 MCC – microcrystalline cellulose;
 OCT – Optical coherence tomography;
 SSG – Sodium starch glycolate;

Acknowledgements

This research was supported by International Fine Particle Research Institute (IFPRI). This research utilised an EPSRC (EP/S02168X/1) funded optical coherence tomography system.