Investigation of consolidation effects during storage and transportation of pharmaceutical powders

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Introduction

Powders are extensively used in the pharmaceutical industry due to their versatility and effectiveness. Lactose and calcium carbonate powders are popular examples of inactive ingredients, known as excipients, used in the production of solid oral dosage forms of drugs. These substances often act as fillers or stabilizers. [1]

In the manufacturing of solid dosage forms from granular materials, powder flow is a crucial parameter for ensuring smooth operation during production. However, many powders tend to increase in bulk strength when stored at rest for prolonged periods due to the compressive stress resulting from their own mass. This time-dependent loss in flowability, known as time consolidation or caking, can severely impact the manufacturing process. [2] Besides the influence of static pressure, powders can also consolidate due to vibrations or shocks experienced during transportation or processing.

As demonstrated in other application notes, modern rheometers can be used to investigate the flowability of various samples. [3,4] This study intends to showcase the applicability of powder rheological techniques to understand the consolidation of powders during both static and dynamic conditions.

Materials and methods

For this study, the flow behavior of commercially available lactose (Meggletose B15) and that of precipitated Ph. Eur.-compliant calcium carbonate powder were investigated.

To characterize the flowability of the powders, a Thermo Scientific™ HAAKE™ MARS™ iQ Rheometer equipped with a powder rheology measuring geometry was used. Figure 1 shows the setup used for conditioning and testing (left) as well as for static consolidation (right).

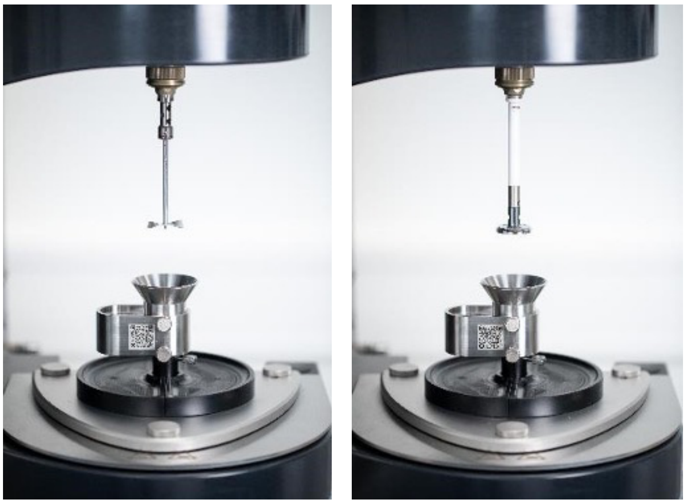

Figure 1. HAAKE MARS iQ Rheometer with powder rheology accessory for powder flow measurements (left) and for static consolidation (right).

To understand the effect of time-consolidation on both samples, the powder was loaded into the funnel and an initial sample conditioning cycle with a tip speed of 40 mm/s was done by using the vane rotor. After conditioning, the rotor was changed to a porous piston to apply the desired consolidation stress. The porous piston allows air to pass through the rotor during this phase.

Depending on the type and volume of the storage vessel as well as the bulk density of the powder, different consolidation stresses can be estimated during storage. [5] A typical consolidation stress range is between 3 and 15 kPa. Therefore, to screen the consolidation behavior of the two powders for storage in different containers, consolidation stresses of 3, 6, 9, and 15 kPa were applied for 10 min each. After the consolidation and splitting of the powder, a single powder flow test step was conducted. In contrast to the complete powder flow test described in [3], here only one downward/upward cycle was performed with a tip speed of 100 mm/s and a helix angle of 5°.

The respective measurement procedure in the Thermo Scientific™ HAAKE™ RheoWin™ Software is shown in

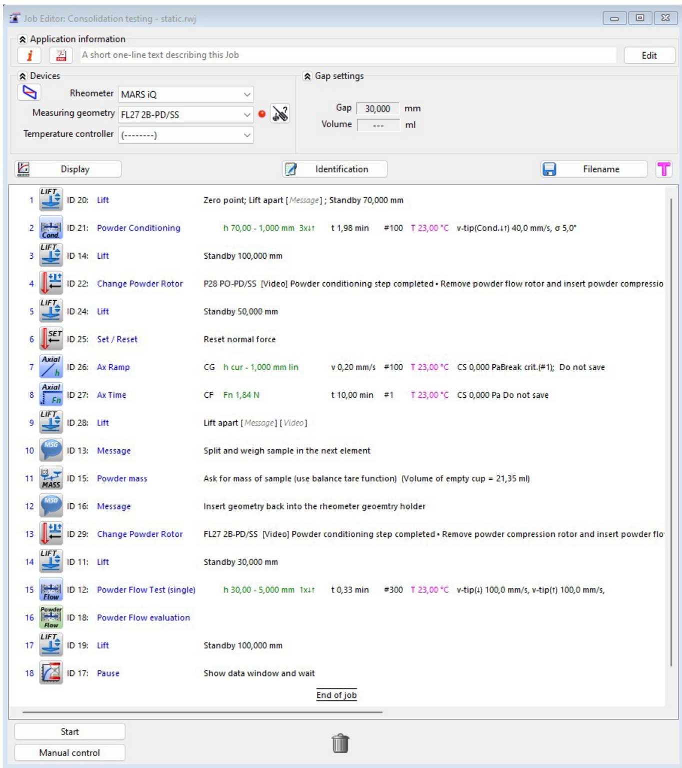

Figure 2. Measurement routine for static powder consolidation tests with a consolidation stress of 3 kPa in the HAAKE RheoWin Software.

Figure 2.

To simulate the effect of vibrations on the consolidation tendency, each sample was prepared, conditioned and tested in the same manner as in static powder consolidation testing. However, dynamic consolidation was done using a jolting volumeter prior to performing a single powder flow test step. To apply the vibrational load onto the sample, the attached powder cell was subjected to controlled jolts or taps, causing the powder to compact and settle. Figure 3 illustrates the working principle of a jolting volumeter with attached powder cell.

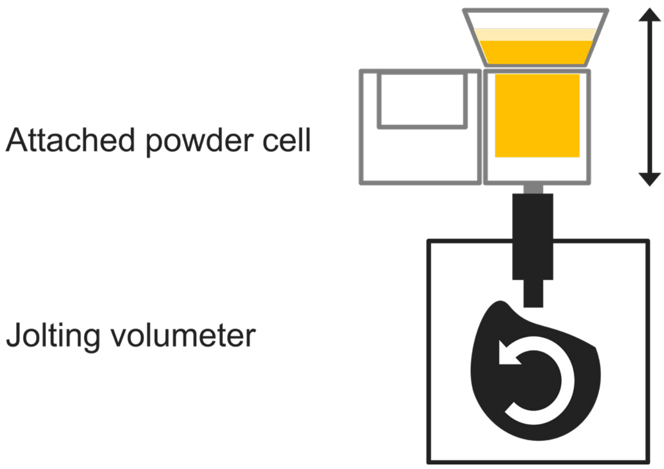

Figure 3. Working principle of a jolting volumeter with attached powder cell.

The device used for this study was a commercially available jolting volumeter fabricated by Funke Gerber™. The number of taps varied between 5, 10, 20 and 50.

The flow energy needed to destroy the consolidated state of the powder during the single powder flow test step was then used as a measure of consolidation tendency after time for a given consolidation stress as well as after vibration.

The respective measurement procedure in the Thermo Scientific™ HAAKE™ RheoWin™ is shown in Figure 4.

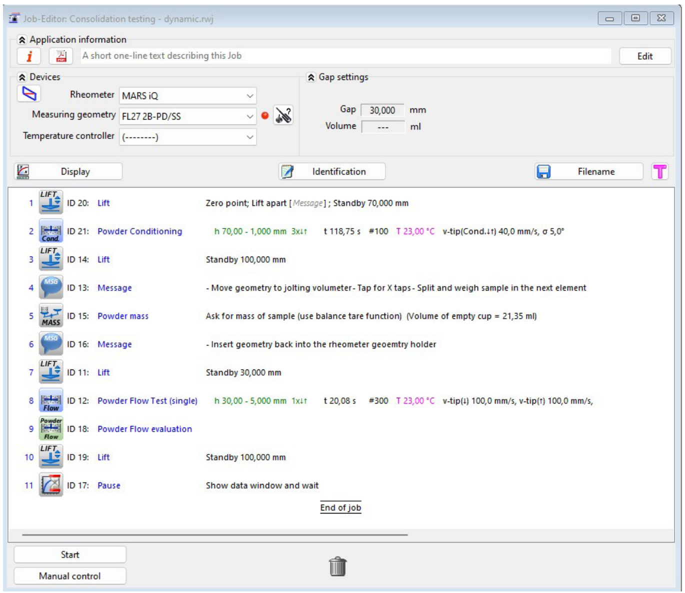

Figure 4. Measurement routine for dynamic powder consolidation tests in the HAAKE RheoWin Software.

Results and discussion

As stated above, depending on the applied consolidation stress, different storage conditions can be mimicked. The larger the stored volume and the higher the bulk density of the granular material, the larger the consolidation stress that needs to be expected. The effect of various stresses on the required flow energy necessary to make the consolidated powder bed flow again is illustrated in Figure 5. An unconsolidated reference sample is also included in the illustration. Despite lactose having an overall higher flow energy compared to calcium carbonate, both powder samples show the same consolidation tendency over time.

In contrast, the dynamic consolidation properties shown in Figure 5 differ quite significantly. Here, lactose shows an almost exponential increase in flow energy as the tap count increases. In comparison, a time-consolidation for 10 min at 9 kPa results in a similar flow energy needed to destroy the consolidated state of the lactose powder, compared to the test after 50 taps. Calcium carbonate shows a much weaker tendency for consolidation due to vibration. It can therefore be assumed that calcium carbonate behaves much more fluidly after transportation compared to lactose. Despite rather short exposure to the environmental factors in this study, the tested powders are significantly affected by consolidation.

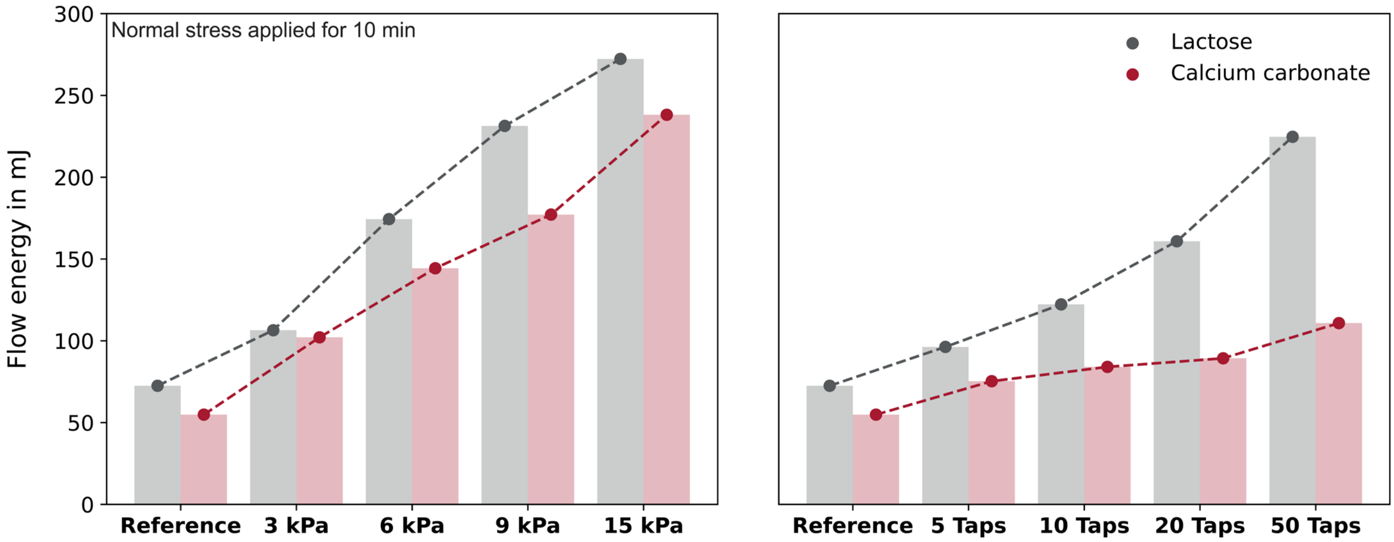

Figure 5. Experimental results for static (left) and dynamic consolidation testing (right).

Conclusion

Two examples of powders commonly used in the pharmaceutical industry, calcium carbonate and lactose, were compared regarding their consolidation behavior. Static testing indicates that time consolidation is likely to be an issue for both samples. In contrast, vibrations seem to influence the consolidation behavior of lactose significantly more than they do calcium carbonate. This type of behavior needs to be considered, especially for longer transportation routes.

In the scope of this report, rather short times and tap numbers were investigated. To mimic real-world applications more closely, granular materials would need to be subjected to consolidation stresses for much longer time periods and under different temperature conditions. To take this into account without occupying the rheometer for a long period, the powder cell could be stored in an external oven while applying the desired consolidation stress using weights. Also, the exposure to vibrations during transportation usually can be expected to be more prolonged.

Consolidation testing is therefore an essential tool to investigate powder flowability throughout the entire supply chain from storage and transportation to processing and distribution.

References

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