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Dwell time sensitivity of pharmaceutical excipients

Lactose

Knowledge of dwell time sensitivity is very useful especially during scale up of directly compressible tablet formulation. However, very limited quantitative data is available in the literature on this property. The main purpose of this study was to quantify the dwell time sensitivity of commonly used grades of directly compression lactose (DCL) alone and in combination with microcrystalline cellulose (MCC).

Materials

Pharmacel® 102 (MCC), anhydrous lactose (SuperTab® 21AN), spray dried lactose monohydrate (SuperTab® 11SD), granulated lactose monohydrate (SuperTab® 30GR) and agglomerated anhydrous lactose (SuperTab® 24AN) produced by DFE Pharma was used in this work (Fig. 1).

Methods

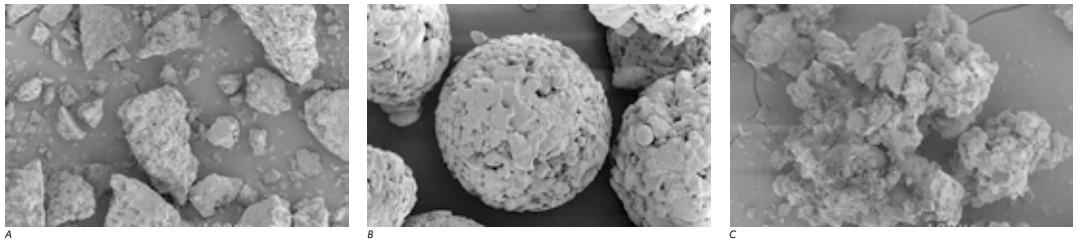
The tableting behavior was studied using a Phoenix hydraulic compaction simulator with dwell times of at 50 mS (slow speed: a typical R &D tablet press) and 5 mS (Fast speed: a typical production press). Excipients studied were Pharmacel® 102, SuperTab® 21AN, SuperTab® 11SD, SuperTab® 30GR and SuperTab® 24AN, tested alone and as blends. Compaction pressure was varied from 30 to 300 MPa. The compaction simulator was programmed with a sinusoidal compression and decompression profile. The dwell time sensitivity index, tensile strength and tabletability were determined. Tabletability was plotted as tablet tensile strength (TS) against compaction pressure, and the linear range of the plot was used to calculate a dwell time sensitivity index as (TS slow-TS fast)/TS slow).

Results and discussion

Pharmacel® 102 exhibited the highest tabletability at both slow and fast tableting speed followed by SuperTab® 24AN, SuperTab® 21AN, SuperTab® 30GR and SuperTab® 11SD. All materials showed low sensitivity to dwell time with the index calculated in the range 0.82 (SuperTab® 11SD) to 0.85 (SuperTab® 30GR and Pharmacel® 102) for all individual excipients and mixtures (Fig. 2) shows a tablettability profile at different compaction pressure for various DC Lactose and Pharmacel® 102. As expected, all tested DC lactoses have higher ejection forces due to the brittle nature of the material causing friction on the die wall. Pharmacel® 102 has low ejection forces.
Lower ejection forces are desired for tablet production because it decreases friction and reduces damage to the tablet on ejection. Adding Pharmacel® 102 at 50% w/w level with the different directly compressible lactose has the effect of significantly reducing ejection force (Fig. 3). A reduction in friction promotes a more even densification on the compact and should result in more consistent tablets.

Conclusion

This study shows that directly compressible lactose grades (four grades) and microcrystalline cellulose (Pharmacel® 102) exhibit little sensitivity to changes in dwell time when changing from times typical for a research press to a those for a production press.



A B C

Fig. 1: Scanning electron micrographs of (A) SuperTab® 21AN (B) SuperTab® 11SD (C) SuperTab® 24AN.

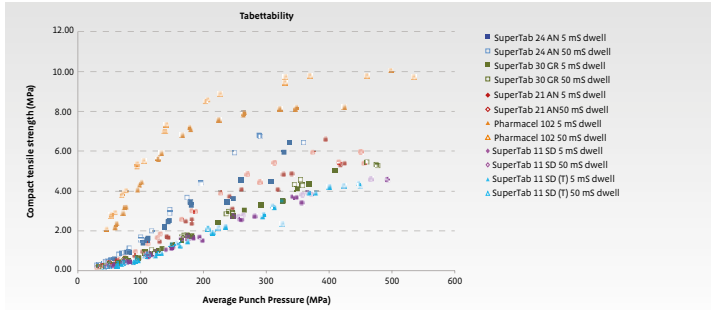


Fig. 2: Tensile strength of different compacts in MPa against average punch pressure at slow and fast speed.

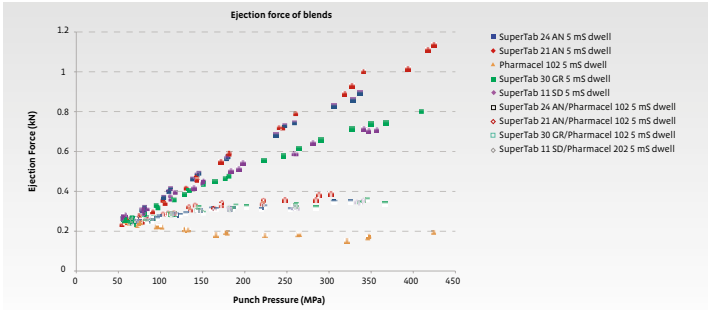


Fig. 3: Ejection forces (kN) of compact blends at various punch pressure (MPa) for individual excipient and at blend (50:50, lactose:MCC) at fast speed.

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