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Effect of Increasing Pharmacel Concentration on the Tableting Properties of DC Diluents

Microcrystalline cellulose is used in a wide variety of oral solid dosage forms, including tablets, capsules, pellets and others. It is one of the most commonly used diluents in drug formulations. MCC is commonly used in combination with a brittle excipient such as anhydrous lactose in which the benefits of high tablet strength and insensitivity to recompaction are combined to give robust dry granulation formulations [1].

Objective

Microcrystalline cellulose (Pharmacel) is the most versatile excipient in Pharma industry. It acts as excellent filler, binder and disintegrant. Because of its neutral mouth feel, it is widely used in oral disintegrating tablet (ODT) formulations. The main aim of this work is to determine the optimal concentration of Pharmacel®102 one can use in DC tablets and to study the effect of increasing concentration of MCC on tablet properties.

Experimental

Material:

Granulated lactose (alpha lactose monohydrate, SuperTab® 30 GR, [D50=144 µm]), anhydrous lactose (beta lactose monohydrate, SuperTab® 21 [D50=159 µm]) and SuperTab® 24AN [D50=123 µm]), spray dried lactose (alpha lactose monohydrate, SuperTab® 11SD, [D50=125 µm]), microcrystalline cellulose (Pharmacel® 102 [D50=110 µm]) and cros carmellose sodium (Primellose®) were from DFE Pharma, Germany (Figure 1).
Mannitol (Pearlitol® 200 SD, 135 µm) and Emcompress® Anhydrous [D50=181 µm] were obtained from Roquette, France and JRS Pharma, Germany, respectively.
Agglomerated anhydrous lactose (SuperTab® 24AN) combines the benefits of granulated and anhydrous lactose; It has excellent flow, superior compaction properties, high mixing efficiency and low lubricant sensitivity.

Methods:

Tablets were processed by direct compression using 9 mm flat punches. Magnesium stearate lubricated mixtures of Pharmacel® 102 at 0, 25, 50, and 75% was compressed in combination with different DC lactoses and mannitol along with superdisintegrant (Primellose®). The excipient blend was prepared on Turbula T2C mixer and compressed on RoTab-T rotary press to produce 250 mg tablets. Tablet ejection force was measured during process. Tablets were evaluated for weight variation, tensile strength and disintegration time.

Results and discussion

The granulated, spray dried and anhydrous lactose has characteristic structure, it consists of clusters of micro-crystals. Typically SuperTab® 21AN contains about 81% of the -isomer. Despite being an anhydrous material, anhydrous lactose exhibits relatively low hydroscopicity. On the hand spherical shape and narrow particle size distribution confer the excellent flow properties of spray dried lactose.

As the Pharmacel®102 concentration increased the ejection force decreased specifically at the higher compaction forces indicating the lubricant properties of MCC. At lower compaction forces, MCC had significant effect on hardness (Figure 2). The tablet crushing strength at 5kN was 49.5 N for 0% of MCC formulation and it increased to 74.5 for formulation containing 50% MCC for SuperTab® 24AN (Figure 3). At low compaction forces, disintegration time decreased with increase in MCC concentration while at high compaction force it increased from 7 min to 11 min when 25% and 75% MCC was used, respectively. This could be due to increased hardness with increase in MCC content. The effect of MCC concentration on tablet hardness varies with the different fillers: with DC lactose a steady increase was observed with increasing MCC concentration whereas for mannitol the hardness is unaffected until 75% MCC.

Conclusion

The selection of diluents played an important role in determining the effect of increasing MCC concentration on placebo tablet properties. The excellent compressibility property of MCC and DC lactoses can be used to make tableting process more economical and efficient.
The recommended range of MCC in direct compression for dicalcium phosphate and lactose is 0 to 50% and for mannitol 0-75%. The stated concentration of MCC is subject to change in presence of other excipients. Next to this, the properties and amount of other filler/binders and drug used in the tablet can affect the tensile strength and disintegration time.

References
1. DFE Pharma-Technical guide on MCC

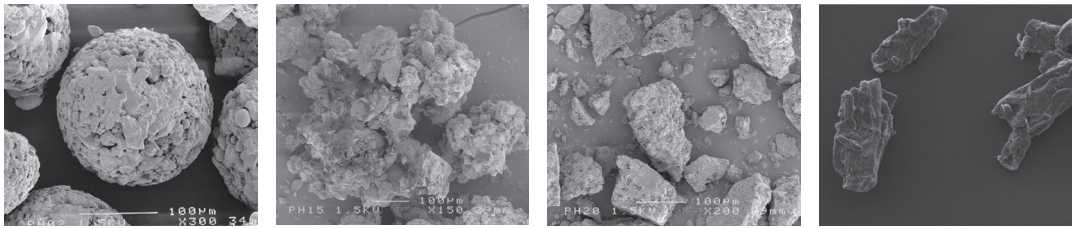
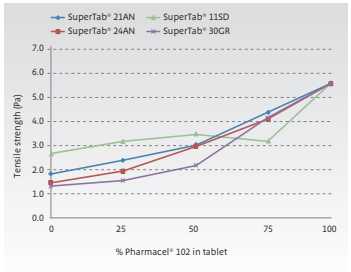


Figure 1: *Scanning electron photomicrograph of different grades of lactose (left) and microcrystalline cellulose (right).*



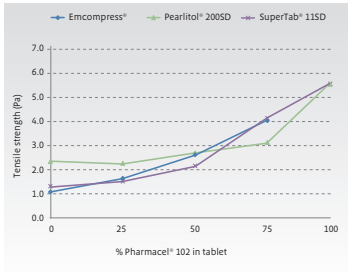


Figure 2: *Tablet tensile strength of tablets prepared with different grades of lactose (ldt), dicalsiumphosphate, mannitol (right) with increasing % of Pharmacel.*

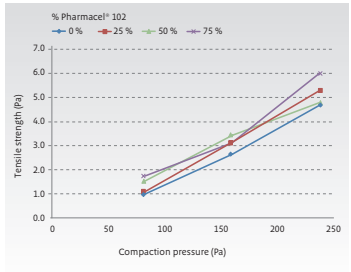


Figure 3: *Tablet tensile strength of tablets prepared with agglomerated anhydrous lactose with increasing % of Pharmacel.*

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