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Research paper

Analysis of particle kinematics in spheronization via particle image velocimetry

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ABSTRACT

Spheronization is a wide spread technique in pellet production for many pharmaceutical applications. Pellets produced by spheronization are characterized by a particularly spherical shape and narrow size distribution. The particle kinematic during spheronization is currently not well-understood. Therefore, particle image velocimetry (PIV) was implemented in the spheronization process to visualize the particle movement and to identify flow patterns, in order to explain the influence of various process parameters.

The spheronization process of a common formulation was recorded with a high-speed camera, and the images were processed using particle image velocimetry software. A crosscorrelation approach was chosen to determine the particle velocity at the surface of the pellet bulk. Formulation and process parameters were varied systematically, and their influence on the particle velocity was investigated.

The particle stream shows a torus-like shape with a twisted rope-like motion. It is remarkable that the overall particle velocity is approximately 10-fold lower than the tip speed of the friction plate. The velocity of the particle stream can be correlated to the water content of the pellets and the load of the spheronizer, while the rotation speed was not relevant.

In conclusion, PIV was successfully applied to the spheronization process, and new insights into the particle velocity were obtained.

1. Introduction

Extrusion/Spheronization (ES) is an established technique for pellet manufacturing on an industrial scale. It is known for producing remarkable pellet properties, such as narrow size distribution and spherical shape [1]. It is a multi-step process, of which spheronization is the most challenging [2,3]. A significant body of research so far has focused on a variety of excipients that are particularly useful for spheronization, called Spheronization Aids [4,5]. However, Microcrystalline Cellulose (MCC) is still the gold standard [6], based on its outstanding properties [7]. Furthermore, several investigations dealt with the influence of process parameters on the pellet properties [8–10]. Thereby, the water content, the speed, the duration, and load were identified as major influences on the pellet properties. In Schmidt's work, the influence of different friction plate designs on the pellet properties was discussed [11]. A cross-hatched structure (Fig. 1) intensified the contacts between the particles and the rotating plate.

Different mechanistic models of pellet formation were suggested during the last few decades [11,12]. However, they have not, so far, been linked to the process parameters of spheronization [13]. The link between the mechanistic models and previous investigations might be the pellet motion. As early as the very first article about spheronization, Reynolds described a "rolling motion" that is related to the particle formation [3]. This motion might be able to link the investigation regarding the process parameters to the mechanistic models of pellet formation. In further studies, this motion is described as an overlay of the toroidal movement induced by the rotating friction plate, and a poloidal movement induced by the centrifugal forces [14]. Quantitative information about the particles' velocities or the impact impulses is still missing, but is of high interest because these are key parameters in explaining the spheronization process.

Particle image velocimetry (PIV) turns back to a review article of Adrian [15] that summarized all relevant velocity-measuring techniques based on images. Initially, PIV was used for measuring the flow of transparent fluid phases with a low fraction of solid or gas tracers and is well established for this application [16,17]. Snapshots of the system are taken after defined time intervals, and the intervals are chosen such that the particle moves only a small fraction of the distance between it and its neighboring particle. The particles are tracked in order to calculate the distances they move between two consecutive images, and thereby determine their velocity. The challenge when using granular materials is to track single particles over time, because the number of similar-looking particles in one volume element is high. Two possible methods to overcome this challenge suggest themselves: adding

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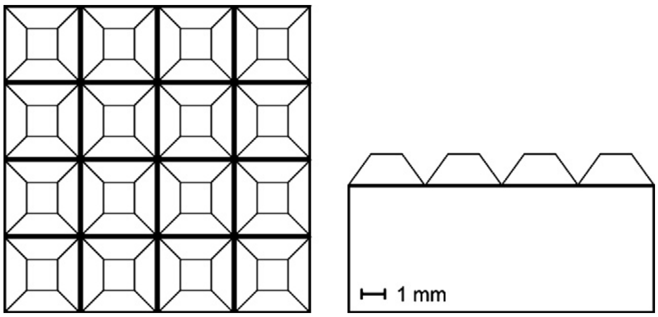

Fig. 1. Schematic drawing of the friction plate's surface structure, viewed from top (left) and side (right) [11].

tracer particles of a different color to facilitate following them or searching for "patterns" instead of single particles. The first method, using different-colored particles, was used by Conway [18]. The second method [19,20] was chosen in this study, because previous studies [21] showed a mass transfer between particles of different color in the spheronizer, which would interfere with colored tracer particles. Another, far more complex, alternative technique for tracking particle velocities would be positron emission particle tracking (PEPT) [22].

The aim of this study was to investigate the pellet velocity in spheronization in order to get deeper insights into the mechanisms of spheronization using a common formulation from microcrystalline cellulose and lactose. To accomplish this, the spheronization process was recorded by a high-speed camera, and the data were evaluated by a PIV algorithm. Several spheronization parameters (water content, rotation speed, loading, duration, and shape of the friction plate) were varied systematically to quantify their effect on the particle velocity. The following subgoals were defined:

– Validation of PIV algorithm
– Visualization of particle movement
– Evaluation of spheronization parameters

2. Materials

Microcrystalline Cellulose (MCC 102G SANAQ®, Pharmatrans Sanaq, Basel, Switzerland) and α-Lactose monohydrate (Granulac® 200, Meggle, Wasserburg, Germany) were used in the 20:80 ratio, and deionized water was added as the granulation liquid (Table 1).

3. Methods

3.1. Extrusion/spheronization

3.1.1. Powder blending

A formulation containing microcrystalline cellulose and α-lactose monohydrate was blended for 15 min at 20 rpm (LM40, Bohle, Ennigerloh, Germany) and loaded into the gravimetric powder feeder (KT 20, K-Tron Soder, Niederlenz, Switzerland) of the extruder (Mikro 27GL-28D, Leistritz, Nuremberg, Germany).

Table 1
Overview about the factors.

Factors	−1	0	+1
Loading (g)	300	900	1500
Rotation speed (rpm)	500	750	1000
Water content (%)	26	32	38
Time (s)	10	–	300
Plate design	Smooth	–	Hatched
Camera position	Top	–	Side

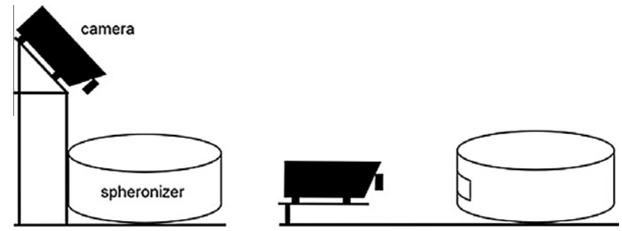

Fig. 2. Camera position from above the pellet stream (left) and through a side window (right).

3.1.2. Extrusion

The formulation was extruded at a screw speed of 100 rpm and a powder feed rate of 33 g/min. The liquid feed was adjusted to obtain water content from 26% to 38% (w/w, based on dry mass) as shown in Table 1. The extruder compressed the wet mass through 23 dies of 1 mm diameter and 2.5 mm length.

3.1.3. Spheronization

Batches of 300–1500 g of extrudates were transferred into the spheronizer (RM 300, Schlueter, Neustadt/Ruebenberge, Germany) and spheronized for 10 s and 300 s with varying rotation speeds from 500 to 1000 rpm.

3.2. High-Speed Imaging

The spheronization process was recorded with a high-speed camera (Fastcam SA4, Photron, San Diego, USA) from two different positions. One camera was positioned to record the top of the torus (Fig. 2, left) and the second was positioned to record at the bottom through a transparent side window in the spheronizer jacket (Fig. 2, right). The particle stream was illuminated using a single high power LED in synchronized pulse mode (High Power LED illumination set, Ila GmbH, Juelich, Germany). For each accumulation, grayscale images (8 bits) of 1024 × 1024 pixels were taken at a frequency of 2000 fps (4000 fps for the side view).

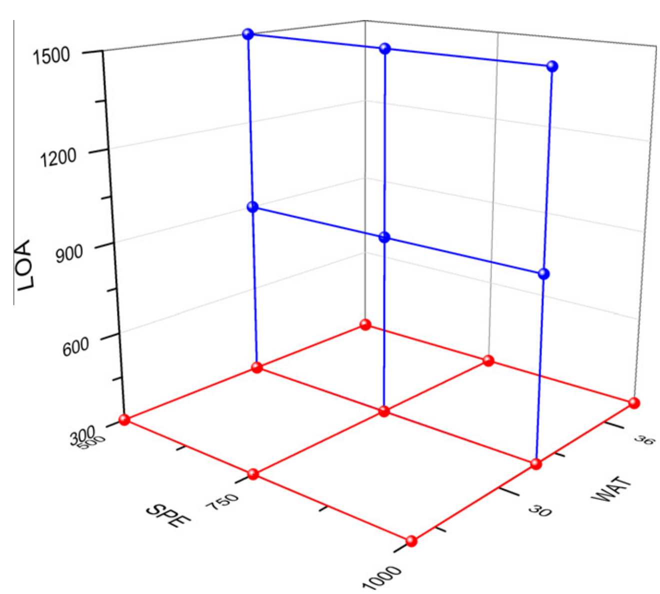

Fig. 3. Designs of experiments (first DoE red, second DoE blue). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)