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Effect of relative air humidity on the flowability of lactose powders

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ABSTRACT

Moisture is known to affect the flowing properties of powders. However, the quantification and the understanding of the observed effects are far to be obvious. To study air moisture influence on powder flowability in a laboratory, a conditioning system and a precise flowmeter are necessary. Simple flow testers, which are commonly used R&D laboratories, are not able to quantify precisely the effect of moisture on powders. The use of advanced techniques is necessary. In this paper, we present how a precise and user-friendly flowability test associated with a dynamic conditioning system can be used to quantify the influence of moisture on the flowability properties of lactose powders. The effect of residence time T in high humidity conditions is analyzed. Afterward, we show that the relative humidity range that optimizes the flowability of lactose powders is between 30% and 50%. For lower values of the relative humidity, the apparition of electric charges inside the bulk induces cohesive forces. For higher relative humidity, the condensation of the air humidity at the contact between the grains forms capillary bridges which favors also the cohesive interactions. A model taking both triboelectric and capillary effects into account is proposed to fit the experimental data.

1. Introduction

Granular materials, fine powders and nanopowders are widely used in industrial applications [1,2]. In particular, lactose powders are commonly used as an excipient for dry powder pharmaceutical formulations (dry powder inhaler, tabs, capsules). Indeed, lactose is inert, non-toxic and cheap. Therefore, any progress in the understanding of lactose powders behaviors could have huge consequences for pharmaceutical industries for the optimization of industrial processes or to avoid technical issues (caking, clogging, noncompliance or unconformity of the by-product). In order to control and to optimize processing methods, these materials have to be precisely characterized. This characterization methods is related either to the properties of the grains or to the behavior of the assembly of grains. The relation between physico-chemical (size, shape, crystallinity, etc.) grain properties and the macroscopic behaviors (flowability, density, cohesiveness, etc.) of the powder is far to be obvious. Therefore, both measurement types have to be performed. Many advanced methods are available to measure physico-chemical grain characteristics: laser diffraction to obtain the grain size distribution, morphometer to measure grains shape, X-ray diffractometer to characterize crystallinity, …However, concerning the physical behaviors of an assembly of grains, most of the techniques used in R&D or control quality laboratories are based on old measurement techniques [3]. During the last decades, some interesting techniques have been developed like shear cells and powder rheometers. However, the evolution of this field is still at his beginning. Indeed, even at the fundamental point of view, the determination of the physical laws that govern the behavior of a granular material is still a matter of intense debates in the physics community [4,5].

Recently, the rotating drum measurement method has been revisited according to the present fundamental knowledge [6]. The existence of the optimized equipment called GranuDrum opens new perspectives due to both its precision and conceptual simplicity. This equipment measures the flowing angle inside a rotating drum as a function of the rotating speed. The cohesion between the grains is also estimated through the fluctuations of the

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flow free surface. Fig. 1 shows two typical flows in the rotating drum: (left) a non cohesive flow and (right) a cohesive flow. In contrary to the shear tester where the powder is loaded, the rotating drum is a free flow test. The free flowing behavior inside the rotating drum is comparable with powder dynamics inside many industrial processes such as conveyor, mixer, granulator, etc.

Granular materials behavior is influenced by (i) steric repulsions, (ii) friction forces (iii) cohesive forces and (iv) interaction with the surrounding fluid (gaz or liquid). The steric repulsion is related to the grains geometry. Friction forces are influenced by both surface state (rough or smooth surface) and chemical nature of the grains. Cohesive forces may be induced by the presence of liquid bridges [7–9], electric charges [10], van der Waals interactions [11] or magnetic dipole-dipole interactions [12–16]. The predominance of one of these forces depends on both the environmental conditions and the physicol-chemical properties of the grains.

Moisture is known to affect both static and dynamic behaviors of a granular materials [8,9,18,19]. However, the effect of moisture is far to be obvious. Indeed, moisture influences surface grains conductivity, capillary bridges formation and relative air permittivity [20]. For low relative air humidity, the electrical conductivity necessary for charge dissipation is reduced and the relative permittivity comes close to vacuum permittivity. Therefore, the electric charges created by triboelectric effects lead to uncontrolled electric field, electrostatic forces between the grains and/or between the grains and the container. For high relative air humidity, the electrical conductivity increases, liquid bridges may be formed at the contacts between the grains and the relative air permittivity increases. Therefore, the electrical charges are dissipated more easily. However, the apparition of liquid bridges induces cohesive forces inside the packing. At intermediate relative humidity values the cohesion is expected to decrease. In addition to these effects, the humidity could also modify the chemical characteristics of the grain surface [21], the strength of the Van des Waals interactions [22] and the friction due to lubrication effects [23].

To measure the effect of relative air humidity on the flowability of a powder sample in a laboratory, a conditioning system is necessary before the flowability measurement. Powders are usually conditioned with a static method. The sample is generally poured in a container, which is put in a climate chamber. The exchanges between the air and the powder bulk is limited. Indeed, only the upper part of the powder bed can have exchange with the controlled atmosphere. In the worse case, a crust forming phenomenon prevents access of the humidity to the powder situated in the bottom of the container. Moreover, the static approach may generate physical and/or chemical heterogeneity in the sample, leading to artefacts during the following measurement. In the present study, the powder is conditioned at controlled relative air humidity in a slowly rotating reactor to optimize the exchanges between the surface grain and the moisture.

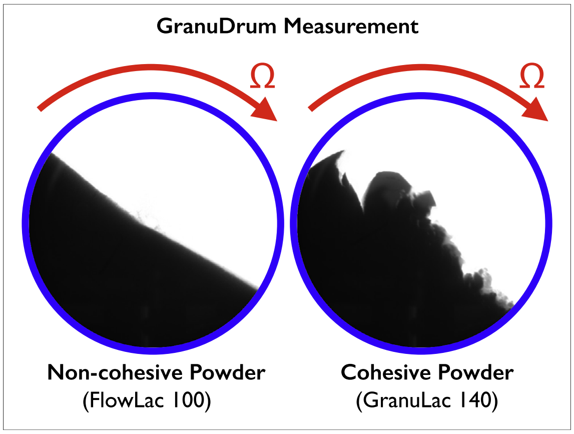

Fig. 1. Two typical flows obtained with GranuDrum Instrument. (left) Regular flow obtained with the non cohesive powder FlowLac 100. (right) Irregular flow obtained with the cohesive powder GranuLac 140. The powder cohesiveness measured with the GranuDrum instrument corresponds to the fluctuations of the air-interface position.

Watling et al. [21] have found a significative aging of lactose powders after an exposure at 75% RH, 40° C during six months. The observed effect was mainly related to a dissolution of the smallest particles covering the big ones leading to a modification of the surface state of the coarse lactose. This effect, which needs long time exposure, is not expected in the present study. The influence of shorter residence times of pharmaceutical powders in controlled humidity conditions has been investigated Crouter et al. [24] (48 h) and by Emery et al. [9] (24 h). In particular, Emery et al. have shown that simple flow testers (tapped density test, angle of repose measurement, flow through an aperture, …) are not able to quantify the effect of moisture on lactose powders. Only the Jenike shear test was found to give acceptable results. Unfortunately, this test is difficult to operate and time consuming. Therefore, to quantify efficiently the effect of moisture on powders, a reliable and user-friendly flow tester is necessary in addition to the simple tests and to the shear cell measurements.

In the present paper, we show how relative air humidity influences lactose powder flowability after a short residence time (only a few hours). The powder samples are first conditioned at controlled relative air humidity in a rotating reactor to optimize the exchanges between the surface grain and the moisture. Afterward, the flowability is measured with the GranuDrum equipment [6].

2. Materials and methods

2.1. Lactose powders

Three lactose powders produced by the company Meggle and widely used in pharmaceutical industries have been used: GranuLac 140 (G140), InhaLac 230 (I230) and FlowLac 100 (F100). All the samples are α-lactose monohydrate powders. Granulac powders come from milling process. Inhalac powders are milled and sieved lactose powders. Finally, FlowLac powders are obtained from spray-dried lactose suspensions. Powders have been selected in order to have similar grain size distributions but resulting from different process.

2.1.1. Particle sizing

The grain size distributions have been measured with the dry method with a laser diffraction particle size analyzer (Malvern, Mastersizer Sirocco 2000). The measurements have been made with an air injection pressures fixed at 1.2 bar. The refractive index of particles was fixed to 1.5 and the default model was selected.

2.1.2. Scanning electron microscopy

Scanning Electronic Microscopy (Philips ESEM XL30 FEG, Eindhoven, NL) with an acceleration voltage of 5 kV was used to analyse qualitatively the grains morphology. Samples were deposited on carbon tapes. Sputtering deposition was done with gold target under argon atmosphere (Balzers, SCD004, Sputter coater).

2.2. Conditioning

Before the flowability measurement, the powder is conditioned during a time T in a slowly rotating reactor. The reactor is a 316L stainless steel tube of internal diameter $D = 48$ mm and length