Drug Development and Industrial Pharmacy, 23(5), 451–463 (1997)

Qualitative Description of the Wurster-Based Fluid-Bed Coating Process

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ABSTRACT

The Wurster-based fluid-bed coating process is often treated as just another fluid-bed coating process. However, there are significant differences between the two types of fluid-bed coatings. The Wurster-based coating process does not contain any fluid-bed regions in the traditional sense, as it is a circulating fluid-bed process. Four different regions within the equipment can be identified: the upbed region, the expansion chamber, the downbed region, and the horizontal transport region. The size of these regions is determined by the dimensions of the coating apparatus. Part of the upbed region constitutes the coating zone where the spray mist hits the substrate (the material that is going to be coated). The coating process consists of three phases: the start-up phase, the coating phase, and the drying/cooling phase. During the coating phase, several processes take place simultaneously. They are: atomization of the film solution/suspension, transport of the film droplets to the substrate, adhesion of the droplets to the substrate, film formation, the coating cycle of the substrate, and the drying of the film. When discussing the coating process, it is important to consider properties of the substrate. Key properties of the substrate determine important process properties such as bed expansion, bubble properties, slug properties, and spouting. The most important properties of the substrate are the density of the particles, their diameter, and their stickiness. The process characteristics are very different in each of the four regions. The upbed region is the most difficult to control. It is here that the most sensitive processes in relation to the coating occur. The product flow in the upbed region is a dilute vertical pneumatic conveying. The pneumatic conveying is controlled by the upbed fluidization air rate. Slugging is a frequent problem with the flow in this region for dense and large substrates. The air flow is the combined air flows of the fluidization air and the nozzle air. Air and substrate velocities are not uni-

form across the upbed. The velocities at the center are significantly higher than those along the walls. There is a risk that substrate might fall down along the partition wall, and that clusters of particles might form in the upbed at certain processing conditions. The particle terminal velocity in the upbed is limited by the height of the expansion chamber. Unfortunately, the particle terminal velocity cannot readily be calculated and must be measured, if attrition of the substrate is a problem. The product concentration in the mist region of the upbed region must be high enough to secure adherence of all spray droplets to a substrate particle. The air velocity in the expansion region must be well below the minimum fluidization velocity. It is the expansion in diameter that secures the drop in air velocity, when the air moves out of the partition and into the expansion region. The downbed region is a slightly expanded bed where the air rate is below the minimum fluidization velocity. This is the region where sticking is most likely to occur, since the movement is gentle and the particles are in close contact with one another. Actually, the product is only slightly expanded over a loosely packed powder. The substrate moves into the upbed via the horizontal transport region. The air flow through this region is very complex. Air rate measurements and pressure drop calculations suggest that some of the air flows from the downbed bottom plate, through the horizontal transport region, and into the upbed region. The Wurster-based coating process is very different from the top-spray coating process, and optimization should be treated from a completely different angle. A stepwise process optimization procedure is suggested involving optimizing the product circulation, adjusting the spray rate, and ensuring that the droplet size of the spray falls within specified limits. The product circulation is optimized by the choice of the correct bottom plate configuration of the downbed and the upbed regions. In conclusion, the Wurster-based coating process is a highly complex process, and sufficient attention should be directed toward optimization of the process.

INTRODUCTION

Coating is an important process in the pharmaceutical industry. Coatings are used to mask the taste, to modify the release of drugs, and to improve the stability of pharmaceutical products. Three different coating principles are used widely for the coating of solid dosage forms. They are: pan coating, top-spray fluid-bed coating, and Wurster-based fluid-bed coating processes.

Traditionally, top-spray fluid-bed coating and Wurster-based fluid-bed coating are grouped together as fluid-bed coating processes, indicating that the processes are more or less the same (1,2). But actually the top-spray coating process and the Wurster-based coating process are very different, indeed, and each shares as much with the pan coating process as they have in common.

In the Wurster process, like in the pan coating process, the product flow through the apparatus and in and out through the coating zone is well controlled. In the top-spray coating process, however, the product movement is arbitrary. This makes a very important difference between the topspray and the Wurster coating processes. Furthermore, there are no fluidized-bed regions in the traditional sense anywhere in the Wurster equipment. Experience shows that the Wurster-based coating is more efficient with respect to the quality of the film that is formed (3–5).

The purpose of the present paper is to present a qualitative overview of the Wurster process with a focus on the substrate transport within the coating equipment. This is done by drawing from the chemical engineering fluid-bed literature and from personal experience with optimization of a Wurster-based coating process. The purpose is not to cover the general use of the Wurster-based coating process for pharmaceuticals, which has been dealt with elsewhere (6).

THE WURSTER EQUIPMENT

The Wurster coating equipment was invented by D. Wurster (7). A schematic drawing of the Wurster equipment is given in Fig. 1. The Wurster equipment is a

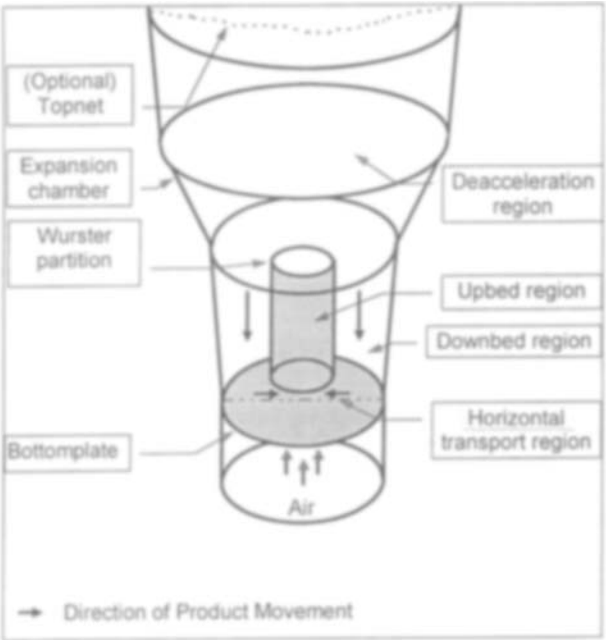

Figure 1. Key regions of the Wurster process.

circulating fluid-bed specially designed for the coating process. It consists of a container with one or more Wurster partition inserts (called the *partitions*). Typical dimensions of commercially available apparatus appear in Table 1.

The product movement in the Wurster process is called a circulating fluid-bed in the chemical engineering literature. Another name for the Wurster process is a *spouted bed* (8). The circulating fluid-bed process contains four distinct zones: a riser, a solids recycle part, a stand pipe, and a feeder. It is claimed that similarly for the Wurster coating process, four zones with distinctly different solid movement patterns can be identified (Fig. 1). The four zones are: the upbed region, the deacceleration region (in the expansion chamber), the downbed region, and the horizontal transport region. The size of each of these regions is determined mainly by the dimensions of the apparatus, but also to some extent by process parameters such as the product load, the coating cycle times etc.

DESCRIPTION OF THE COATING PROCESS

The coating process consists of three phases: the start-up phase, the coating phase, and the drying phase. These phases are discussed in the following.

The start-up phase consists of an optional preheating of the equipment and a heating of the substrate. The preheating of the equipment is an advantage when the substrate is fragile and the heating period should be as short as possible. Heating of the substrate is done to prevent overwetting during the initial application of the film solution/suspension as heating increases the rate of evaporation of the coating solvent just after the start of the coating. The heating might also facilitate the film formation.

The coating phase, in which the coating is applied to the substrate, has several key elements. One of these is the atomization of the coating solution/suspension which distributes the solution/suspension to the surface of the substrate. From a process point of view, the coating solution/suspension does not enter the fluid bed. It is the mist formed by the nozzle that enters the equipment. The formation of the spray is an important part of the overall coating process but is not covered in this paper (9). Typically, spray mists consist of droplets with an average diameter of 10–30 μm.

Once the droplets have been formed they have to be transported to the substrate. Ideally, all newly formed droplets hit the substrate with enough solvent left to

Table 1

Typical Apparatus Dimensions Relating to Different Wuster Equipment

Supplier Equipment Scale	Glatt GPCG 200 Production	Glatt GPCG 3 Laboratory	Aerocoater MP-1 Laboratory
Upbed diameter (cm)	21.5	7.3	4.8
Upbed height (cm)	76	17.5	18
Number of partitions	3	1	1
Volume of downbed (liter)	360	8	~1
Opening under partitions (mm)	15–40	10–30	7–15
Product load (kg)	300	3–5	0.8–2

ensure spreading over the surface of the substrate, and enough to ensure coalescence of the droplets into a film. This process is repeated for each film layer that is applied. It is important that the evaporation is slow enough to let the new film layer dissolve a sufficient part of the layers below to secure proper adhesion between layers. It is, of course, equally important that the first layer formed adheres to the substrate. But the drying must not be too slow, either, as this will facilitate agglomeration of substrate particles. The drying of the film starts as the solvent evaporates from the film droplets in the spray mist and continues from the film droplets adhered to the substrate.

The time is takes a particle to go through a complete cycle of coating and drying is termed the *coating cycle*. Typical coating cycles are 15 to 60 sec even for full-scale equipment such as Glatt GPCG 200. The diversity between the coating cycle time of each of the individual particles of the substrate is of great importance for the homogeneity of the product, in particular if some particle properties (e.g., particle size) influences the coating cycle time for the individual particles in a systematic way (10).

The circulation time in a Wurster equipment is controlled by the opening beneath the Wurster partitions. The substrate circulation rate must be set high enough to ensure that all the coating in the coating mist will hit a substrate surface. However, the circulation rate should not be too high, since this will cause slugging of the product in the upbed. If the product is friable, the circulation rate must also be kept at a minimum, since increased circulation rate will lead to an increase in attrition.

To finalize the coalescence of the polymer, and to prevent adherence between the individual particles, the substrate is dried after the coating has been finalized. This step is also necessary to remove residual solvent in the film. After drying the substrate is cooled, most often to room temperature.

THE COMPONENTS

Each of the materials used in the coating process is characterized below with respect to the properties relevant for the fluidization process.

The Substrate

The material to be coated is called the *substrate*. The substrate is a batch of particles, typically tablets, hard or soft gelatin capsules, pellets, crystals, or granules. The substrate is referred to as the *solids*, the *powder*, or simply the *particles* in the fluidization literature. Even though the powder/particles when fluidized behave much like a liquid, the properties of the particles are still important for the fluidization behavior of the substrate. Typical fluidization properties of different substrates appear in Table 2.

As seen from Table 2, substrates with rather different properties are coated in the Wurster equipment. The Geldart classification of solids, according to their fluidization properties (11), appears in Fig. 2. Using this classification, tablets and capsules are group D solids, pellets and granules are group B solids, and crystals are either group B or group D solids depending upon their

Table 2

Typical Fluidization Properties of Examples of Different Substrates

Substrate	Characteristic Diameter[a] (mm)	Volume of Particle[b] (mm^3)	Substrate Density (g/cm^3)	Bulk Density (g/cm^3)
Tablets	8.0	500.	1.0	0.7
Capsules	6.6	580.	0.8	0.4
Dense crystals	0.8	0.51	2.1	1.2
Light crystals	0.5	0.13	1.0	0.8
Pellets	0.6	0.11	0.8	0.8
Small crystals	0.3	0.014	1.0	0.8
Granules	0.3	0.014	0.5	0.5

[a]The diameter as determined by a sieve analysis.
[b]Estimated using relevant simple geometry (cubes, spheres, etc.).

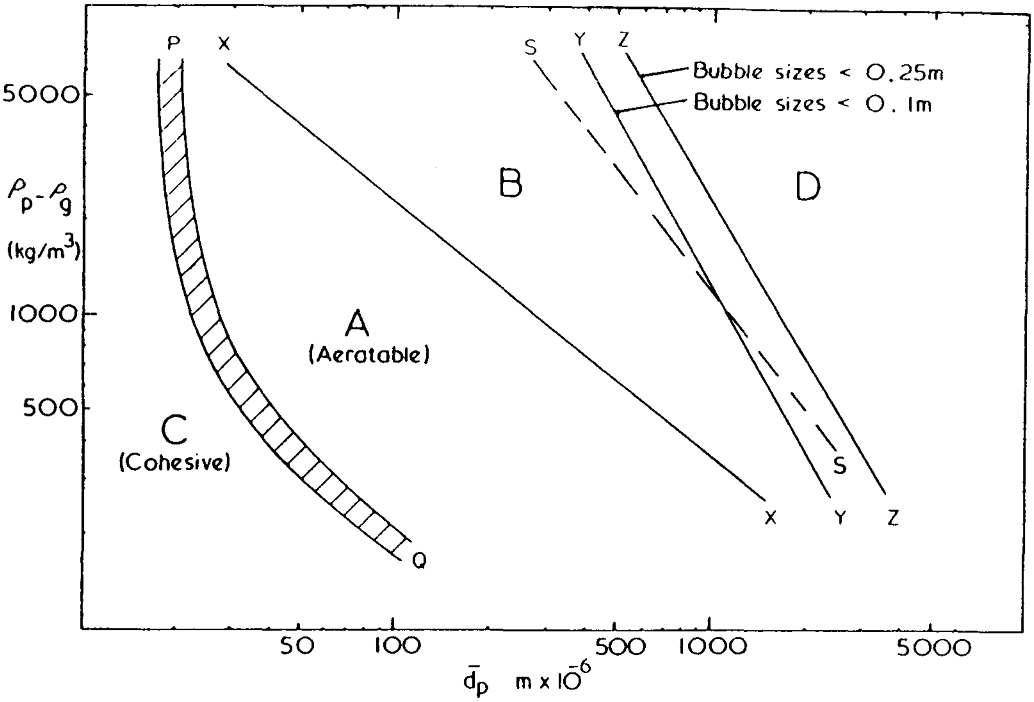

Figure 2. Diagram for classifying powders into groups having broadly similar fluidization characteristics in air at atmospheric temperature and pressure. d_p denotes the sieve diameter of the particles, $\rho_p - \rho_g$ is the difference in density between particles and gas. From Ref. 12; taken from Ref. 11. Copyright 1986 John Wiley & Sons, Ltd. Reprinted by permission of John Wiley & Sons, Ltd.

density and diameter. The denser and larger the crystals are, the more they behave like group D solids. Thus some crystals will be fluidized in the same manner as pellets are, and some crystals will be fluidized as tablets.

The key fluidization properties of solids from the different groups appear in Table 3. Group B solids expand moderately when fluidized or placed in an expanded bed. With group D solids, the bed expansion is minimal, even less than for the group B solids. The more a solid tends toward group D, the more it will tend to spout and to form slugs in the bed. Thus spouting and slugging is a greater problem for tablets and heavy large crystals than for granules.

Another very important feature of the substrate is its surface properties. The surface properties, especially the total surface area, the smoothness of the surface, and the form of the particles are important for the properties of the final product. These coating properties of the substrate have been covered elsewhere (13). They are not discussed here, as it is believed that they do not significantly contribute to the fluidization behavior of the solids.

The Fluidization Medium

The fluidization medium is either atmospheric air, nitrogen, or vacuum. Atmospheric air used for fluidization is typically heated to an inlet temperature of about 50° to 80°C. At times the humidity of the inlet air is controlled as well. If the vapors of the coating solvent could explode in the presence of oxygen, either nitrogen or vacuum fluidization is used. In vacuum fluidization, the fluidization medium is the solvent vapors. Typical properties for fluidization media appear in Table 4. When using nitrogen for fluidization, the fluidization medium is recycled and thus contains a certain concentration of vapors from the coating solvent.

The Coating Solution

The coating solution consists of a polymer and various excipients dissolved or suspended in a liquid. The liquid is a vehicle for the transport of the polymer to the substrate. The liquid also ensures satisfactory distribution of the polymer over the whole of the surface of the substrate. Furthermore, the liquid facilitates the forma-

Table 3

Summary of Group Properties

	A	B	D
Most obvious characteristic	Bubble-free range of fluidization	Starts bubbling at minimum fluidization velocity	Coarse solids
Typical pharmaceutical substrates	Microparticles	Pellets; granules; light, small crystals	Tablets; capsules; heavy, large crystals
1. Bed expansion	High	Moderate	Low
2. Deaeration rate	Slow, linear	Fast	Fast
3. Bubble properties	Splitting/recoalescence predominate Maximum size exists Large wake	No limit on size	No known upper size Small wake
4. Solids mixing	High	Moderate	Low
5. Gas backmixing	High	Moderate	Low
6. Slug properties	Axisymmetric	Axisymmetric; asymmetric	Horizontal voids, solids slugs, wall slugs
7. Spouting	Not except in very shallow beds	Shallow beds only	Yes, even in deep beds

Source. Excerpted from a table in Ref. 14.

Table 4

Key Fluidization Properties of Typical Fluidization Media

Fluidization Medium	Density (kg/m^3)	Viscosity (10^{-6} Pa·sec)
Heated air (60°C)	1.05	20
Dry air	1.16	18
Nitrogen	1.25	18

tion of a film by coalescence of the polymer during the evaporation.

Formulations of film coating solutions/suspensions are given in Refs. 15 and 16.

DESCRIPTION OF THE MATERIAL TRANSPORT PROCESS

The Total Process

The total Wurster coating process is controlled by one or more limiting process balances. The balances can be described by their limiting parameters. The subprocesses of the Wurster coating process are highly dependent upon one another, as some of the limiting parameters are controlled by parameters determined by other subprocesses. As an example, for one set of coating conditions, the total solution spray rate might be limited by the lower explosion limit of the coating solvent. In that case, the maximum allowable spray rate will depend upon the amount of fluidization air in the upbed region, as the ratio between the solution spray rate and the fluidization air in the upbed region determines the solvent concentration, which must be below the lower explosion limit. If the maximum allowable amount of fluidization air in the upbed is limited to air rates that will not cause particle attrition, particle attrition becomes limiting for the spray rate, and thus for the overall process time.

Obviously, the pressure drop over any closed circle in the equipment must be zero. Thus the pressure drop over the downbed and horizontal transport regions must equal the pressure drop over the upbed region. Calculations on pressure drops indicate that the pressure drop over the horizontal region is considerable, because the amount of the product within a column in the downbed region is several times higher than within a column in the upbed region. The acceleration of the product in the upbed does not balance this pressure difference.

Since the total amount of substrate in the equipment is fixed, and since the equipment is in a steady state during operation, the amount of substrate that passes through any of the four regions at any time is the same. In other words, the amount of substrate that passes through any surface across the regions during a fixed time will be the same. Therefore, one can measure the circulation rate of the system at any surface across a region.

Werther uses the Reh fluidized-bed state diagram for the bed porosity to classify the fluidized-bed processes (17). Werther points out that for circulating fluidized-bed processes, the circulating solids mass flow rate per unit area must also be taken into account to properly understand the bed porosity. The solids mass flow rate per unit area thus becomes a key parameter for the state of the Wurster fluidized-bed process.

The Upbed Region

In the upbed region, the particles are accelerated by the fluidization medium. Geldart and Rhodes (18) characterized the upbed region as as vertical pneumatic conveyor. The process is an entrainment of particles in the fluidization medium. Vertical pneumatic conveying is either dilute or dense, depending upon the volume of solids relative to the volume of the fluidization medium. In Wurster production equipment, typical fluidization medium rates are 5 m/sec and higher (corresponding to 0.1 m^3/sec per partition). With particle entry rates per partition of approximately 5 kg/sec and less, the particles typically constitute less than 5% (v/v), often less than 1–2% (v/v) of the upbed flow. Thus upbed flow is like a dilute pneumatic conveying process.

Usually the particle flow in vertical pneumatic conveyors develops fully over a range of several meters. In a typical Wurster apparatus, the partitions are only between 0.5 and 1.0 m high. Thus the flow is not fully developed when the particles leave the partitions.

Upbed Fluidization Air Rates

Since the substrate is transported up through the partitions, the air must be well above the minimum fluidization velocity. The air rate must also be above the transport velocity for the material in question, as the function of the air is to accelerate the particles and to overcome the gravitational drag on them. Typical air rates appear in Table 5.

One of the problems in vertical pneumatic transport is slugging or choking. The slugging phenomena is illustrated in Fig. 3. The vertical pneumatic transport process is characterized by a minimum slugging velocity. The minimum slugging velocity is the minimum air velocity above which no slugging occurs. The minimum slugging velocity depends upon the rate at which the solids enter the upbed region. For higher entry rates of solids, the minimum slugging velocity increases, as illustrated in Fig. 4. Also Fig. 4 illustrates that a minimum pressure drop is found with air velocities somewhat above the minimum slugging velocity.

As appears from Table 3, different types of slugging will develop depending upon which group the substrate belongs to. For group D powders, horizontal voids can develop in the upbed if air velocities are below the minimum slugging velocity. If slugging occurs, the pressure drop over the bed will fluctuate in a characteristic

Table 5

Air Rates Measured at 20°C Under the Bottom Plate in a Wurster GPCG 200 with 3 Partitions at Different Process Air Volumes

	Downbed			Upbed	
Process Air (m^3/hr)	Close to Container Wall (m/sec)	Close to Partition Wall (m/sec)	Between Partitions (m/sec)	Close to Partition Wall (m/sec)	Center (m/sec)
2000	0.3	0.7	1.3	4.0	7.5
2500	0.35	0.7	2.0	4.4	8.5
3000	0.5	1.0	2.0	3.3	9.5

Note. 300 kg KCl crystals were used. The Wurster height was 40 mm. Bottom plate hole areas: upbed 25%; downbed 6.5%.

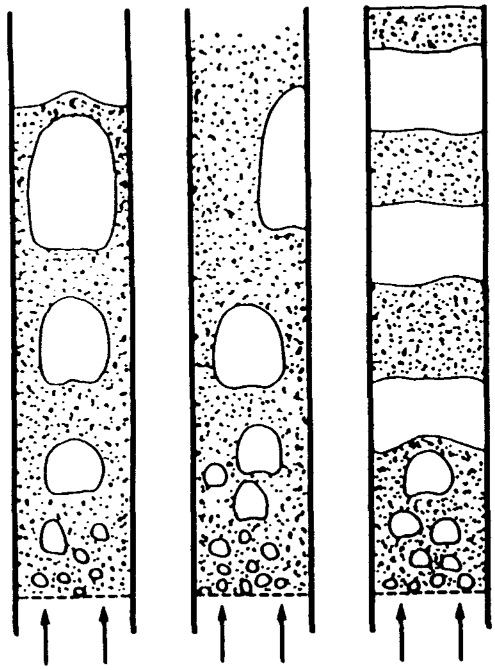

Figure 3. Types of slugs formed in fluidized beds: (a) axial slugs—fine smooth particles; (b) wall slugs—fine rough particles, rough walls, high velocity; (c) flat slugs—large particles. Reprinted from Ref. 19. Copyright 1991 by Butterworth-Heinemann. Reprinted by permission of Butterworth-Heinemann Ltd.

manner. The slugging can also be observed looking at the substrate exiting from the Wurster partition.

Upbed Solids Mass Flow Rate

The total solids mass flow rate through the upbed is the same as the total solids mass flow rate through the horizontal transport region, which actually, under normal operational conditions, controls the upbed solids mass flow. The pressure drop (as well as the bed porosity) is controlled by the fluidization air rate and the solids mass flow rate in the upbed, as illustrated in Fig. 4. If slugging occurs and the upbed fluidization air rate cannot be increased, the slugging can be reduced by decreasing the upbed solids mass flow rate (20).

Pressure Drop Through the Upbed Region

The upbed pressure drop will differ with the height above the bottom plate, as shown in Fig. 5. Two regions with clearly different pressure drops of $1 \cdot 10^4$

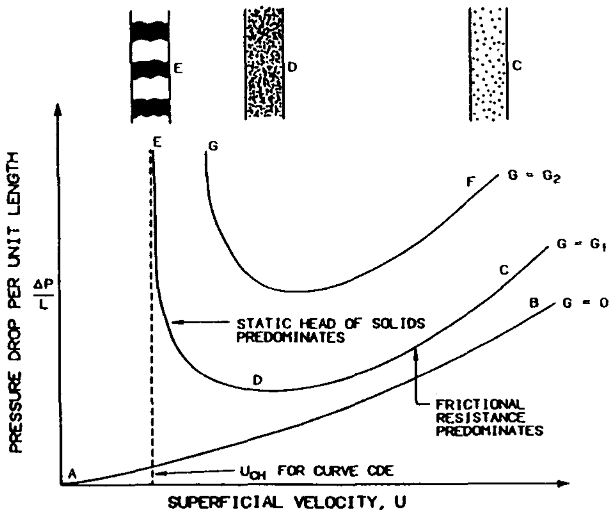

Figure 4. Phase diagram for dilute phase vertical pneumatic conveying. The pressure drop over a vertical tube is plotted versus the superficial velocity (air velocity relative to solids velocity) for pure air and for two different solid loads (G_1 and G_2). From Ref. 20. Copyright 1986 John Wiley & Sons, Ltd. Reprinted by permission of John Wiley & Sons, Ltd.

Pa/m and $1 \cdot 10^3$ Pa/m were found in the upbed region. Rhodes and Geldart (21) demonstrate how the riser region in their circulating fluid-bed at certain operating conditions contains a fluid-bed region at the bottom of the riser and a traditional vertical pneumatic region above the fluid bed. The presence or absence of such a fluid-bed region at the bottom of the riser, depends upon the gas velocity and the solids flux in the upbed region. Others have also found both a dense region in the bottom and a dilute region in the upper part of the riser although this occurred in risers that were 10 times as high as the Wurster partitions (22).

Reynolds number formed with the air flow and the diameter of the partition is ≈60,000 in a Glatt GPCG 32 with atmospheric air at an air rate of 800 m^3/hr per partition presuming an 80:20 distribution of the air between up- and downbed regions. Thus the air flow is highly turbulent in the upbed region. The air from the spray nozzle will further add to the turbulence with air velocities up to about 20 m/sec, compared to a maximum of about 10 m/sec for the fluidization air at the center of the upbed region.

The air velocity differs across the tube, and the air velocity is lower close to the walls of the tube than in the center of the tube. Thus particles close to the walls will rise slower and may even fall down along the wall.

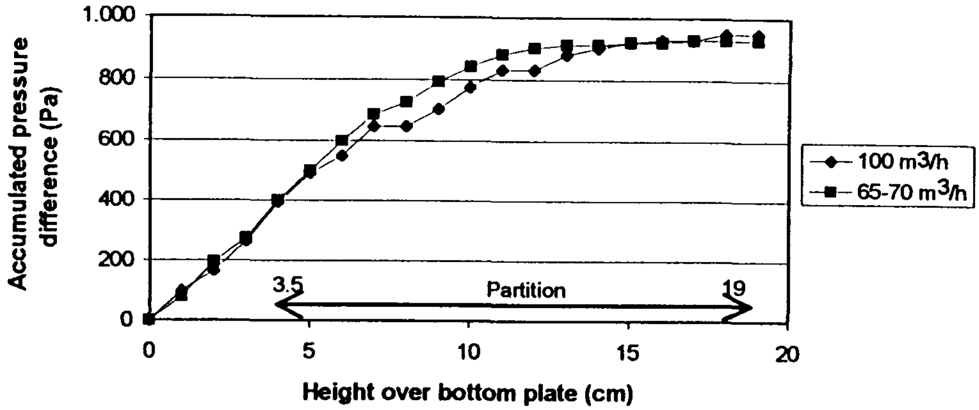

Figure 5. Vertical pressure difference at two different air flows in the upbed region in a Glatt GCPG-3 fluid-bed apparatus.

The particle flow in the riser was studied by Bader et al. (23) for high-speed fluidization processes (Fig. 6). Especially, there is a risk that particles will adhere to the wall. This problem is accentuated if the particles are sticky themselves or become sticky when the coating is applied. Such adherence of particles may become a significant problem if uniform coating of all the particles is important for the final quality of the product. In our own experience, the lower part of the inside of the Wurster partition is an Achilles heel for the Wurster-based coating process.

In high-speed fluidization processes, particles may form clusters in the upbed region. Clusters of particles will behave as larger particles. The clusters will rise more slowly than the unclustered particles, or they might even fall down through the bed. As the clusters leave the upbed region or fall down deeper into the upbed, the cluster will dissociate into individual particles. It is not clear from literature whether particle clusters form in risers with heights as low as the partitions used in the Wurster coating process. In our own work we have not observed any clusters in the expansion chamber, but since clusters might dissociate before they can be observed, it is unclear whether clusters form in the Wurster coating process.

The maximum allowable terminal particle velocity in the upbed is controlled by the height of the expansion region. To avoid having the particles smashed against the topnet or the ceiling, the free fall of the particles must be long enough to stop them. The velocity of the upbed air determines the terminal particle velocity. Thus the maximum allowable velocity of the upbed air is limited by the height of the expansion chamber. The height of the Wurster partition will also determine the terminal particle velocity, since the particle flow does not develop fully through such short tubes. The shorter the partition, the smaller the terminal velocity.

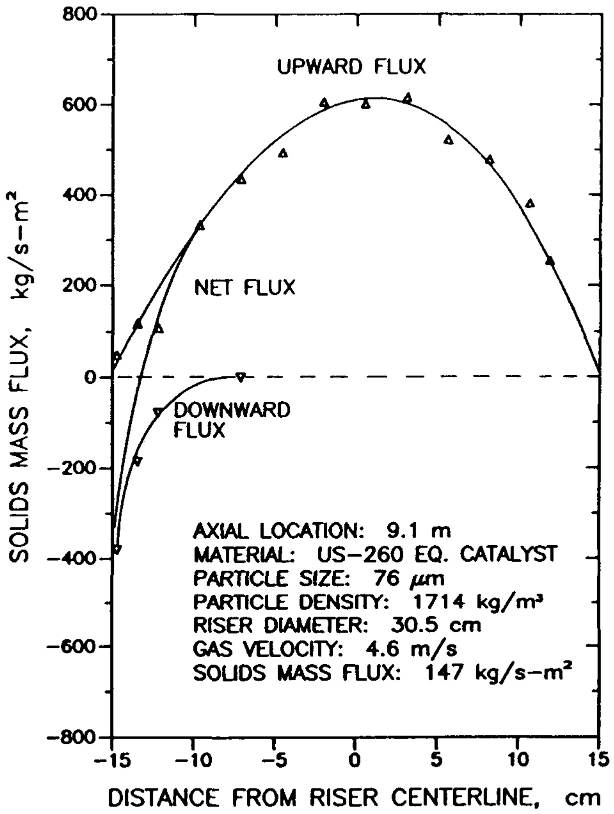

Figure 6. Radial solid flux profiles from Ref. 23. Reprinted by permission of P. Basu (ed.).

Using the same conditions as those given above, Reynolds number will be about 29 for the terminal velocity of the KCl crystals. Since crystals are nonspherical the terminal velocity cannot readily be calculated (for calculations of particle terminal velocities, see Ref. 24). If attrition of particles in the equipment is a problem, terminal velocities should be measured or collision with the top of the equipment should be evaluated experimentally. In our experience, collision with the topnet does occur even in production-scale equipment.

The Mist Region

The spray mist constitutes a special part of the upbed region. When (as is usual) a two-component nozzle is used, the spray air will have a considerable higher air rate than the air rate of the fluidization air of the upbed region. This will increase the turbulence in the central region of the partition, as already discussed. The mist is a region of its own in the fluid-bed apparatus. Once the spray adheres to the particles, it moves together with the particles through the bed.

The concentration of particles in the mist region should ideally be high enough to ensure that every spray droplet in the spray mist meets a particle. Thereby it is ensured that all the spray is used for coating the product. In other words, the product density in the upbed region (or in the spray mist part of the upbed region) should be so high that the surface of the partition viewed from the spray nozzle is always covered by a curtain of product. As discussed above, the concentrations of particles are usually below 5% (v/v). The concentrations of particles are controlled by the fluidization air rate and the solids mass flow rate in the upbed (25). The concentrations of particles also differ across the riser, with a higher (at some air rates significantly higher) concentration close to the wall of the Wurster partition (26).

The Expansion Region

When the particles leave the upbed region to enter the expansion region, the air velocity drops to a level well below the minimum fluidization velocity. Thus the particles enter a free fall (actually a fall in a counter-flowing fluidization medium) towards the downbed region. The particles have an upward exit velocity due to the acceleration through the upbed region. Unfortunately, as discussed previously, this exit velocity of the particles cannot easily be calculated. It must be measured or calculated indirectly. Because of the upwards velocity of the particles as they leave the upbed region, they will travel a certain distance upwards before they start to fall down again. Thus a minimum height of the expansion chamber is required to avoid topnet collisions. This minimum height is determined by this exit velocity, the surface area, and the density of the substate.

The upwards air velocity in this region is controlled by the combined fluidization air and nozzle air volumes, and by the diameter of the equipment in the expansion region. Thus most fluid-bed apparatus are designed so that they have a significantly larger diameter in this region to bring the air velocity well below the minimum fluidization velocity. Typical air velocities are given in Table 5.

The drying of the solvent in the film on the particles continues as the particles enter the free fall in the expansion region.

The Downbed Region

The downbed region is a slightly expanded bed. As discussed above, beds constituted by both type B and type D solids expand very little. The air velocity is below the minimum fluidization velocity for the material in question. The particles are newly coated and the movement rather gentle, at least compared to the movement in the other three regions in the bed.

As the film has not yet completely dried, it tends to pass through a sticky phase. Sticking of the particles is most likely to occur in this region, since the particles touch one another in the downbed and since the air flow is laminar.

The downbed region is a container for particles to enter into the upbed region. It also allows for additional drying of the particles before they enter the upbed region again. The size of the downbed region thereby control the drying time for the particles, before they again pass through the spray mist.

Downbed Fluidization Air Rates

The downbed fluidization air rate must be below the minimum fluidization velocity. Typical air rates appear in Table 5. In most fluidization, the control of the air rate (actually air flow and thus air rate) in the downbed is achieved by the hole area in the bottom plate under the downbed region versus that under the upbed region. In reality two separate balances must be considered regarding the fluidization air rates: the air rate in the upbed and the air rate in the downbed. Thus ideally it should be possible to control the air rates of the two regions separately.

The Reynolds number formed with the air flow and the diameter of the downbed container is ≈10,000 in a Glatt GPCG 32 with atmospheric air at an air rate of 800 m^3/hr per partition presuming an 80:20 distribution of the air between up- and downbed regions. Thus the air flow is highly turbulent even in the downbed region.

In our experience the height of the downbed region is smaller close to the partitions than close to the container, at least for some products. The difference in heights depends upon the operating conditions. The difference is further discussed below.

The Horizontal Transport Region

The opening under the partition of the Wurster controls the flow of particles into the upbed and thus controls the solids mass flow rate per unit area in the upbed region. The bottom of the downbed and the opening under the partition constitute a separate region with horizontal transport of the particles. The horizontal transport is a pneumatic transport. Because of the complex air movement it is more complex than a simple horizontal pneumatic transport through a tube.

The horizontal transport in the GPCG for KCl crystals amounts to about 200 kg/m^2·sec. Since the same crystals have a powder flow rate of about 300 kg/m^2·sec,* it is possible that it is the free fall of crystals into the upbed which is responsible for the horizontal flow. However, there must be a significant resistance to particle flow from the friction of the particles against the bottom plate and against the bottom of the partitions. As discussed above, it is probable that there is a certain pressure drop across the horizontal region, which would then contribute to the product movement through the opening under the partition.

Air rate measurements show that air rates under the bottom plate increase considerably near the partitions (Table 5). This pattern has been observed consistently in all air rate measurements performed at the Nycomed production facility. In most cases the air rates close to the partitions are above the minimum fluidization velocity for the material in question (the minimum fluidization velocity was determined to be 0.42 m/sec for the KCl crystals used). One possible explanation is that some of the air that passes up through the downbed plate enters the upbed region through the opening under the partition (cf. Fig. 1). It is, however, also possible that the height of the downbed is smaller close to the partitions, as the substrate is removed more rapidly from the area close to the partitions, while most of the substrate is returned into the downbed region by sliding down along the outside walls of the container, and thus the substrate will locate itself away from the partitions. If the latter is the cause, this would suggest that a fluidized-bed region exists in the downbed close to the partitions and in the horizontal transport region. This air will reduce the friction between the particles and the bottom plate, and perhaps further help the movement of the particles into the upbed region.

CONCLUSIONS

The Wurster-based fluid-bed coating process is a high-velocity circulating fluid-bed system. It does not contain any simple fluidized-bed regions in the traditional sense, as the top-spray fluid-bed coating process does. This circulating fluid bed involves several regions with rather different fluidization properties. Wurster-based fluid-bed coating has well-defined product movement into and out of the spray zone, in common with the pan-coating process. Apart from this minor similarity, the Wurster-based fluid-bed coating process is different from and considerably more complex than both top-spray coating and pan-coating processes. This complexity is caused by the high number of interrelated subprocesses, and by the presence of several individual regions within the equipment, with different controlling parameters.

When running a Wurster-based fluid-bed coating process, several balances have to be kept under control. These are:

- The product circulation through the apparatus must be adequate, but not too fast. This implies:
  - Upbed air velocity should be above minimum slugging velocity but not so high as to cause attrition for the product in question.
  - Expansion chamber and downbed air velocities should be below minimum fluidization velocity.
  - Horizontal pneumatic transport must be secured just above bottom plate.

Thus proper product circulation is secured by adjusting the opening under the Wurster partitions as well as the air velocities in the different regions. The air rates cannot be fixed for a given apparatus since the minimum fluidization and the minimum slugging velocities both depend upon product properties such as the particle size, the shape, and the product density. The opening under

*As determined by the flow rate through an opening with the same diameter as the opening under the Wurster column.

the partitions must also be adjusted to compensate for air rates as well as particle friction.

- The spray rate of the coating solution must be adjusted to:
  - The drying capacity in the downbed region.
  - The product movement in the upbed region.
  - The lower explosion limit in the upbed and expansion chamber regions.

Since the drying capacity, the product movement, and the lower explosion limit all depend either upon the air flow or on the air velocities in one or more of the regions, the spray rate must be adjusted to fit the air velocities. Furthermore, the product concentration in the upbed region is controlled by the opening under the Wurster partitions, and thus the spray rate must be adjusted according to this as well.

- Finally, the droplet size in the spray mist must be within limits that secures:
  - Adequate spreading of the coat over the surface of the product.
  - Sufficient slow drying of coating solution before hitting the product to secure proper film formation and avoid spray drying.

Thus the nozzle size and nozzle air rates must be adjusted to the acceptable spray rates and the product flow in the upbed region.

The Wurster-based coating process is a complex process with many interrelated cocurrent processes. It is suggested that because of these highly complex processes, much effort should be directed towards the optimization of the process parameters. If the process is treated like a standard process that should be run with the same standard parameters for all kinds of different products, it is very likely that the process will run less than optimally. Especially in the pharmaceutical industry, where the tradition is to rely on standard processes for production, and where important product features (e.g., the control of drug release) are highly influenced by the coating process, is it important to stress the complexity of the process and the need for adequate process optimization for most, products if not for all.

ACKNOWLEDGMENTS

We are indebted to Dr. Hungerbach from Glatt Gmbh. in Binzen, Germany, for the most relevant information and for many interesting comments based upon his long experience with Wurster-based coating. His suggestions on the interpretation of the air rate measurements have also been very valuable. Mr. Knud Helmo from Nycomed Pharma has developed the equipment that enabled us to measure the air rates under the bottom plate. These measurements were instrumental for the understanding of the process. This paper would not have been possible without Mr. Helmos' support.

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