FLOW CHARACTERIZATION METHODS OF GLIDANTS

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Abstract

The applications of nanoparticles or ultrafine glidant particles are increasing over the last years. In most of these industry applications the flow behavior of the particles is critical issue for the proper design of the processes and devices. Therefore, flowability tests including ratio ffc (consolidation stress to unconfined yield strength), bulk properties measurements and novel patented angle of repose Zenegero method were performed. The new method is based on a continuous flow of particles whose flow dynamics doesn't affect with the fall of bulk material the target arrangement of material pile. Evaluation of pile angle is performed at 8 views rotated around the perimeter of the pile ensuring more accurate result. The most commonly used glidant such as Aerosil®, Cab-O-Sil® and magnesium stearate were taken for three type of flowability tests evaluation. In order to understand the nanoparticles flow behavior was also determined their particle size distribution, compressibility and cohesion. Initial results show that new Zenegero method gives more comprehensive flow information and good sensitivity. In addition, it was confirmed that the flowability of glidant with a narrow particle size distribution leads to good flow conditions. This study reveals how choice of flow characterization method can play a key role in multi-factorial determination of the glidant type.

Keywords: Flowability, angle of repose measurement, glidant, bulk properties

1. INTRODUCTION

Glidants are incorporated into solid dosage forms to improve the flow properties of powders or granulates [1]. These are excipients adsorbing during mixing (preparation of tableting mixture) on the surface of the powders - particles of other excipients or active pharmaceutical substances. In the phase of pouring the tableting mixture from the hopper into the tableting press die glidants reduce friction between particles and between particles and the wall of the hopper. The consequence of friction reduction (i.e. improving of the mixture flowability) is the uniform die filling with the powder mixture, ensuring of required weight and content uniformity of produced tablets. Glidants also prevent sticking of pressed powders on compression thorns and tablets capping [2]. For capsules, addition of glidants ensures a high accuracy of metering and a uniform distribution of active ingredients. There is some controversy over the exact mechanism, but two theories exist. The first is that fine glidant powders coat the relatively larger host powders, increasing interparticle distance and decreasing interparticle forces. The second one is that the glidant powders act in a manner analogous to ball-bearings, decreasing friction of rough surfaces [1]. Finely divided amorphous silica, silicon dioxide and magnesium stearate are commonly used glidants. The above listed were therefore used in this study. This work compares accessible and simple flowability methods for glidants which can be used and show a new patented method of angle of repose determination in order to classify powders into particular flowability modes. Methods for powder flowability characterization described in the literature are numerous and exist in many variations [3, 4]. But only one individual test is not always able to measure small differences in flow between similar powders and to rank their flow properties [5]. In this study were therefore used several methods for determining of glidants flowability and data were mutually compared in order to gain reliable measurement result. The particle size distributions, compressibility and cohesion of glidants were selected as the basic characteristics.

2. MATERIALS AND METHODS

2.1. Materials

Three commonly available and often used glidants were used in this study. These are Aerosil® 380, Cab-O-Sil® M5 and magnesium stearate (**Figure 1**). Aerosil® and Cab-O-Sil® are fumed silica (SiO_2+4HCl). Magnesium stearate is also known as octadecanoic acid and magnesium salt with chemical formula $C_{36}H_{70}Mg_4$.

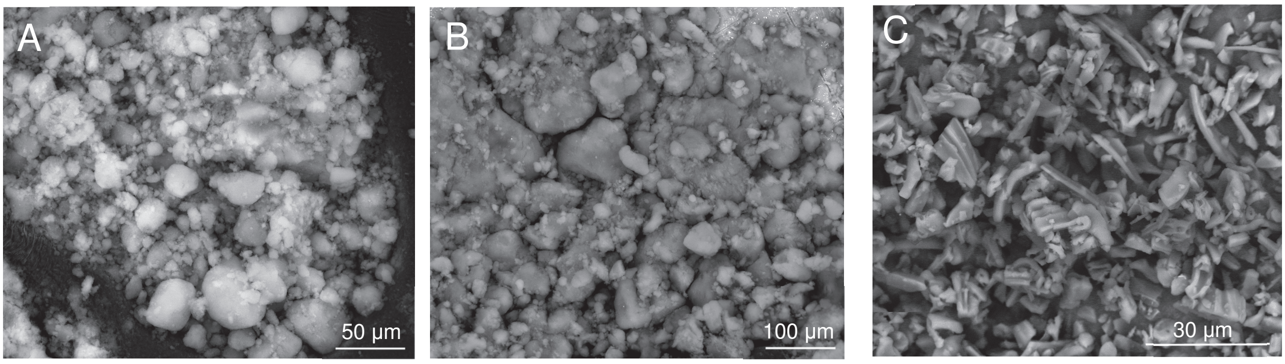

Figure 1 SEM images of Aerosil® 380 (A), Cab-O-Sil® (B) and magnesium stearate (C)

The figure shows that fumed silica (namely Ca-O-Sil®), which is produced by flame hydrolysis of chlorosilanes, cannot be captured as isolated primary particles but as agglomerated aggregates. For the mechanism of glidants action are their primary particles indispensable (**Figure 2**). Agglomerates are broken down by the shear forces that occur during powder processing.

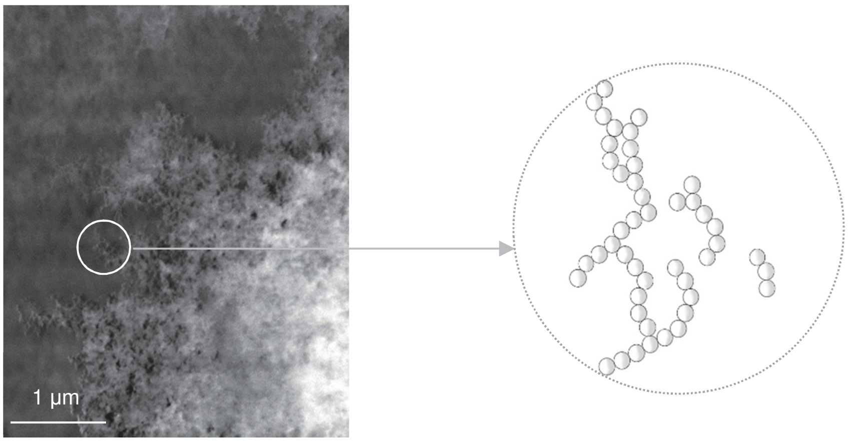

Figure 2 Detail of the primary spherical Cab-O-Sil®. particles necessary for the mechanism of glidant action

2.2. Particle size distribution

A particle size analyzer CPS Disc Centrifuge DC24000 was used for measuring particles size distribution. The analyzer measures particle using centrifugal sedimentation within an optically clear spinning disc that is filled with fluid. Sedimentation is stabilized by a density gradient within the fluid, and accuracy of measured sizes is insured through the use of a known size calibration standard before each test. The concentration of particles at each size is determined by continuously measuring the turbidity of the fluid near the outside edge of the rotating disc.

2.3. Bulk properties

The device used for bulk properties measurement was an FT4 Powder Rheometer. FT4 is a universal powder tester, combining patented blade methodology for measuring flow energy. The methodologies allow measurement of flow energy in relation to many variables and all packing states, shear properties of consolidated or unconsolidated powders, bulk properties - bulk density, compressibility, cohesion, angle of internal friction *AIF* and flowability *FFC*. The procedure for bulk properties measuring without automation devices is given below. An accurately weight amount of glidant was poured into a 200 ml glass cylinder. The bulk volume was recorded and then the cylinder was tapped for 10, 500 and 1250 taps. Every reduced apparent volume was recorded (V_0 - V_{1250}). Bulk density *BD* (weight and V_0 ratio), tapped density *TD* (weight and V_{1250} ratio), Carr's index *CI* (**Equation 1**) and Hausner ratio *HR* (**Equation 2**) of each glidant was calculated as follows [6].

$$CI = \frac{(TD - BD)}{TD} \cdot 100 \qquad (1)$$

$$HR = \frac{TD}{BD} \qquad (2)$$

The packability was determined from the tapped density according to Kawakita and Ludde equation (**Equations 3 and 4**) [4].

$$\frac{n}{C} = \frac{n}{a} + \frac{1}{ab} \qquad (3)$$

$$C = \frac{(V_0 - V_n)}{V_0} \qquad (4)$$

Where n is the tap number, *C* donates the volume reduction and V_0 and V_n are the glidant bed volume as the initial and nth tapped state respectively. The plot of *n/C* versus *n* is linear. The compactibility *1/a* can be obtained from the slope *a*. Cohesivity *1/b* is obtained from the intercept *1/ab* of the plot.

2.4. Angle of repose

New patented device (Zenegero method) for an angle of repose measurement is in the **Figure 3** [7]. The device consists of a frame which comprises a horizontal beam (1) and attached vertical beam (2), on which is using clamp with a hand lever (3) fastened the arm (4). On the arm is placed holder (5), into which is fastened the funnel (6). To the beam (1) is mounted rotary stand (7) with the camera (8) and contrast wall (9). Beneath the beam is places collecting vessel.

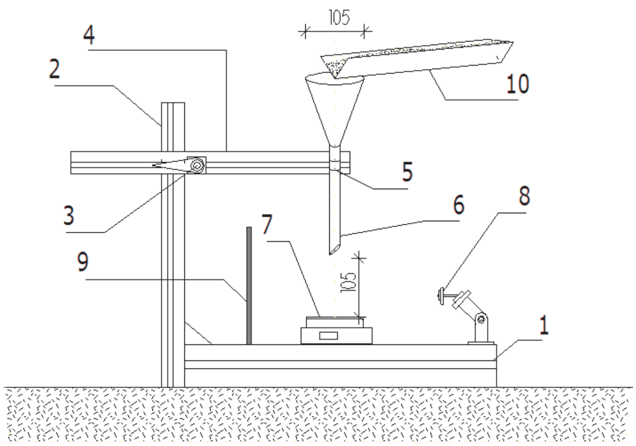

Figure 3 Schematic representation of the device for angle of repose measurement

Measured material is transported into the funnel using vibrating conveyor (10). Material is poured into the bowl, while gradually creating the pile and surplus material falls into the receptacle. After the pile creation starts the drive giving the bowl rotation. The bowl rotates around its vertical axis and the camera (8) successively records a pile of all eight sides. The results are processed by the eScope software.

3. RESULTS AND DISCUSSION

Particle size distribution of Aerosil® 380, Cab-O-Sil® and magnesium stearate are represented in **Figure 4**. The **figure 4** shows that Cab-O-Sil® exhibits the monomodal distributional distribution of particle sizes with a significant in the area of about 90 µm. Unlike Aerosil® 380, this has bimodal distributional curve and multimodal distribution of magnesium stearate.

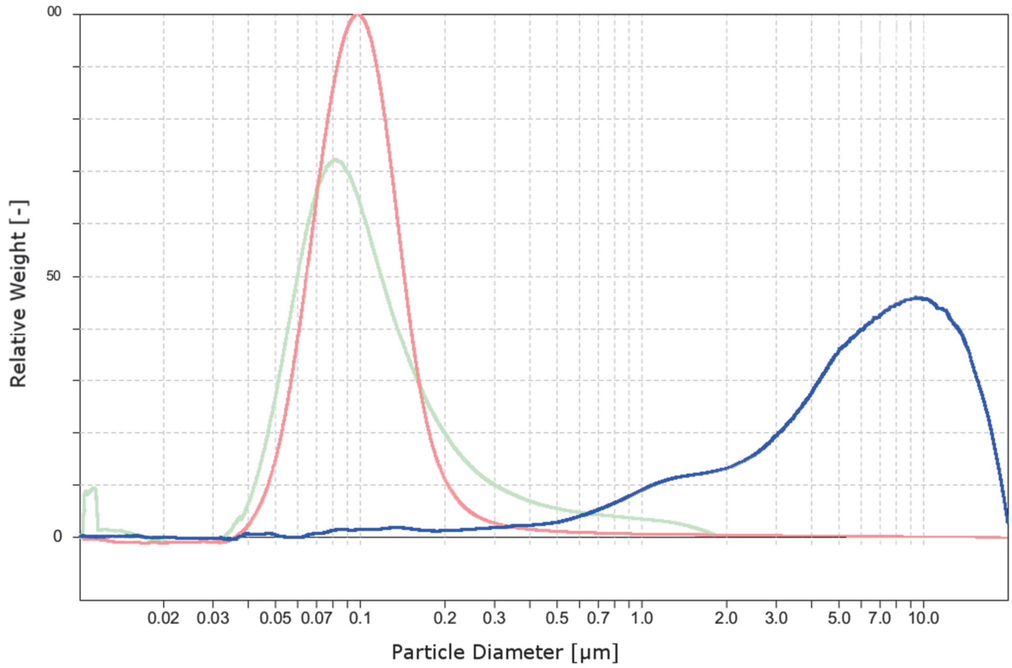

Figure 4 Particle size distributions (—— Cab-O-Sil®, —— Aerosil® 380, —— magnesium stearate)

Cab-O-Sil® contains 96 % particles to 98 µm, Aerosil® 85 % and magnesium stearate only 2.15 % particles to the same size.

Data obtained using powder rheometer Freeman FT4 and calculated from bulk properties are given in **Table 1**. Parameters of compressibility and cohesion based on automated measurements are in good agreement with calculated results of compactibility and cohesivity. The compactibility *(1/a)* defines the degree of volume reduction and the cohesivity (*1/b*) is a constant related to cohesion [4]. Compressibility determining changes in a powder's density as a result of a directly applied consolidation load (related to compactibility). Compressibility of powder is very important. Good compressibility is required for example to ensure sufficient strength of tablets in order to get problem-free manipulation and transport.

Aerosil® and Cab-O-Sil® show similarly high value of compressibility (they comprise nanoparticles and large amount of air) unlike magnesium stearate with significant lower value. The same is in case with parameter of compactibility. The cohesion factor is minimal for Aerosil®, and increases for Cab-O-Sil® and magnesium stearate (again in accordance with calculated cohesivity (*1/b*)). For the initial indication of glidants (powders) compression ability parameters and its cohesion degree is normally possible to use only measurements of bulk properties (bulk and tapped densities) from which it is very easy to deduce these parameters.

Table 1 Comparison of cohesion and compressibility values measured using powder Rheometer FT4 and calculated from bulk properties

Material	Aerosil®	Cab-O-Sil®	Magnesium stearate
Compressibility, %	37.1 ± 0.6	34.2 ± 0.8	18.8 ± 0.1
Cohesion, kPa	0.09 ± 0.02	0.72 ± 0.17	1.07 ± 0.04
Compactibility (*1/a*), -	5.9 ± 0.4	3.1 ± 0.2	2.4 ± 0.2
Cohesivity (*1/b*), -	19.4 ± 1.7	36.9 ± 1.8	47.8 ± 2.4

Values of Carr's index, Hausner ratio, angle of repose and angle of internal friction are shown in **Table 2**. The angle of repose has been evaluated using newly developed Zenegero method which is based on continual flow of particles thereby reducing the flow dynamics and increasing reproducibility of the particle arrangement (section 2.4). Another advantage of this method is reduction of the human factor by automated scanning of formed pile at eight different rotations. Evaluation according to the angle of repose has got seven levels, thus also little difference in the value of the angle of repose may indicate the different classification into flow regimes of powders. Evaluation of flowability (classification into regimes) of tested powders according to various indicators is in **Table 3**.

Table 2 Flowability indicators for glidants, *CI* - Carr's index, *HR* - Hausner ratio, *AOR* - Angle of repose, *AIF* - Angle of internal friction

Material	*CI*, %	*HR*, -	*AOR*, °	*AIF*, °
Aerosil®	17	1.2	40.1±0.5	30.5 ± 0.29
Cab-O-Sil®	28	1.4	36.7±1.0	30.6 ± 0.9
Magnesium stearate	39	1.7	42.1±1.3	24.2 ± 0.6

Table 3 Evaluation of glidants flowability using various methods

Classification according to	Aerosil®	Cab-O-Sil®	Magnesium stearate
Carr's index [8]	Good flow	Poor flow	Very poor flow
Hausner ratio [8]	Good flow	Poor flow	Very poor flow
Angle of repose [8]	Adequate (no needed help) on limit with average flow (may linger)	Adequate (no needed help) on limit with good flow	Average flow (may linger)
Flow index [6]	Free flowing	Free flowing	Easy-flowing

Generally, the best flowability exhibits material with larger particles. In this case it would be the magnesium stearate, which contains a fraction of up to about 20 µm. An important parameter is also particle shape and cohesiveness. Particle shape of magnesium stearate (leaf shape, sharper edges) contributes to an easier locking of particles and therefore also to the worse flowability and compressibility. Conversely, spherical particles with a smooth surface of the colloidal silica exhibit good flowability. Aerosil® and Cab-O-Sil® show similar bulk properties. Classification of Aerosil® a Cab-O-Sil® is the same as in case of assessment of flowability according to flow index. According to Carr's index, Hausner ratio and angle of repose is Aerosil® classified into the two levels higher regime (better flowability) than Cab-O-Sil®. It is possible to say, that best flow properties from tested glidant has Aerosil®. According to angle of repose indicator is, however, Aerosil® classified into the proportional regime as Cab-O-Sil®, but on the limit with average flow, which is one level lower. According to AOR exhibit the best flow properties Cab-O-Sil®. Aerosil® and Cab-O-Sil® are chemically identical substances i.e. colloidal silica, but each prepared by a slightly modified technology (depending on the producer). Both substances are recommended as glidants. Even so, there are between them differences in flowability and cohesion. The role of the technologist remains to use the most of this knowledge to compile the optimum formulation of solid dosage forms.

4. CONCLUSION

In this study, the basic characteristics of glidants were determined. It has been demonstrated, that Cab-O-Sil® exhibits monomodal distribution curve, unlike multimodal particle distribution of magnesium stearate. Values of compressibility and cohesion of glidants were determined by two different methods, which were in relative agreement. In particular, four different flow characterization methods of glidants were compared and discussed. Determination of flowability regime according to flow index has discovered that Aerosil® and Cab-O-Sil® belong into the same group always having trouble-free of flow. Dividing according to the flow index classifies magnesium stearate into the group belonging immediately before group of Aerosil® and Cab-O-Sil®. Minor differences in the flowability of Aerosil® and Cab-O-Sil® were recognized in case of using method according to Carr's index, Hausner ratio and angle of repose. Carr's index and Hausner ratio are straightforward and well-established method that allows good differentiation for fine glidants. But the results are strongly affected by the initial pouring of the powder. These limits are removed by angle of repose Zenegero method, where fine material is continuously transported by the vibrating conveyor. This method is therefore suitable for fine nanoglidants.

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