DFE pharma

Adequate flow properties of direct compression excipients

An industrial view

The pursuit of excipient excellence

Contents

1 Introduction

Controlling powder flow is key to the success of many industrial processes [1,2]. In the pharmaceutical industry, adequate powder flow is a prerequisite for weight control during tablet manufacturing.

Poor powder flow of the excipient in a formulation will lead to uncontrolled variations in tablet weight, poor content uniformity and inconsistent tablet properties. Poor flowing formulations can lead to under-utilization of fast speed tableting machines.

To investigate the powder flow versus the tablettability of excipients in time, six (6) excipients were characterized and tableted.

2 Experimental

Tableting was carried out on a ZPS08 (Shanghai Tianxiang, China) tableting press equipped with a gravimetric feeder system. The equipment has 8 stations (punches). The speed of the press was set at 22 rpm (10.560 tablets per hour). Two types of tooling were installed being a round flat beveled 7 mm tooling and an elongated (14 mm*6 mm) tooling.

Tablet weight was targeted to 225 mg, after initial setup to reach targeted tablet weight and hardness the press was run for 65 min. 10 tablets were taken from the start and every 5 minutes following. The average, standard deviation and relative standard deviation (RSD) of tablet weight were calculated.

A ring shear cell tester (Brookfield PFT, UK) was used for measuring the powder flow properties. Flowability was measured using a flow function (FF) test, applying 5 normal stresses (between 0.4 and 4.0 kPa) and three over-consolidation stresses at each normal stress.

Particle size distributions were measured using dry powder laser diffraction (Sympatec, Germany) and bulk and tapped densities were measured using a Vankel Tap density tester, following the USP method [3]. Excipients were mixed with 0.5% w/w Magnesium Stearate for 5 min in a multi directional motions mixer at 20 rpm to avoid punch sticking.

3 Results and discussion

Tablet weight variation was very low (<2.0%) for the examples shown, indicating excellent powder flow (Figures 1A and B). For the round flat beveled tablets SuperTab® 24AN (anhydrous granulated) showed the lowest variation of tablet weights in time compared to the other SuperTab® lactoses used in this study.

Even while having the highest tablet weight variation, widest particle size distribution, highest amount of fines and lowest flow factor (10) of the SuperTab® products tested, SuperTab® 21AN (anhydrous) is still considered free flowing and having excellent flow properties for tableting. Improvement in weight variation may be addressed by using a force feeder rather than the gravimetric feeder used in this study. Interestingly, Pharmacel® 101 and 102, excipients with low bulk densities, showed good flow behavior resulting in relatively low tablet weight variation (Table 1).

During the test carried out with Pharmacel® 101 (an excipient chosen to be on the borderline of good and poor flow) we observed some inconsistent die filling, which is reflected in the tablet weight variation (Table 1). The finding is in line with CC. Sun (2010)[4], who indicated that low density (<0.5 g/ml) powders having flow factors above 6.7 can be used for high speed tableting (=50.400 tablets per hour) [3].

The study from CC Sun (2010) suggests that tablet weight RSD's below 2.5% are acceptable for high speed tableting. The differences in tablet weight variation found between tooling shapes are likely due to ability to overcome arching of an elongated tablet. The consistency in tablet weight variation in time shows that after

tablet machine set-up little or no intervention has to take place to achieve good tablet weight control during a tablet production trail, with the excipients used in this study.

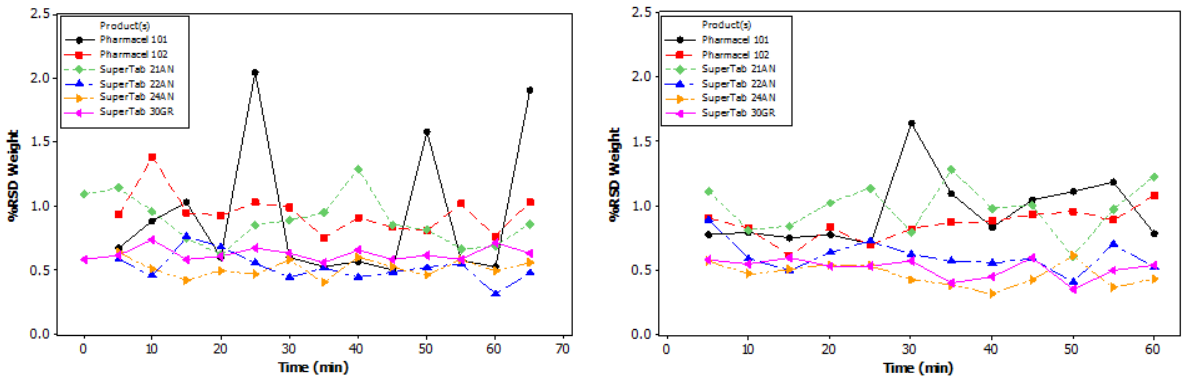

Figure 1(A). Tablet weight variation of various excipients for round beveled tablets (B) for elongated tablets. Each point is calculated from a total of ten tablets collected every 5 min during the study.

Table 1: A summary of the typical physical parameters and tableting results of the different excipients tested in this study.

	Particle Size (micron), n=3			Density (g/ml), n=3		HR	CI	Flow function, n=3	Tablet wt RSD (mean +/- SD, n=13-14)	
	X10	X50	X90	Bulk	Tapped				round	elongate
21AN	12.2 (0.1)	159 (1)	351 (17)	710 (28)	896 (37)	1.26	20.8	10	0.89 (0.19)	0.92 (0.19)
22AN	64.7 (0.3)	223 (1)	394 (2)	670 (8)	786 (9)	1.17	14.8	40	0.52 (0.11)	0.61 (0.12)
24AN	42.6 (0.3)	129 (1)	275 (10)	502 (16)	620 (22)	1.24	19.0	30	0.52 (0.07)	0.46 (0.09)
30GR	41.8 (0.7)	140 (3)	302 (16)	548 (22)	671 (30)	1.23	18.3	30	0.63 (0.07)	0.52 (0.08)
MCC 101	19.5 (0.4)	66.3 (2)	135 (6)	294 (12)	442 (15)	1.50	33.5	6.8	0.98 (0.40)	0.96 (0.26)
MCC 102	29.2 (0.4)	94.2 (2)	190 (8)	317 (9)	450 (17)	1.42	29.6	11	0.94 (0.17)	0.86 (0.12)

4 Conclusion

The study shows that the SuperTab® range of lactose's tested are ideal for formulations targeted for high speed tableting. The border line between acceptable and poor flow for high speed tableting as described in literature was confirmed to be in the range of powders having a flow function of 6.5.

As exemplified by Pharmacel® 101, an excipient designed for wet granulation. A powder with poorer powder flow properties and/or lower bulk densities may cause significant tablet die filling problems and is therefore not recommended.

The SuperTab® grades with higher densities lead to less weight variation than the less dense Pharmacel® grades and can be used alone or in combination to provide adequate flow properties required for high speed tableting in formulation.

5 References

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2. S.V. Crowley, et al., Influence of protein concentration on the physical characteristics and flow properties of milk protein concentrate powders, J. Food Eng. 135 (2014), p. 31-38.

3. USP <616>, United States Pharmacopoeia Method 616 – Bulk and tapped density

4. C.C. Sun, Setting the bar for powder flow properties in successful high speed tableting, Powder Technology 201 (2010), p. 106-108.

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