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Choosing the optimal lactose and MCC grade for formulating moisture sensitive drugs

Purpose

The development of robust and cost effective formulations of moisture sensitive drugs is complicated due to poor flow of drug, variable dissolution rates, and/or instability. Excipients like microcrystalline cellulose (MCC) and lactose with low moisture levels can accelerate their formulation development. The main objective of this study is to show the tabletability performance of low moisture MCC and anhydrous lactose in moisture sensitive tablet formulation.

Methods

Low moisture MCC (Pharmacel® 112), anhydrous lactose (SuperTab® 21AN, 22AN) and anhydrous granulated lactose (SuperTab® 24AN) were evaluated for physical-chemical parameters like particle size, shape and flow properties. Dwell time sensitivity of the individual excipients was studied at fast and low tabletting speeds in a placebo formulation. The dwell time study was performed on Phoenix hydraulic compaction Simulator. A model moisture sensitive drug was incorporated in 250 mg tablets composed of anhydrous lactose alone and in combination with Pharmacel® 112.

Results and discussion

The mean particle size of three anhydrous lactose grades is in the range of 120-220 µm and that of the MCC grade between 90-100 µm. Microscopy (SEM) (Fig. 1) confirmed the fibrous/agglomerated nature of MCC, the irregular kite like shape of anhydrous lactose and the spherical shape of anhydrous granulated lactose. Anhydrous lactose showed superior flow functions coefficients compared to Pharmacel® 112 (moderate flow) when tested in pure form (Fig. 2).

All the directly compressible excipients showed very stable flow and robust tabletting properties (low dwell time sensitivity) at high speed of 5 ms and low speed of 50 ms demonstrating the robustness of excipient performance during scale up (Fig. 3).

The formulation containing anhydrous lactose (50% w/w) and Pharmacel® 112 (50% w/w) was selected to incorporate 20% w/w moisture sensitive drug in 250 mg tablets compressed at 10 kN.

Tablets were produced with different grades of anhydrous lactose and in combination (50-50% w/w) with Pharmacel® 112 showed similar thickness, friability and weight variation profiles. The tensile strength at 10 kN was higher for SuperTab® 24 AN (anhydrous granulated lactose, 5.4 MPa) followed by SuperTab® 22AN and SuperTab® 21AN, which showed similar tensile strength (3 - 4 MPa) (Fig. 4).

Granulated anhydrous lactose (SuperTab® 24AN) forms compacts with greater strength, and is ideal excipients for directly compression process. Addition of Pharmacel® 112 (50% w/w) to anhydrous lactose further improved the compactibility without changing the disintegration time to large extent. MCC together with lactose showed synergistic effect on tabletability and lowered ejection forces.

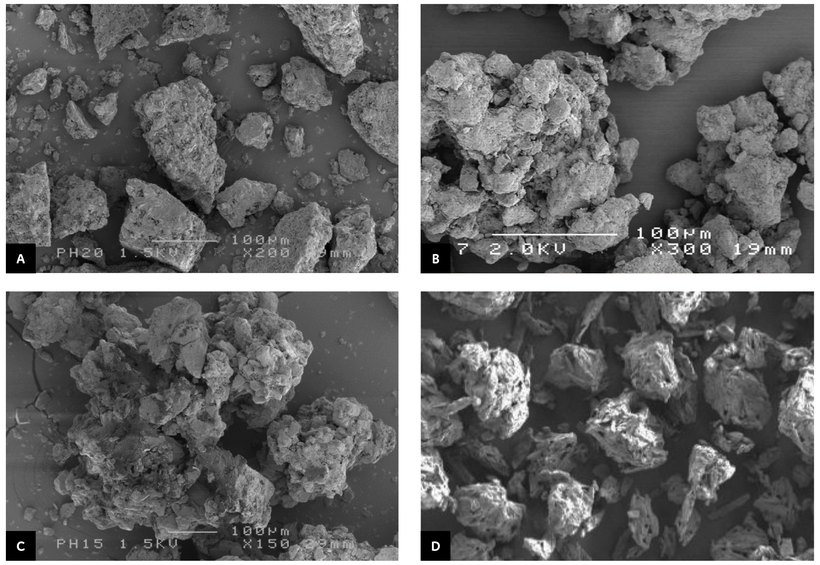

Figure 1: *Scanning electron micrographs of (A) SuperTab® 21AN (B) SuperTab® 24AN and (C) SuperTab® 30GR (D) Pharmacel® 112.*

Conclusion

Low moisture MCC and anhydrous lactose offers a perfect combination of plastic and brittle behavior, respectively enabling the rapid formulation development of moisture sensitive drugs. Moderate flow of MCC can be further improved by addition of lactose while increased tabletability can be achieved by addition of MCC. The combined offering of the both anhydrous grades of lactose and low moisture MCC grade by DFE Pharma allows therefore the formulator choice to find the most optimal solution for their formulation challenge.

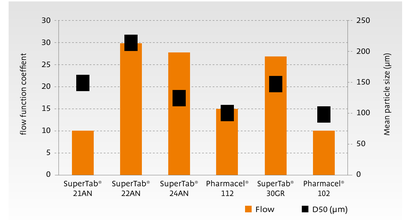

Figure 2: *Flow function coefficient (FFC) and mean particle size of anhydrous directly compressed lactoses (SuperTab® AN series) and Pharmacel®112.*

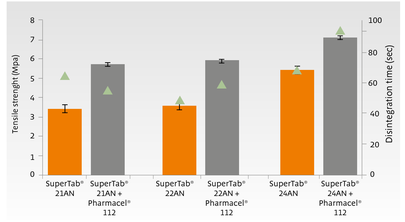

Figure 4: *Tensile strength (Mpa) and disintegration time (sec) of tablets compressed at 10 kN using anhydrous lactose alone and in combination with Pharmacel® 112.*

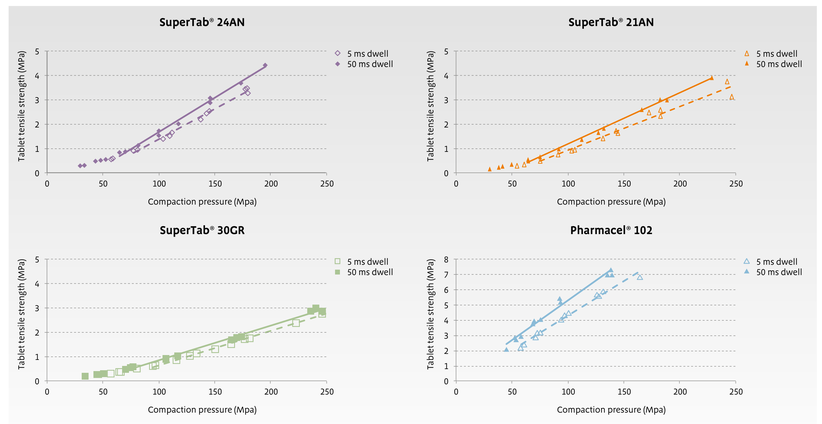

Figure 3: *Tensile strength (MPa) of different anhydrous grades of lactose and Pharmacel® at fast and low tabletting speed. The dwell time sensitivity index was calculated from the ratio of slop of both speeds at compaction pressure of 125 MPa.*

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