GRANUTOOLS™ POWDER FLOW CHARACTERIZATION

Influence of rheological behavior of lactose powders on the weight consistency of tablets

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INTRODUCTION

Lactose is one of the most widely used excipients in the pharmaceutical industry. There are many reasons for its popularity, such as the fact that lactose is largely inert, relatively inexpensive, safe, many different grades are available, and it has a long history of usage in successful formulations world-wide. For direct compression processes like tableting, lactose excipients can be used as a filler-binder to provide bulk density, compaction and flow to the formulation. Good flow of a pharmaceutical formulation is critical to produce uniform dosage forms. In this study, the rheological properties of lactose powders have been investigated with the rotating drum method (GranuDrum) and correlated with the actual consistency of flow achieved in a tableting system. The investigation of powder flowability at different drum rotating speeds gives useful information on the evolution of powder processability at a higher shear rate. Indeed, with classical characterization method like the angle of repose, the stress state at which the powder is tested is far from what the powder experiments in the tableting machine. In this study, we demonstrate the importance of the powder rheology to get useful insights that allow relevant prediction of the powder processability[1].

MATERIALS AND METHODS

Lactose powders:
Two SuperTab® grades
(DFE Pharma, Goch, Germany)

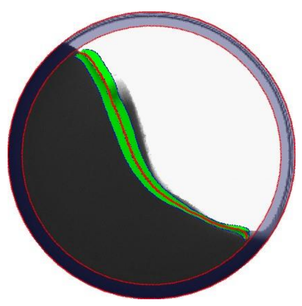
Lactose	Shape	x10 [µm]	x50 [µm]	x90 [µm]
SuperTab® 11SD	Spherical	44	119	223
SuperTab® 21AN	Shards	24.1	180	387

Tablet properties

- 99.5%w/w filler is blended with 0.5 %w/w MgSt (2 min Turbula blender T2 at 96rpm).
- Blends are compressed on a RoTab rotary tableting press at 25 rpm (9 mm flat beveled punches (iHolland), 10 kN).
- Target tablets of 250 mg at 10 rpm agitator (optfiller) speed.
- The agitator speed from 10-45 rpm in steps of 5 rpm.
- Twenty tablets are analyzed on weight by using an automated tablet tester (Sotax AT50).

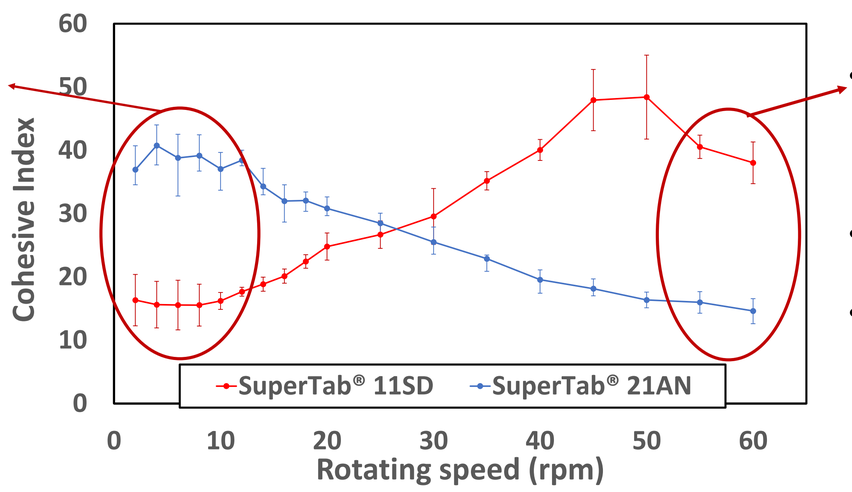
Powder rheology evaluation

- Rotating drum: GranuDrum [2] (Granutools, Awans, Belgium)
- Rotating speeds: 2 to 60 rpm
- Cohesive index based on temporal flow fluctuations

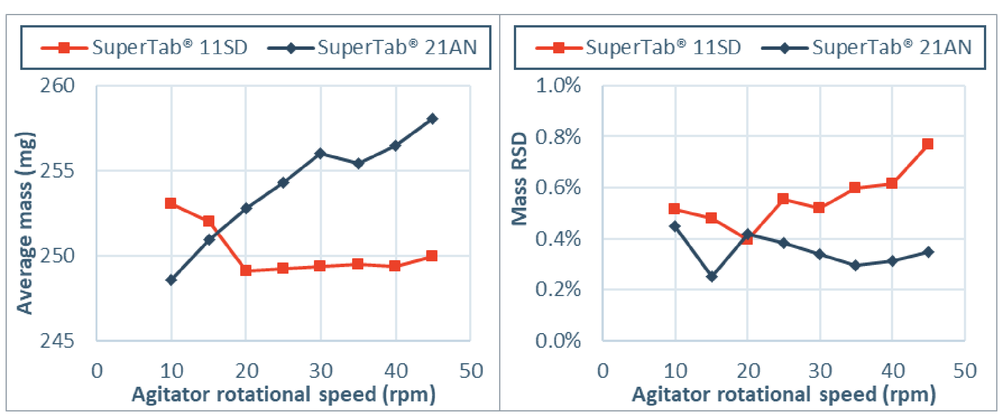


RESULTS

- Higher flowability for SuperTab® 11SD at low stress state
- Can be explained by spherical particle shapes for spray dried powder
- Same classification for other low stress method (Angle of repose, tapped density)



- Two opposite rheological behavior: shear-thinning for SuperTab® 21AN / shear-thickening for SuperTab® 11SD
- The classification is inverted at high stress state!
- Good / bad flowability classification directly depends on the stress applied to the powder during the process



- SuperTab® 11SD: Average tablet mass decreases with agitator speeds + higher variability
  - ➢ Reduction of flowability
- SuperTab® 21AN: Opposite behavior, increase of tablet mass + lower variability
  - ➢ Improvement of flowability
- The classification inversion predicted in the GranuDrum is also seen in the tableting machine
- Low stress state classification fails to predict behavior at high agitator speeds !

CONCLUSIONS

In this study, the rheology of two lactose powders has been investigated with a rotating drum method and correlated with the mass variability of produced tablets. The two powders exhibit different rheological behavior: a shear-thickening and a shear-thinning, leading to an inversion of flowability classification at high stress state. The inversion of the flowability classification predicted by the GranuDrum has also been observed in the tableting machine. Indeed, the shear-thinning properties of SuperTab® 21AN leads to an increase of flowability at high agitator speeds and consequently to an increase of tablets mass. These results demonstrate the importance of taking into account the rheological properties of the powder in order to get a relevant prediction of the tableting performance. Furthermore, this highlights the necessity to use a powder characterization method able to mimic the stress state at which the powder will be submitted during its processing.

REFERENCES

1. Janssen, P.H.M.; Depaifve,S.; Neveu, A.; Francqui, F.; Dickhoff,B.H.J. Impact of Powder Properties on the Rheological Behavior of Excipients. Pharmaceutics 2021, 13, 1198.
2. Lumay, G.; Boschini, F.; Traina, K.; Bontempi, S.; Remy, J.C.; Cloots, R.; Vandewalle, N. Measuring the Flowing Properties of Powders and Grains. Powder Technol. 2012, 224, 19–27.