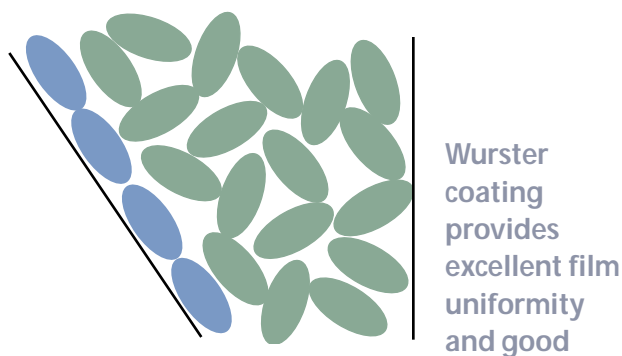


Positron Emission Particle Tracking Studies of a Wurster Process for Coating Applications

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Wurster coating provides excellent film uniformity and good active-component distribution. The authors describe the results of a study using the Wurster method with positron emission particle tracking technology.

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The coating of particles, agglomerates, and compacts is an important operation in the pharmaceutical, food, and chemical industries. Various types of equipment have been used for such a purpose, including rotating pans, fluidized beds, and spouted beds (1–4). This article describes the Wurster system, a high-velocity, circulating-bed unit widely used for coating pharmaceutical pellets and tablets. Figure 1 shows a schematic diagram of a Wurster coating unit. The system typically consists of a relatively short cylindrical column with a truncated conical chamber base, a cylindrical insert (draft tube) in the center of the chamber, and a centrally located air distribution plate below the conical base. A spray nozzle, located in the center of the air-distribution plate, enables the introduction of coating solutions and suspensions.

In a typical operation, two concentric streams of gas are used; namely, a jet of low-flow rate but high-pressure gas from the nozzle for atomizing the liquid spray and a stream of high-flow rate but low-pressure gas entering the chamber through the distributor for fluidization and the drying of particles. In operation, particles are propelled upwards in a central spout of low solids concentration and high solids velocity and move downward under the force of gravity in a slowly moving annular region of high solids density. The particles ascend in the spout until they reach the freeboard region located at the top of the bed, rain down on the annulus in the form of a fountain, and move down the annulus until they are re-entrained into the spout. A cyclic pattern of solids motion thereby is established. Particles used in spouted-bed processes generally are rather coarse, belonging to Group D in the Geldart diagram (5). The spray nozzle is located in the center of the air-distribution plate and below the draft tube, and a distinct spray zone is established within the lower portion of the draft tube.

Because the Wurster coating method provides excellent heat and mass transfer within the bed, it often is the preferred approach when uniform film and good active-component distribution are important (e.g., for precision coating or modified-release tablets) (6,7). However, because the method creates relatively high-speed solids motion in the spout region, attrition and hence elutriation may limit its application. Furthermore, dead zones may occur near the wall region in the annulus where particles move very slowly.

Table I: Particle cycle time obtained by PEPT measurements.

Run number	Batch size (g)	Gap height (cm)	Flow rate (m ³ /h)	Particle cycle time		
				Mean (s)	% RSD	Range (s)
1	400	1	62	88.1	228.3	3–736
2	700	1	55	88.2	115.6	18–373
3	700	1	48	8.7	79.3	3–54
4	1200	1	48	16.6	74.1	4–66
5	400	2	62	7.1	285.9	3–278
6	700	2	55	8.6	81.4	3–42
7	700	2	48	11.2	83.9	3–75
8	1200	2	48	15.4	76.0	4–54
9	1200	2	41	36.9	102.4	4–248
10	400	3	62	17.6	296.6	3–697
11	700	3	55	9.3	81.7	3–59
12	700	3	48	9.0	71.1	4–55
13	1200	3	48	12.3	65.9	4–41
14	1200	3	41	96.0	181.3	11–823

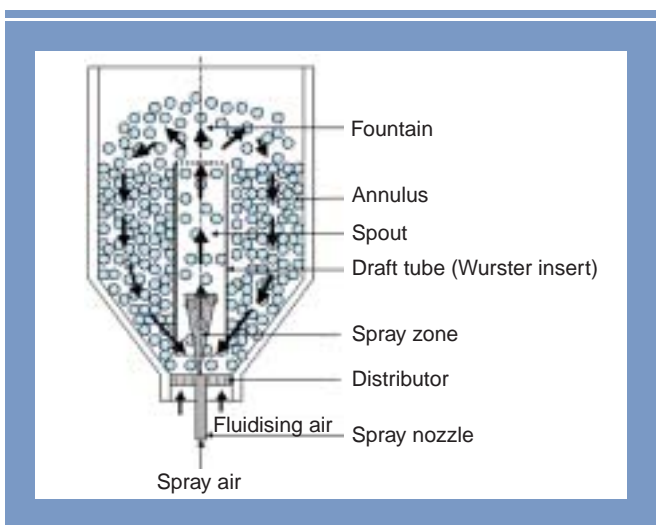


Figure 1: Schematic diagram of Wurster coating system.

However, attrition and elutriation can be minimized by controlling the operating conditions and increasing the tablet or pellet strength, and dead zones can be prevented by changing the operating conditions. The prime objective of this study was therefore to examine the effects of operating conditions (e.g., airflow rate and particle loading) and coater configuration (e.g., the gap between the draft tube and the air distributor) on solids motion. The formation of dead zones and the possibility of segregation of binary tablet mixtures also were studied. The positron emission particle tracking (PEPT) technique was used in the work, which allowed an accurate, noninvasive measurement of three-dimensional particle motion.

Materials and methods

Figure 2 provides a schematic representation of the experimental system used in this study. The system consisted of a Wurster coating device (Aeromatic Strea-1, Aeromatic-Fieldler, Switzerland), which was similar to that shown in Figure 1. The device was placed within the PEPT facility of the Positron Imaging

Centre at the University of Birmingham. The Wurster coater had a built-in fan to supply the fluidizing air, which was calibrated using a Furness Controls flowmeter. The results presented in this article were corrected against this calibration. A wire mesh installed at the top of the chamber ensured that no tablets were elutriated with the exhaust air. The air distributor of the device was more porous in the central region (below the draft tube) than in the outer area, causing a higher air velocity below the draft tube and promoting pneumatic transport up the tube. In this study, the percentage of open area of holes in the annular distributor area was 8%. The atomizing air pressure was maintained at 1 barg, which created exit velocities in the nozzle center

of ~ 120 m/s. Despite the high nozzle-exit velocity, the atomizing air contributed comparably little to the total gas flow. The gap between the air distributor and the bottom end of the draft tube was, unless stated otherwise, set to 1 cm. The Wurster coating unit allowed changes in the flow rate of the fluidizing air. The minimum flow rate of the fluidizing air was chosen as the point at which tablets could exit the Wurster column in a regular manner. The maximum flow rate was selected as the point at which the majority of tablets in the fountain contacted the wire mesh at the top of the column. The temperature of the fluidizing air was maintained at 26 ± 3 °C (i.e., slightly above ambient temperature).

The PEPT facility at Birmingham is derived from a medical positron emission tomography system. It has been used previously to study solids motion in rotating drums (8), fluidized beds (9), and mixers (10). A detailed description of the device is available elsewhere (11,12). The PEPT technique incorporates a single positron-emitting tracer particle that is placed within the bulk particles in the device of interest. Each emitted positron annihilates with a local electron in the bulk, leading to the production of two collinear, back-to-back γ rays. The γ rays are detected by two parallel detectors, enabling the line along which the positron emitter is situated to be determined. Such detections placed in succession enable the tracer to be located in three dimensions by triangulation. The two detectors have a cross sectional area of 50×40 cm² and a maximum separation of ~ 80 cm, which is sufficient to study the entire Wurster column. The detectors at the PEPT facility have very high spatial and time resolutions such that a particle moving at 1 m/s can be located within 1 mm more than 1000 times per second (12).

The raw data obtained from the experiments are tracer particle x , y , and z coordinates as a function of time. Upon processing these data, one may obtain information such as particle velocity profiles, residence time distributions within specific zones, and frequencies of particles entering specific zones. A pseudo-real time visualization of the tracer movement also can be obtained, which enables the technique to be used for rapid diagnostic and development studies.

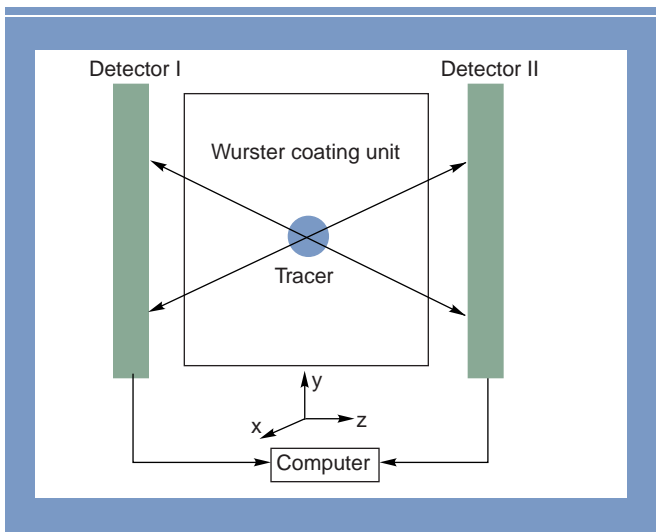


Figure 2: Schematic diagram of the experimental system.

Four round convex placebo tablets were used in this study: 100 mg (diameter = 6.5 mm), 200 mg (diameter = 7.5 mm), 300 mg (diameter = 9.0 mm), and 400 mg (diameter = 10.5 mm). Resin beads of 500–600 μm , activated by ion exchange with radioactive water produced in the Birmingham in-house cyclotron, were used as tracers. In a typical experiment, a small hole was drilled in a tablet taken from the bulk and the tracer placed in the hole, which was subsequently sealed with epoxy resin. The tracer tablet had a similar weight and size to the remainder of the batch of tablets. A Geiger counter was used to locate the tracer tablet at the end of each run and to confirm that the tracked tablet had remained intact.

Because the work was aimed at understanding solids motion, all experiments were conducted in the absence of liquid spray to prevent the introduction of additional variables (e.g., an underdrying of tablets leading to sticking and changes in tablet weights).

Results and discussion

Particle trajectory. Figure 3 shows a typical record of the y -direction (vertical) displacement. The origin of the y coordinate is located at the level of the air distributor. Figure 3 shows the existence of extensive vertical motion and that particles spend a considerable length of time in the lower part of the annulus. Figure 3 also shows a variation in the highest positions of the tracer particle and hence a range of trajectories in various cycles. The differences may arise from a variety of radial positions of the tracer tablet at the inlet of the draft tube; nonuniform gas velocity distribution in the draft tube (i.e., a zero value at the wall surface and a maximum value at the centre line) (13); rotation of the tablets in the draft tube as a result of the nonuniform gas-velocity distribution; and particle-particle and particle-draft tube wall interactions.

Particle cycle time. In particle coating processes, the time taken for a particle to go through one complete cycle of coating and drying is termed the *coating cycle time*. Because no liquid spray was used in this work, the cycle time is thus defined as the time elapsed between a particle moving up from the bottom part of

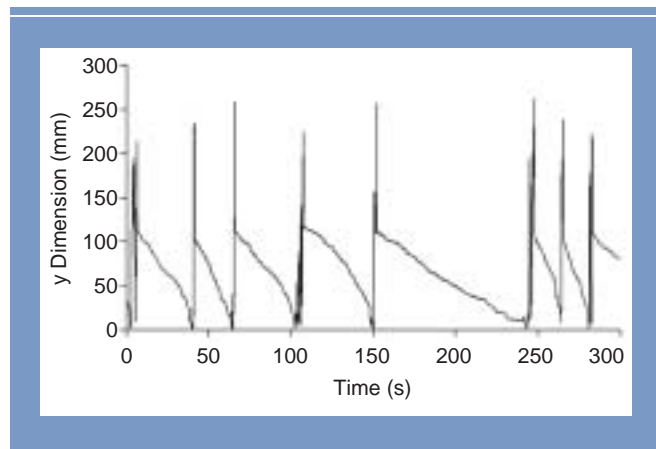


Figure 3: Vertical (y direction) displacement of the tracer, 10.5-mm tablets, 2-cm gap, and 130 m^3/h fluidizing air.

the bed through the draft tube, the fountain, and the annulus and then back to the lower part of the bed. The cycle time is often defined with reference to a particular y -coordinate. Several techniques have been used to measure particle cycle time in spouted beds, including radioactive-particle tracing (14,15), magnetic particle tracing (16,17), and an optical fiber probe technique (18–20). These studies, however, focused on spouted beds without internals, which are expected under similar operating conditions to give higher solids circulation rates than a spouted bed with a draft tube (1). The PEPT technique used in this work is more accurate than the methods described previously and also allows for particle velocities and residence times in specified zones within the equipment to be calculated.

Several parameters that may affect the particle cycle time have been examined. Figure 4 shows the effect of particle size on the cycle time. At a given airflow rate, large or heavy particles give a longer mean cycle time because smaller particles move more quickly in the draft tube for a given airflow rate and also pass more easily through the gap between the distributor and the draft tube. As expected, an increase in the airflow rate causes a decrease in the mean particle cycle time.

The batch size and the gap between the draft tube and the air distributor also have been found to have a significant effect on the particle cycle time: A large batch size leads to a long particle cycle time, whereas a large gap between the draft tube and the distributor leads to a short particle cycle time and a fast solids circulation rate. These results are in agreement with those of other published studies (21). The first observation is relatively straightforward. The latter, however, requires some clarification because it involves two competing processes. When the gap is increased, less of the gas enters the draft tube because a larger portion flares out into the annulus, thereby leading to an increase in the residence times in both the spout and the annulus. On the other hand, particles experience less resistance when they pass through a large gap. Because the resistance to particles passing through the gap is a rate-limiting step under the conditions of these runs, the overall result is that a large gap results in a short particle cycle time.

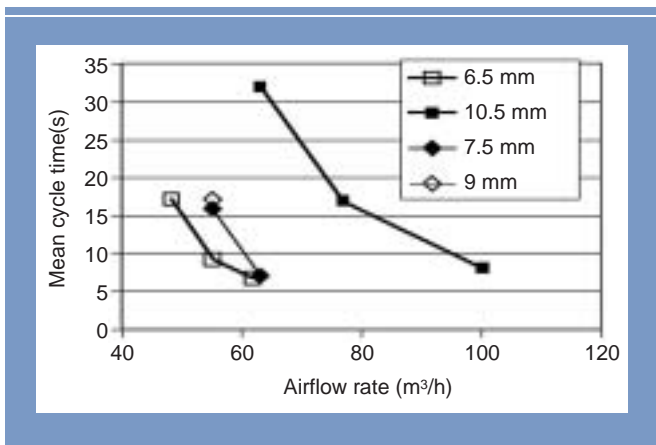


Figure 4: Effect of particle size on the mean cycle time (8% distributor opening, 2-cm gap).

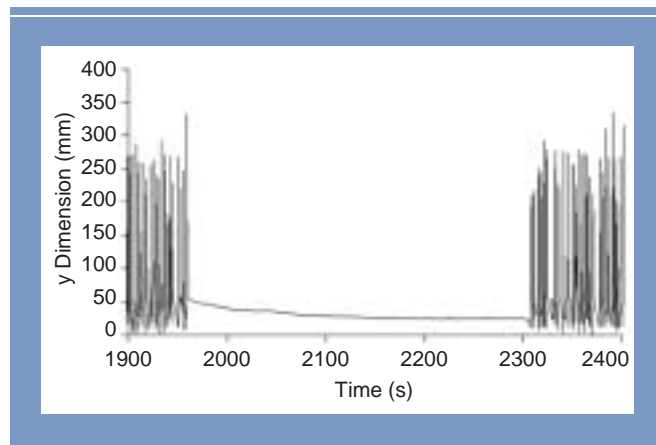


Figure 5: Vertical (y direction) displacement of the trace, showing a dead zone where particles are nearly stationary.

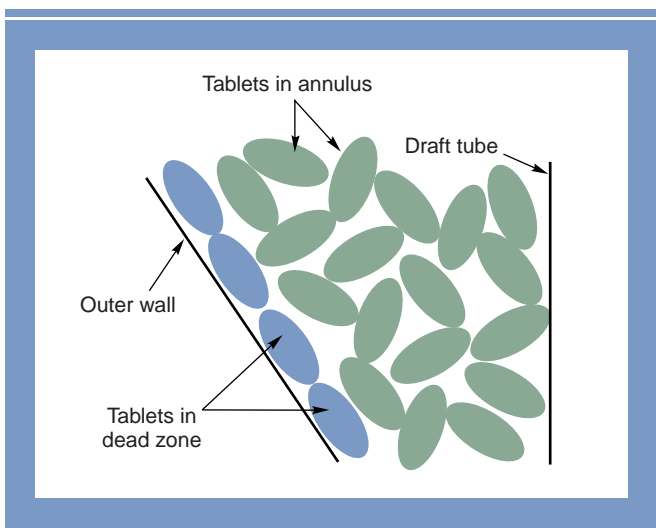


Figure 6: Schematic structure of the dead zone (tablets shown in dark gray) occurring in the lower portion of the annulus adjacent to the inner wall of the chamber.

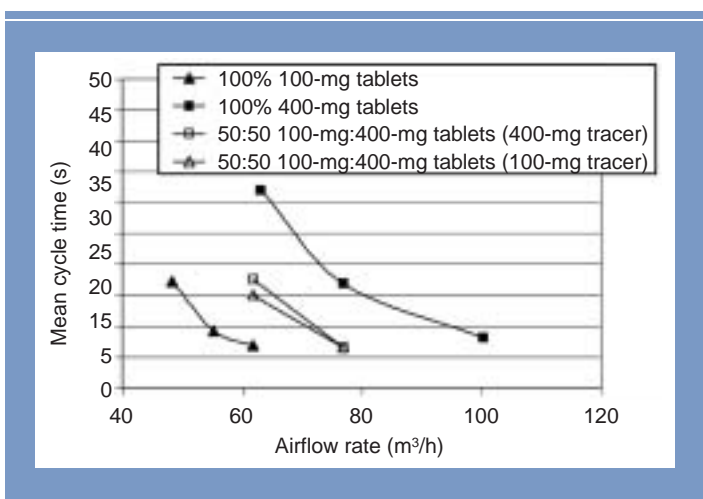


Figure 7: Mean particle cycle times of small and large tablets in binary mixtures.

Deviation from the mean particle cycle time and formation of a dead zone. The experimental results show a significant spread of cycle times for all runs, with the percent relative standard deviation (% RSD) being typically in the order of 70–80%. Table I summarizes the experimental results obtained using 6.5-mm diameter, 100-mg tablets. When the equipment is operated with either a small batch size (400 g) or a lower airflow rate (48 m³/h), the % RSD increases to more than 200%. A major contributory factor in this wide variation is the presence of a dead zone where tablets are stationary for a significant length of time. Figure 5 clearly shows the presence of the dead zone. In this figure, the y position of the tracer tablet is plotted against time for a study with a 400-g batch size, a 2-cm gap, and a 62 m³/h airflow. From ~1900 s to 2400 s, the tablet is shown to be essentially stationary. Because of a very slow solids exchange between the dead zone and the moving bed in the annulus, the tracer tablet re-entered the moving bed after being trapped in the dead zone for 500 s. The exact reason for the formation of the dead zone is unclear. Observations made during the course of experiments suggest that the dead zone occurs at the lower part of the annulus adjacent to the inner wall of the chamber, where particles pack in a regular array at the wall (i.e., the flat end facing the chamber wall) (see Figure 6). The size of the dead zone can change with time and operating conditions, a higher gas flow rate generally creates a smaller dead zone size. Avalanches were observed in the dead zone, which may be the predominant mechanism of solids exchange between the dead zone and the moving bed.

The appearance of dead zones is unacceptable for tablet coating because it will contribute to significant inhomogeneity in the quantity of coat applied to the tablets within a batch. It appears that the dead zone may be overcome by increasing gas flow in the annulus and/or by introducing tangential gas flow at the chamber wall (22).

Particle cycle time for binary mixtures. During the initial development of a formulation for a new drug candidate, one often desires to prepare small batches of a film-coated formulation for further testing (e.g., for an assessment of the effect of the film coat on stability). The availability of drug

for these studies is often limited, so the quantity of formulated material available for film coating may be in the order of tens of grams. For a laboratory-based Wurster system such as an Aero-matic Strea-1, the minimum batch size is in the order of several hundred grams. Small batch sizes lead to high mean deviations in the mean particle cycle time and hence poor coating quality, as discussed previously. To overcome the limitations on batch size, the material of interest can be bulked out with placebo tablets. The placebo tablets are usually a different size from the active tablets so that a rapid separation on the basis of size can be undertaken at the end of the coating operation. Such an approach implies coating a binary mixture of small and large particles. However, binary mixtures tend to segregate (the inverse of mixing). If segregation occurs, small and large particles may have various cycle times and hence different coating quality. This aspect has also been investigated in the present work. Figure 7 shows the experimental results, from which no significant difference in cycle times can be seen. The average cycle times of the small and large tablets in the mixture are approximately the same, but considerably different from those when the two tablet components are used alone.

Conclusion

The authors investigated the motion of solids in a Wurster coating process using the noninvasive positron emission particle tracking (PEPT) technique. The following results were obtained:

- The mean particle cycle time increases with increasing batch and tablet size and with decreasing airflow rate and gap between the distributor and the draft tube.
- A significant spread exists in particle cycle time for all runs with the % RSD typically around 70–80%. The % RSD increases with decreasing airflow rate and batch size and can be more than 200%. This results in a distribution in coating mass over a short time of operation. Whether this distribution will narrow over time remains to be investigated.
- The spread in % RSD values is attributed primarily to the formation of a dead zone in the lower portion of the annulus, which is adjacent to the inner wall of the chamber. Dead zones generally have a depth of only one tablet layer and arise from ordered packing at the wall.
- No significant difference in particle cycle times was observed for the binary mixtures tested (tablet mass ratio was 4:1).
- The average particle cycle time of a binary mixture lies within the cycle times of the two component particles, which were operated at similar conditions.

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FYI

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