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Continuous micro-feeding of fine cohesive powders actuated by pulse inertia force and acoustic radiation force in ultrasonic standing wave field

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ABSTRACT

Stable continuous micro-feeding of fine cohesive powders has recently gained importance in many fields. However, it remains a great challenge in practice because of the powder aggregate caused by interparticle cohesive forces in small capillaries. This paper describes a novel method of feeding fine cohesive powder actuated by a pulse inertia force and acoustic radiation force simultaneously in an ultrasonic standing wave field using a tapered glass nozzle. Nozzles with different outlet diameters are fabricated using glass via a heating process. A pulse inertia force is excited to drive powder movement to the outlet section of the nozzle in a consolidated columnar rod mode. An acoustic radiation force is generated to suspend the particles and make the rod break into large quantities of small agglomerates which impact each other randomly. So the aggregation phenomenon in the fluidization of cohesive powders can be eliminated. The suspended powder is discharged continuously from the nozzle orifice owing to the self-gravities and collisions between the inner particles. The micro-feeding rates can be controlled accurately and the minimum values for RespitoseSV003 and Granulac230 are 0.4 mg/s and 0.5 mg/s respectively. The relative standard deviations of all data points are below 0.12, which is considerably smaller than those of existing vibration feeders with small capillaries.

1. Introduction

Continuous micro-feeding of powders has recently gained importance owing to the rapidly increasing interest in many industrial operations, and is a topic of intense research. Such operations include the micro-feeding of powder in pharmaceutical research, development, and production, in particular for high-potency active pharmaceutical ingredients (HPAPI) (Mehrotra, 2010) with only a few mg (or less) of an active pharmaceutical ingredient (API) in a drug product. In such cases, feed rates below 10 g/h might be needed. However, most of the API and its excipient powders (e.g., α-lactose monohydrate powder) are cohesive materials and made of very fine or sticky particles (Hertel et al., 2018). In these powders, the size of individual particles is reduced below several microns, the interparticle cohesive forces begin to play a major role in the bulk powder behavior. Van der Waals forces are the main cohesive forces between fine powders (Li et al., 2004). The strong interparticle attraction forces determine the formation of aggregates (Barletta and Poletto, 2012), which influence powder flowability and may cause the micro-feeding process to be unstable and inaccurate. Because of this, the operations to fill capsules or blisters with such small powder quantities are generally very difficult, especially in a commercial-scale manufacturing process.

In recent years, many continuous mass powder feeding techniques, such as pneumatic (Kaur et al., 2017; Graham et al., 2013), volumetric, screw/auger, and electrostatic methods, have been emerging in the research field of solid freeforming (Yang and Evans, 2007) and pharmaceuticals. The pipeline gas pressure is the driving force in the pneumatic conveying of fine powders and it is suitable for feeding massive amounts of powder in several industries, such as coal fired thermal power plants (Mittal et al., 2014). Corona/tribo charging guns are widely used in electrostatic methods to spray fine powders. The powder is actuated in an electric field generated by the ionization of air by imposing a high voltage on a sharp, pointed needle-like electrode. However, its complexity makes their use impractical (Yang et al., 2017). Thus, continuous powder feeding at mass flow rates above 300 mg/s is possible on a routine basis with some restrictions for strongly compressible or cohesive materials.

The accurate continuous micro-feeding of fine powders appears to remain a critical step in practice, and has recently gained importance in many fields, especially in pharmaceutical development. In cohesive fine powder micro-feeders (feed rate below 100 mg/s), the most commonly used are vibration methods, the most common of which are the acoustic vibration feeder (Yang and Evans, 2005; Chen et al., 2012a,b) and ultrasonic vibration feeder (Lu et al., 2008) according to the vibration

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frequency. In vibration feeders, small capillaries (Matsusaka et al., 1996; Qi et al., 2011; Lu et al. 2009) with orifices of a diameter in the same order of magnitude as the particles are often used. The feed rate can be controlled, e.g., via the frequency or the orifice diameter. For metal, ceramic, and glass powders, the small capillaries may obstruct the powder flow via arching, plugging, and blocking in the absence of agitation (Lu et al., 2006; Lu et al., 2007). However, for API and its excipient powders, the influence of powder/wall interactions cannot be neglected owing to the high surface-to-volume ratios, e.g., in small cavities, channels, or tubing, of such small powder quantities. When gravitational forces are comparatively small, interparticle forces become important (Zhu et al., 2017). Powders that are cohesive and of low density tend to block the capillary tube owing to particle aggregates, which are not able to break under mechanical vibration.

To avoid the technical problem of the cohesive fine powder blocking phenomenon in capillaries, Besenhard et al. (2015, 2016) demonstrated the feasibility of a micro-feeder with a vibratory sieve system mounted on a chute. Feed rates in the range of 3–10 g/h were obtained. However, the powder properties required special attention. To solve this problem, they presented a volumetric micro-feeder based on a cylinder piston system (Besenhard et al., 2017). The feed rate ranging from 1 to 100 g/h can be conveniently adjusted via the piston speed or the cylinder diameter and the powder properties do not have a considerable effect on the feed rate.

To solve the problem of the cohesive fine powder blocking phenomenon in capillaries, this paper describes a novel method of continuously feeding cohesive fine powders simultaneously actuated by a pulse inertia force and an acoustic radiation force in an ultrasonic standing wave field. The micro-feeding process can be divided into two steps. First, the powder in the nozzle moves forward toward the nozzle outlet section actuated by the pulse inertia force in a consolidated columnar rod mode. Second, the powder rod breaks into several small agglomerates actuated by the ultrasonic radiation force, and is discharged from the nozzle orifice into the capsule body or other micro vessels continuously.

2. Materials and methods

2.1. Materials

Lactose is a well-known and widely used sieved carrier for inhalation APIs (Kou et al., 2012; Faulhammer et al., 2014) because of its wide availability and, in particular, its historically good record of safety and tolerability. As typical very fine α-lactose monohydrate powders, RespitoseSV003 (DFE Pharma, Goch, Germany) and GranuLac230 (Meggle, Wasserburg, Germany) were used as the feeding materials in the experiment. Their micro morphologies and characteristics were studied using scanning electron microscopy (SEM, ZEISS EVO18), which shows that there are many small particles adhering to the larger ones and most of the larger particles have irregular prism shapes, as shown in Fig. 1. Furthermore, the small particles adhering to the larger ones in GranuLac230 powder (Fig. 1(b)) are much smaller than that of RespitoseSV003 (Fig. 1(a)) and are in nanometer Scale. This micropattern indicates that GranuLac230 has a stronger cohesive force between particles than RespitoseSV003 because the powder with nanoparticles adhering to the surface of cohesive powders has larger interparticle van der Waals force (Ruzaidi et al., 2017; Zhu et al., 2017).

Properties of the two kinds of powders are described in Table 1. The angle of repose (AoR) was determined using a glass funnel by an AoR determinator (FT-104B2, Beijing Zhongyiwancheng Technology Co., Ltd). The aspect ratio (AR) is the ratio between F_{min} and F_{max} (Feret diameters), which describe the shape of the particles; its value is between 0 and 1. The higher the value, the more spherical the shape. Thus, the low aspect ratio of 0.69 and 0.68 show that the powder particles have an irregular shape, which may cause the aggregation phenomenon more seriously. The powders were stored at a relative humidity (RH) of < 55% and a room temperature of < 25 °C.

2.2. Micro-feeding system

As shown in Fig. 2, the experimental facility consists of a pulse inertia force providing system, an ultrasonic standing wave generating system, a glass nozzle, lab scale (220 g ± 0.1 mg, AUY220, Shimadzu, Japan), and digital microscope (AM4113ZT4, Dino Lite). The pulse inertia force providing system was developed to produce a sufficient inertia force for powder in a glass nozzle and drive the consolidated powder in the columnar rod mode to continue moving toward the outlet section of the nozzle. The ultrasonic standing wave generating system was developed to apply acoustic radiation force to the powder rod to suspend it and break it into several small agglomerates. The glass nozzle was fixed with the down face of the PZT stack actuator and its outlet orifice was placed above the lab scale. During feeding into a weighing dish, the weight was recorded once per second via the scale's serial port. A digital microscope with frame rate of 30 fps was used to record the micro-feeding process. All of the micro-feeding experiments in this study were conducted at an RH < 55% and a room temperature of < 25 °C.

2.2.1. Pulse inertia force providing system

The pulse inertia force providing system comprises a connector A, PZT stack actuator (PAL200VS25, NanoMotions, China), connector B, power amplifier, and function generator. The micro-nozzle is clamped by connector B, which is vertically fixed with the down face of the PZT stack actuator while the upper face is fixed with connector A and kept stationary. As shown in Fig. 3, the PZT stack actuator is constructed of several disc-shaped piezoelectric ceramic pieces, the thickness of which is in the range of 0.02–1 mm. There is an approximate linearity between the applied voltage amplitude and the down face displacement of the actuator. The typical waveform of the driving signal is one quarter of a sine wave. The amplitude (U_p) and frequency ($f_p = 1/T$) are in the range of 10–110 V and 1–256 Hz, respectively.

As shown in Fig. 4, when applied to the driving signal of a one-quarter sine wave, the PZT stack actuator stretches and exerts a driving force F_1 on the solid wall of the glass nozzle. Therefore, the glass solid wall and powder move along the nozzle axis. Then, the interparticle cohesive force f_0 (wall-particle and particle-particle friction) within the powder transfers the movement and the powder obtains a velocity v. When the applied pulse driving signal decreases rapidly to zero in magnitude, the actuator contracts and the glass solid wall obtains a pulse acceleration. In that the system is not an infinitely rigid system, the pulse acceleration is a definite value. The acceleration is measured by a piezoelectric accelerometer (CA-YD-103, SINOCERA PIEZOTRONICS. INC.), a charge amplifier (YE5852, SINOCERA PIEZOTRONICS. INC.) and an oscilloscope (TDS-2022, Tektronix), as is shown Fig. 5(a). The value of acceleration can be calculated by:

$$a = \frac{U_m}{S_c \times S_a} \tag{1}$$

where U_m is the peak voltage shown in an the oscilloscope; S_c is the amplification factor of charge amplifier which is 1.82CP/m·s^{-2}; S_a is the sensitivity of the piezoelectric accelerometer which is 10 mV/CP. The waveform of the acceleration in two driving periods is shown in Fig. 5(b). The acceleration values are shown in Fig. 5(c) when the amplitude is in the range of 10–110 V and the frequency is 1 Hz. It can be seen that the values increase sharply with increasing signal voltage. The maximum value reaches 400 m·s^{-2} when signal amplitude voltage is 110 V.

Consequently, the powder inside the nozzle obtains a pulse inertia force F_{inertia} relative to the solid wall of the glass nozzle. If the inertia force F_{inertia} is small in magnitude, the resultant inertia force F_{inertia} and local gravity G_0 of the powder itself is less than the interparticle cohesive force f_0', and the powder and glass solid wall will move back. If