POSTER 75

CMAC FUTURE MANUFACTURING RESEARCH HUB

Enhancing virtual tablet formulation design

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Introduction

Despite the fact that the pharmaceutical industry has produced tablets for more than a hundred years, the development of a new formulation and the choice of manufacturing processes and excipients is often based on trial-and-error approach. This trail and error approach poses several challenges during tableting (e.g. low tensile strength, excessive friability, and strain rate sensitivity) See pictures below

A mechanically compromised tablet is unsuitable for use by patients for many reasons including the loss of potency associated with a split or fragmented product. Accurately predicting to what extent a material and their formulation is sensitive to changes in strain rate is vital for developing a robust formulation

Aim

Developing models to predict the strength [**Fig. 2**] and porosity [**Fig. 1**] of directly compressed pharmaceutical powders, including understanding the influence of strain rate and additional surface modifying components such as lubricants.

Objectives

- Detailed characterisation of physical & mechanical properties of representative materials.
- Detailed compaction of these materials including influence of strain rate & extent of lubrication.
- Detailed characterisation of tablets, including strength, structure & disintegration performance.
- Developing and apply models to describe individual component contributions to bulk strength, tablet porosity and disintegration performance.

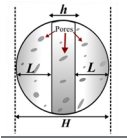


Fig. 1. Tablet porosity

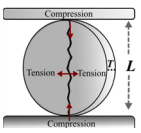
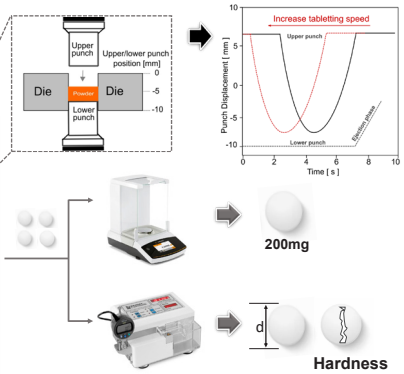


Fig. 2. Tablet Strength

Methods

Mixture components

Excipient	% (w/w)
Microcrystalline cellulose	66 %
lactose	33 %
Magnesium stearate	1%



Results

Compaction profile

- Single-ended compaction mode
- Punch Position control
- Sinusoidal compaction profile
- Various total compression time

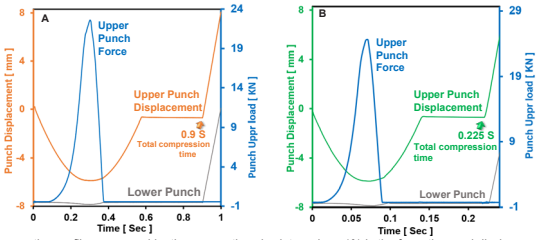


Fig. 3. Compaction profiles measured by the compaction simulator, where (**A**) is the force-time and displacement-time profile for tablets produced at total compression time of 0.9 sec, and (**B**) is the force-time and displacement -time profile for tablets produced at total compression time of 0.225 sec.

Characterisation of the compaction process:

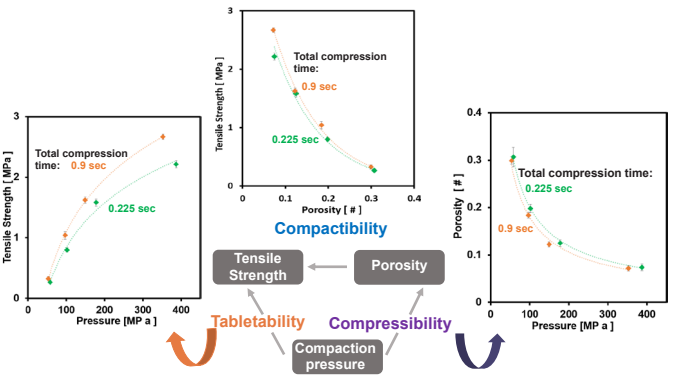


Fig. 4. Effect of total compression time on tablet (**A**) tabletability, (**B**) compactibility and (**C**) compressibility profile.

- A higher compression pressure makes a stronger tablet [**Fig. 4.** A]
- A higher compression speed makes a weaker tablet [**Fig. 4.** A, B]

Conclusion

- The mixture shows sensitivity to changes in strain rate
- Strength shows a reduction in all cases as speed is increased
- Deformation is a more time- dependent process
- The pressures required to achieve given porosities increase as the machine speed is increased

Acknowledgment

- The authors would like to acknowledge the contributions of Gavin Reynolds, Catherine Hallam, Liz Meehan, Pratik Pankaj, Jack Creswick, and the CMAC National Facility Team for their technical support. MO would also like to thank AstraZeneca, Macclesfield, UK for funding.

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