DFE pharma

Re-compaction properties of anhydrous lactose and microcrystalline cellulose

Excipient blends

The pursuit of excipient excellence

Summary

The recommended starting ratio of SuperTab® 21AN to microcrystalline cellulose for dry granulation is in the range 65:35 to 55:45.
Pharmacel® 102 (microcrystalline cellulose) is beneficial to dry granulated formulations to reduce the compaction pressure needed to form hard tablets, but above a level of 35% to 45% reduction in tabletability of granules is observed.

1 Introduction

Part 1 of this series of papers on dry granulation showed that SuperTab® 21AN (anhydrous lactose) was the preferred form of lactose for dry granulation processes [1].
This paper examines the tableting properties of mixtures of SuperTab® 21AN combined with Pharmacel® 102 as both powders and as densified granules.

Footnote

To avoid confusion, in this paper the term “densification” is used to mean the first compaction step by roller compaction or by slugging, and “tableting” is used to mean tableting of the granules formed by the densification process as in the schematic process below.

Relative density (used to describe the degree of densification) is calculated as

RD = density of the compact / true density of the components of the compact.

Porosity (used to describe the porosity of the final tablets) is calculated as

*Porosity = 100 * (1 – RD)*

2 Experimental section

2.1 Materials

SuperTab® 21AN and Pharmacel® 102 are available from DFE Pharma.

2.2 Densification and milling

SuperTab® 21AN and Pharmacel® 102 were blended and densified by compaction on a single punch tablet machine (Korsch EK0) fitted with 13 mm punches. The blends were densified to a target relative density (RD) of 0.9.

Tablets so produced were milled using an oscillating granulator fitted with a 0.8 mm screen, following pre-milling through a 1.6 mm screen if necessary.
The fraction 63 µm to 710 µm was used in the tableting experiments.

2.3 Density measurement

Poured and tapped bulk densities were measured on a 30 ml sample of granules in a 100 ml measuring cylinder. The measuring cylinder was tapped 1250 times using a Jel STAV tap bulk density tester.

2.4 Tableting

Powder blends (that is blends of the excipients as supplied) and densified granules were lubricated by blending with 1% magnesium stearate for 5 minutes using an Erweka AR400 cube mixer. The lubricated granules were tableted using a single punch tablet machine fitted with 11mm punches to target porosities of 20%, 15%, 10% and 5%.
Tablet strength was determined after 10 days using an Erweka TBH 30 tester.

3 Results and discussion

3.1 Granule density

Increasing the proportion of MCC in the granules decreases both the poured and the tapped bulk densities (figure 1) as would be expected from the results in reference 1.

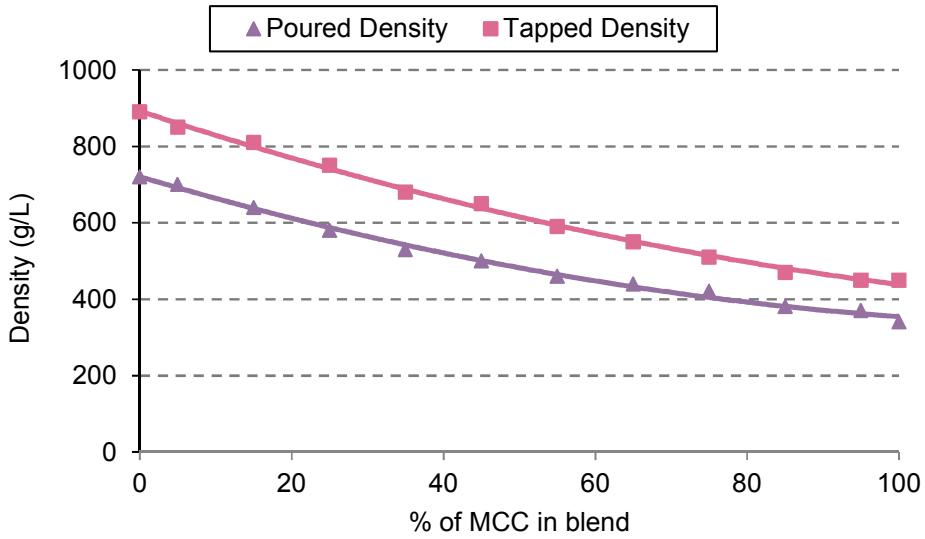

Figure 1: *Poured and tapped densities of excipient blends and granules*

3.2 Tableting powder blends and granules

The simple plots of tablet strength against compaction pressure for the powders and the granules (figures 2 and 3 respectively) are not very revealing. For the powders there is a clear and predictable improvement in tabletability as the proportion on Pharmacel® increases, but no such relationship exists for the granules.

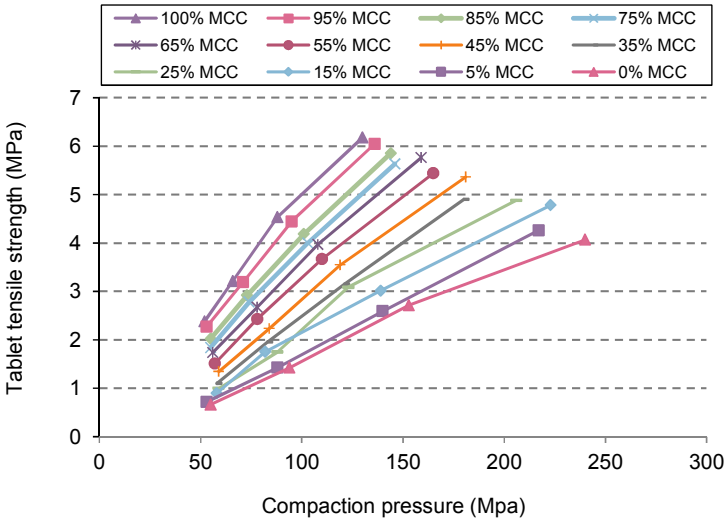

Figure 2: *Tabletability plots for blends of anhydrous lactose and MCC*

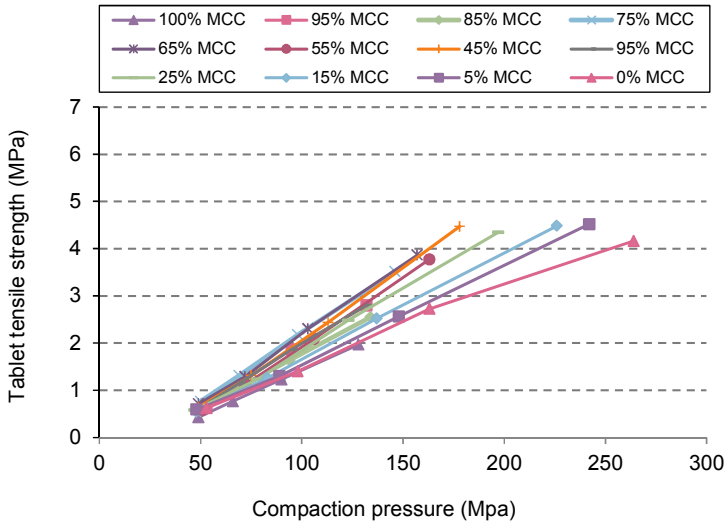

Figure 3: *Tabletability plots for granules of anhydrous lactose and MCC*

Comparison of the strengths of tablets made from powders or granules at the four target porosities reveals that separation of the tabletability of the granules and powders occurs with increasing proportions of MCC in the formulations (figure 4).

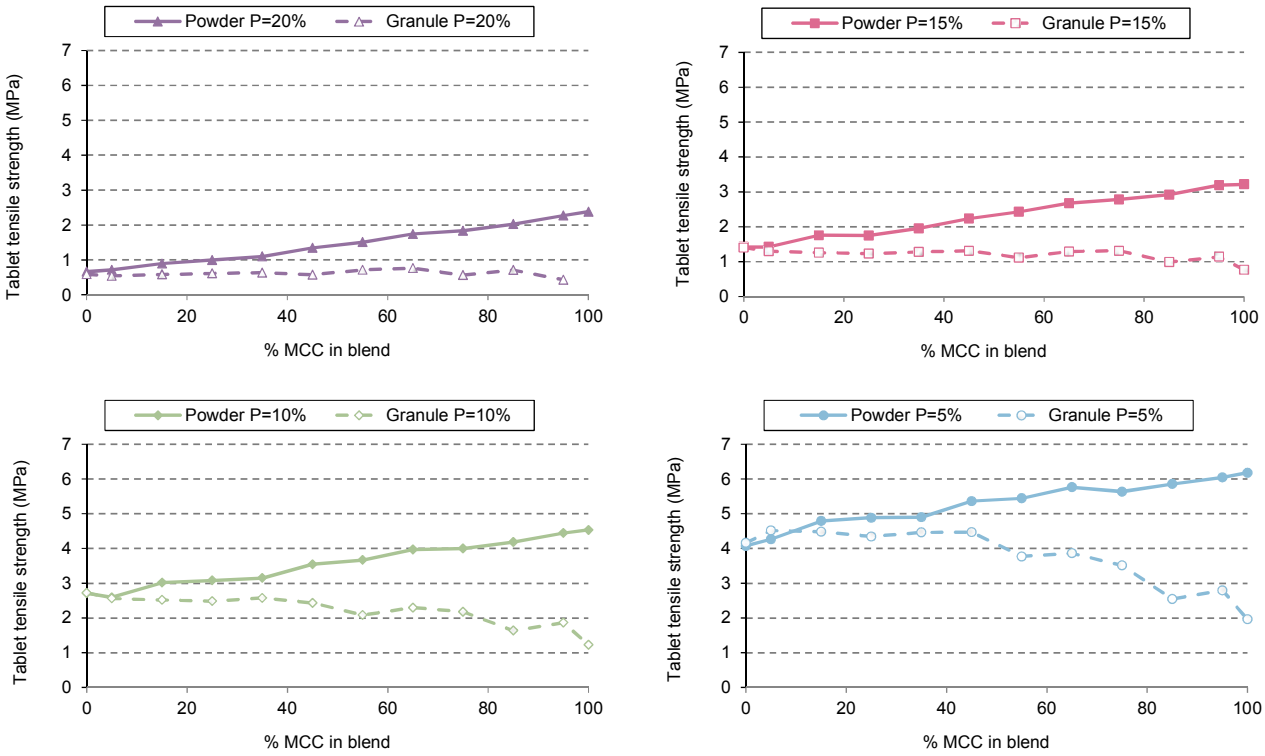

Figure 4: *Tabletability of anhydrous lactose / MCC blends and granules to 4 porosities*

As expected, all of the powders show an increase in tabletability with increasing MCC, but this is not the case for the granules. The tabletability of the granules remains more or less constant for tablets made at higher porosities of 20% and 15% (upper two plots). However, for tablets made at low target porosity of 10% and 5%, tabletability decreases when the MCC proportion rises above about 35% to 45% (lower two plots).

Figure 5 shows the importance of MCC in the granules. These plots show that increasing the proportion of MCC in the granules reduces the pressure required to achieve the target tablet porosity, especially for the lower porosity tablets. Inclusion of MCC in the formulation reduces applied pressure during tableting, and therefore potentially maximises the lifetime of tablet tooling.
An almost identical picture is obtained for the powders.
Thus the powders and the granules of the same composition show similar compressibility (similar compaction pressure results in similar tablet porosity) but different tabletability (similar compaction pressure results in lower tablet strength) when the formulation contains more than 35% to 45% of MCC.

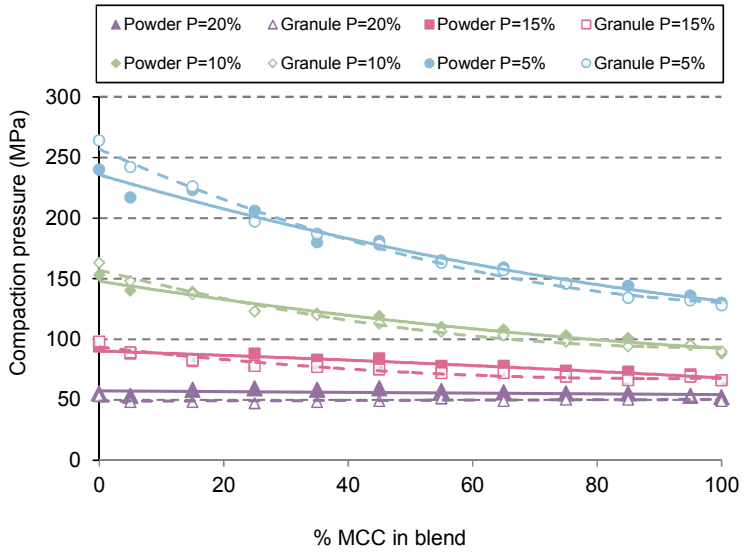

Figure 5: *Compaction pressure required to achieve the target porosity of tablets made from anhydrous lactose / MCC blends and granules*

4 Conclusions

It is clear that there is a balance to be found between the proportions of brittle anhydrous lactose and plastic MCC in the tablet formulations.
MCC is important in allowing tablets to be made at relatively low compaction forces, but when the amount of MCC rises above about 35% to 45% the loss of tabletability of the granules starts to become a factor.

Overall then, the optimal starting point for a roller compaction formulation is a ratio of anhydrous lactose to MCC of about 65:35 to about 55:45.

References

1. DFE Pharma technical paper: Recompaction of lactose and microcrystalline cellulose: Individual excipients

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