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Effect of increasing microcrystalline cellulose concentration on the flow properties of DC diluents

MCC

Microcrystalline cellulose (MCC) is commonly used together with direct compression lactose (DCL) in tablet formulations. The coarse grades of MCC have been reported to exhibit the minimum flow required for high speed tableting whereas DCL exhibit better flow than MCC. The aim of this work is to examine the powder flow behavior of MCC-lactose combinations relevant to direct compression (DC) using an annular shear cell tester.

Methods

The powder flow behavior was evaluated using an annular ring shear tester (RST-XS, Dietmar Schulze, Wolfenbüttel, Germany), using consolidation forces of 1000, 2000, 4000 and 8000 Pascal. Four types of DCL, being: anhydrous (SuperTab® 21AN), spray dried (SuperTab® 11SD), granulated (SuperTab® 30GR) and agglomerated anhydrous (SuperTab® 24AN) were evaluated in blends having increasing amounts of MCC (Pharmacel® 102). Scanning electron micrographs of the excipients are shown in Figure 1. The blends were prepared in the ratios of 100%, 75%, 50%, 25% and 0% w/w lactose with 0%, 25%, 50%, 75% and 100% w/w Pharmacel® 102 in a Turbula T2 blender. The flow factor (ff), density and effective angle of internal and external friction were evaluated. All measurements were performed in duplicate.

Results and discussion

At low consolidation forces (1000 Pa), little differentiation between the individual excipients was observed, with flow factors between 4.0 - 5.2. The differentiation was more obvious at higher consolidation forces. The flow behavior of the individual excipients at 4000 Pa consolidation force are shown in Table 1. The data shows that the flow factor for the individual excipients ranges between 8.5 and 27. According to the Jenike classification (Jenike AW, 1965/1980), SuperTab® 11SD, 24AN and 30GR are free flowing and SuperTab® 21AN and Pharmacel® 102 are easy flowing. In Figure 2, the flow factors, ff, of the excipient blends utilizing a consolidated force of 4000 Pa are plotted. The figure shows that the flow behavior of the blends having 25% w/w Pharmacel® 102 in their formulation, the flow characteristics are driven by the lactose component in the blend. At 50% w/w the flow behavior the differences between the blends become smaller at 4000 Pa consolidation force, the flow factors being between 11 - 14 (Table 2). This means that the MCC component in the blend is getting dominant. At higher percentages MCC in the blends, there is limited difference in terms of flow between the blends.

The measured effective angles of internal friction of the blends did not show significant differences at 4000 Pa consolidation force. The angle of linearized yield locus showed a decreasing value for SuperTab® 24AN and 30GR with increasing amounts of Pharmacel® 102. This was not clearly observed for SuperTab® 21AN and 11SD. For all blends, the density measured on the shear cell tester decreased with increasing amounts of Pharmacel® 102. The reason for the difference in flow behavior may be due to the different morphology of the lactoses used.

Conclusion

The shear cell analysis revealed the differences in the flow of excipients that are typically not apparent using common flow indicating methods (like angle of repose and orifice tester, data not shown). The shear cell technique showed that granulated anhydrous DC lactose (SuperTab® 24AN) and granulated monohydrate lactose (SuperTab® 30GR) are the most free flowing of the excipients studied. Increasing amounts of Pharmacel® 102 in the binary blends reduced the flow properties of the blends to the level of 100% Pharmacel® 102.

Ref: Jenike AW (1964/1980) Storage and flow of solids. Bull. No. 123, 20th printing, revised 1980. Engng Exp. Station, Uni. Of Utah, Salt lake City, USA.

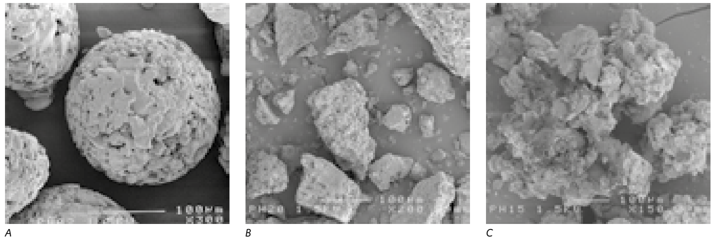

Fig. 1: Scanning electron micrographs of (A) SuperTab® 11SD (B) SuperTab® 21AN (C) SuperTab® 24AN.

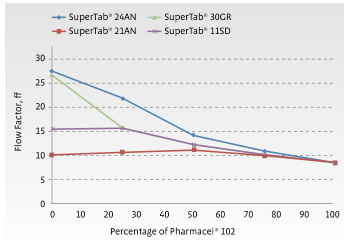

Fig. 2: Flow Factor (ff) of different DC Lactose : Pharmacel® 102 blends.

Table 1: Summary of flow properties of individual DC lactoses and Pharmacel® 102.

Parameter (s)	SuperTab® 21AN	SuperTab® 24AN	SuperTab® 30GR	SuperTab® 11SD	Pharmacel® 102
Major principle stress, kPa	7.02	7.13	6.93	6.77	7.07
Unconfined yield strength, kPa	0.69	0.26	0.26	0.44	0.83
Flow Factor, ff	10	27	27	15	8.5
Bulk Density, kg/m	587	417	481	530	321
Effective angle of internal friction, °	36.2	35.4	35.0	33.9	35.4
Angle of linearized yield locus, °	33.8	34.5	34.2	32.4	32.4
Angle of internal friction at steady state flow, °	32.8	32.7	32.0	31.0	32.5

Table 2: Flow factor (ff) values of Pharmacel® 102/DCL blends.

Pharmacel® 102 concentration	SuperTab® 24AN	SuperTab® 21AN	SuperTab® 30GR	SuperTab® 11SD
0% w/w	27	10	27	15
25% w/w	21	10	15	15
50% w/w	14	11	12	12
75% w/w	10	10	10	9.9
100% w/w	8.5	8.5	8.5	8.5

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