European Journal of Pharmaceutical Sciences 104 (2017) 72–81

Contents lists available at ScienceDirect

European Journal of Pharmaceutical Sciences

journal homepage: www.elsevier.com/locate/ejps

# Comparison of video analysis and simulations of a drum coating process

P. Boehling[a,*], G. Toschkoff[a], R. Dreu[b], S. Just[b], P. Kleinebudde[b], A. Funke[d], H. Rehbaum[e], J.G. Khinast[a,c]

[a] *Research Center Pharmaceutical Engineering GmbH, Graz, Austria*
[b] *Institute of Pharmaceutics and Biopharmaceutics, Heinrich Heine University, Düsseldorf, Germany*
[c] *Institute for Process and Particle Engineering, Graz University of Technology, Graz, Austria*
[d] *Chemical and Pharmaceutical Development, Bayer Pharma AG, Berlin, Germany*
[e] *L.B. Bohle Maschinen + Verfahren GmbH, Ennigerloh, Germany*

## ARTICLE INFO

*Keywords:*
Tablet coating
Simulation
DEM
Experiments

## ABSTRACT

Tablet coating is a common unit operation in the pharmaceutical industry. To improve currently established processes, it is important to understand the influence of the process parameters on the coating quality. One of the critical parameters is the tablet velocity. In this work, numerical results are compared to results obtained experimentally.

Tablet movement in the drums was simulated using the Discrete Element Method (DEM). The simulation parameters were adapted to fit the simulation to the experimental data. A comparison of the experimental and simulation results showed that the simulation correctly represents the real tablet velocity. A change in the velocity over time and its dependence on the rotation rates and the baffle position in the simulation were similar to the experimental results.

In summary, simulations can improve the understanding of tablet coating processes and will thus provide insights into the underlying process mechanics, which cannot be obtained via ordinary experiments.

## 1. Introduction

In the pharmaceutical industry, tablet coating is commonly performed as the last step of the drug production process. Perforated pan coaters are generally the equipment of choice since they provide a gentle yet effective mixing of the tablet bed. Mixing, spraying and drying may occur simultaneously during coating. Understanding the underlying processes involved results in a better quality of the final product. A low coating variability is often required, especially for active coatings. Coating variability is significantly affected by the drum design, the rotation rate, the number of nozzles, the spray rate, the coating time and the drying temperature (Porter et al., 1997; Tobiska and Kleinebudde, 2003; Smith et al., 2003). Good mixing in the tablet bed is essential for the homogeneous quality of the end product. Mixing is influenced by the pan speed, which in turns controls the mechanical energy introduced into the system.

Image analysis software for particle tracking, in combination with tracer tablets, was used in previous studies (Alexander et al., 2002; Mueller and Kleinebudde, 2007; Rantanen and Khinast, 2015; Ketterhagen et al., 2009) to automate the analysis of tablet motion. The effects of pan loading, pan speed and particle shape on the circulation times, surface appearance times, projected area of particles per pass and cascading velocities were investigated. Most of these studies were only performed on the laboratory scale. Some studies reported rules that govern the cascading velocities (Mueller and Kleinebudde, 2007) when the process is scaled up. In this work, we propose an alternative approach, which combines a high speed camera with an image analysis spatial cross-correlation algorithm, to calculate the velocity fields in the tablet bed without tracer tablets. By computing the difference in the tablet position between two images, the velocity of the tablets can be calculated.

Experiments are expensive and can be material- and time-consuming. Furthermore, dedicated experiments are generally unfeasible after implementing final changes to the process. When planning a new process or optimizing an existing one, simulations can be used to reduce the number of experiments required (Rantanen and Khinast, 2015). The Discrete Element Method (DEM), which is increasingly applied in the pharmaceutical industry to simulate various processes (Ketterhagen et al., 2009), can help to improve the understanding of granular material flows. Due to a low number of particles and a relatively large size of tablets, tablet coating is particularly suitable for the DEM analysis (Just et al., 2013a; Kalbag and Wassgren, 2009; Dubey et al.,

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* Corresponding author.
*E-mail address:* peter.boehling@rcpe.at (P. Boehling).

http://dx.doi.org/10.1016/j.ejps.2017.03.031
Received 9 September 2016; Received in revised form 27 February 2017; Accepted 23 March 2017

2011). When applying DEM, matching the simulations with experiments is crucial (Toschkoff et al., 2015). Spheres were often used to simplify the tablet shape in the simulations (Kalbag and Wassgren, 2009; Kalbag et al., 2008). However, since the tablet shape influences the bulk behavior and the validity of the simulation results (Freireich et al., 2011; Suzzi et al., 2012), the way the tablet shape is modeled greatly influences the simulation outcome. There are several methods to imitate the shape of the real tablets. In this work, we followed the glued-sphere approach (also termed the multi-element model) (Favier et al., 1999), which was successfully used in numerous works (Freireich et al., 2011; Suzzi et al., 2012; Toschkoff et al., 2013; Ketterhagen, 2011). It involves several simple shapes (spheres) arranged to mimic the real tablet shape. In this work, we employed the “eXtended Particle System” (XPS), an in house developed DEM software that uses the CUDA programming language to parallelize DEM on graphics processing units (GPUs) (Radeke et al., 2010; Jajcevic et al., 2013).

The validity of the experimental results is shown first. A base configuration was chosen and the simulation material parameters were fitted to best reflect the experimental results. A full numerical DOE was performed on the laboratory and pilot scales using the parameters that fit the experiments best. The results show that it is possible to realistically simulate the behavior of a tablet bed and determine the tablet velocity. Moreover, they can predict the tablet velocity on larger scales. Finally, we investigated the influence of the material on the process outcome (coefficient of variation) and established that the elastic properties have a major effect on this quality parameter.

## 2. Material and Methods

### 2.1. Drum and Tablets

This work is a part of an active-coating-process optimization for the production of tablets that contain two active pharmaceutical ingredients (APIs): one with immediate release in the coating layer (active coating) and the other with sustained release in the core. For studying the process of tablet-core coating, gastrointestinal therapeutic systems (GITS 30) were used as a starting material (Bayer Pharma AG, Leverkusen, Germany). GITS 30 are round biconvex two-layer tablets that contain the API Nifedipine. They have a diameter of 9 mm and a height of 5 mm and are pre-coated with cellulose acetate and polyethylene glycol. The tablet shape used in the simulations can be seen in Fig. 1 which is taken from (Boehling et al., 2016a).

The tablet velocity assessment experiments were performed on the laboratory scale using a perforated drum coater BFC 5 with a 5 kg drum and on the pilot scale using a BFC 50 using a 25 kg drum (both L.B. Bohle Maschinen + Verfahren GmbH, Ennigerloh, Germany). The 5 kg and 25 kg coating drums for the experiments and the detailed geometry of the drums were provided by the manufacturer.

### 2.2. Experimental Determination of Tablet Velocity

Drum filling degrees of 12.6% and 16.9% were used in the experimental part of our study. Experiments were done in cooperation with Dreu et al. (2016). Rotation rates of the 5 kg and 25 kg coating drums were varied in order to achieve circumferential drum speeds of 8.3, 16.5, 24.8, 33.1, 41.1 cm/s and for the 25 kg-coating drum, additionally, of 49.6 cm/s. In order to determine tablet surface flow velocities, a 560 or 1180 mm borescope (88590DF, 88770DF, Karl Storz GmbH, Germany) was inserted sideways into the coating drum and mounted to a high-speed camera (MotionBLITZ EoSens mini 2, Mikrotron GmbH, Germany). A high-speed video of the externally-illuminated tablet surface flow was taken at a frame rate of 1 kHz and with a shutter time of 350 or 450 μs. Image pairs from the high-speed tablet surface flow video were analyzed via a cross-correlation algorithm (VidPiv 4.7, ILA GmbH, Germany). High-speed video data were imported as successive image pairs with a time gap of 1 ms and masked for the area of ~300 × 300 pixels that had sufficient sharpness and illuminance. To extract a velocity vector field for each time step, we first applied a cross-correlation algorithm with an interrogation area of 128 × 128 pixels and an interrogation grid separation of 20 pixels and continued with an adaptive cross-correlation algorithm with the same grid settings. A window filter was used to filter out velocity vector outliers. The minimum downward tablet surface flow velocity was set to one half of the drum circumferential speed. To determine the maximum threshold for the downward tablet velocity, tablets that moved to the highest location in the drum were used and a free-fall trajectory was assumed, yielding the maximum possible velocity. In order to attain the correct captured image magnification, the borescope-to-tablet-bed distance was measured in-line by an ultrasonic distance sensor (UM18, SICK, Germany). Representative tablet bed dynamic angles of repose were established by analyzing a separate sideways video (24 fps) of the tablet bed surface contour movement. The obtained spatially averaged velocities in pixels/s were transformed to velocity units by applying a distance-dependent scale and corrected for misalignment between bed dynamic angle of repose and optical axis angle, using Eq. (1):

$$|\vec{v}| = \frac{|\vec{u}|}{\cos(\Theta - \alpha)} \tag{1}$$

where $|\vec{v}|$ is the tablet surface flow velocity magnitude aligned with the tablet bed, $|\vec{u}|$ is the video-extracted tablet velocity, $\alpha$ is the optical axis angle of inclination measured from the vertical line and $\Theta$ is the local dynamic angle of repose measured from the horizontal line. The whole model is describe and shown by Dreu et al. (2016) (Fig. 1). The time averaged tablet bed distance and dynamic angle of repose was used in the transformation to determine from video the final absolute tablet velocity.

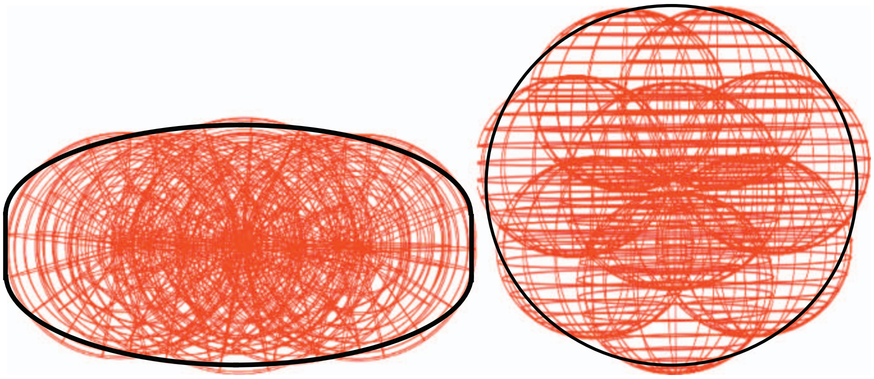

**Fig. 1.** Tablet shape modeled via the glued sphere approach taken from (Boehling et al., 2016a).