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CHALLENGES DURING SCALE-UP IN WURSTER COATING

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Abstract:

Wurster Technique for Coating of powders or particles can be performed using bottom-spray where the nozzle is spraying from the bottom or using rotary module with a nozzle spraying from the side or tangentially. The fluidization pattern in the Wurster process is very critical. The bottom-spray Wurster method is very popular in the pharmaceutical industry for active layering and for coating to modify or control drug release. It was used for development of various dosage forms of Multiple Unit Particulate Systems with better therapeutic efficacy. The Wurster process has number of variables. The batch size, spray liquid viscosity, concentration, spray assembly setting, air distributor plate, column height, and dew point, etc. are easy to establish. To fix dependent variables like air volume, atomization air pressure, spray rate, product temperature trials were performed. Finally by using Quality by design optimize the critical parameters in the process. Before scale-up, key variables and their effect on output should be identified during lab and pilot scale. This process is particularly suitable for a controlled release/ extended release and delayed/ enteric coating of active ingredients layered in the form of pellet. In the Wurster process, a complete sealing of the surface can be achieved.

Keywords: Pelletization techniques, Wurster process, Quality by design.

1. Introduction

Multiparticulate drug delivery systems are widely used in the pharmaceutical industry due to their formulation flexibility for the manufacturers and clinical benefits that they offer to the patients. Multiparticulate systems are developed in a wide range of sizes, i.e., as small as 150 µm or as large as 2–3 mm in diameter and offer superior clinical and technical advantages over many other specialized drug delivery technologies. Due to their multiplicity of units and small sizes, they exhibit reduced risk of dose dumping, spread along the gastro-intestinal tract (GIT), when taken orally, and therefore, offer specific biopharmaceutics advantages over the larger single units. Their transit time through different segments of the GIT is more predictable, reducing inter- and intra-subject variability. Multiparticulates possess large surface area for drug release and when dispersed along the gut, maximize drug absorption without possible local irritation in the GIT. Pellets are so flexible intermediate that can fill in capsule, compressed to tablets, add in suspension or make lyophilized tablets. Commercially, there are three most accepted pelletization technologies i.e. Suspension/solution loading, powder loading and extrusion-spheronization. However suspension/solution loading is most accepted technology at industry level due continuous process, less manual interruption and batch to batch reproducible assurance. Successful pellet coating process optimization at lab level using small capacity Wurster is half work done. Successful scale up of Wurster based coating process at commercial scale is a challenging task. The present review focuses on process variables involved in coating process and challenges in scale up of pellets from lab scale to industrial scale batch to get consistent results.

Fluidized Bed Processing-

Fluidized bed equipment is used extensively for multiparticulate processing [1]. Typical applications include drug layering onto a core material (sugar spheres or microcrystalline cellulose pellets), seal coating, and modified release coating. Substrates range broadly in particle size, typically from below 100 microns up to and including mini-tabs and traditional tablets. The fluidized bed is available in various configurations, depending on the machine manufacturer (vendor), but principally, they are based either on a conventional top spray, bottom spray, or tangential spray, referred to as a rotor or centrifugal processor. In 1959, Dr. Dale Wurster, then at the University of Wisconsin, introduced an air suspension technique now known as the Wurster system. The Wurster process enjoys widespread use in the pharmaceutical industry for pellet core manufacturing and film coating of particles and pellets [5]. Inserts typically range in size from 3.500 (100–500 g batch sizes) to 4600 (up to approximately 600 kg). The Wurster is widely used commercially for coating particles from less than 100 microns to more than 1 mm and for solution or suspension layering to produce drug pellets.

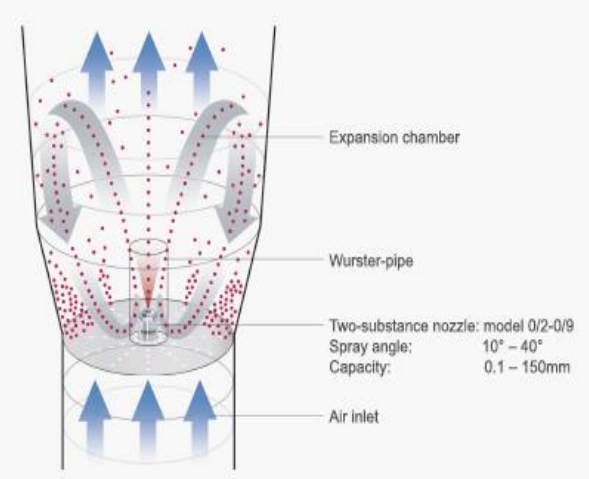

Fig. 1 Wurster Product Container

A diagram of the Wurster product container, shown in Fig.1 illustrates the regions of air and substrate flow in the process. The region outside of the partition is referred to as the down bed. The configuration of the orifice plate in this area depends on the size and density of the material to be processed. The purpose of the air flow in the down-bed region is to keep the substrate in near-weightless suspension, irrespective of its distance to either the wall of the product container or the partition. The goal is to have it travel rapidly downward (to minimize cycling time) and then to be drawn horizontally toward and ultimately into the gap at the base of the partition

General Processing Considerations for Fluidized Bed Processing-

The fluidized bed techniques described above have several process variables in common. Irrespective of the technique used, process efficiency and robustness is dependent on four major factors, listed below:

1. Heat and mass transfer
2. Substrate flow
3. Droplet size
4. Liquid properties

1. Heat and Mass Transfer-

The rate of evaporation of the application media (solvent or water) can significantly affects the properties of the applied layer or film using both aqueous and/or organic solvent systems. The coating material suppliers should recommend product temperatures for processing at which their materials will perform as intended. Process air volume, temperature, and dew point are the three components of this variable. For an aqueous process, water will move from the substrate surface to air in an attempt to reach an equilibrium condition, determined by thermodynamics. The proximity to saturation can be read from a phase diagram or psychrometric chart. The rate at which water will move from liquid on the substrate surface to vapor in the air stream increases, the further away the system is from equilibrium (the greater the driving force). Evaporation of water is impacted by the absolute humidity of the process air (commonly referred to as the dew point), whereas evaporation of a solvent is more dependent on its vapor pressure.

Inlet and Product temperature-The inlet drying air is usually heated before passing into the coating chamber to enhance the evaporation of coating material sprayed onto the cores. Control of the air temperature is important as it affects the quality of coats formed. Generally, excessively dry environment leads to spray drying effect and attrition while overwetting causes agglomeration (Maronga and Wnukowski, 1998). The optimal temperature allows the evaporation of solvent to take place at a rate that is sufficiently slow for adequate spreading of spray droplets and coalescence of polymer particles, and fast enough to avoid agglomeration and drug migration into the liquid layer (Yang and Ghebre-Sellassie, 1990). When the temperature of the air is too high, sprayed droplets dry quickly and do not coalesce when impinged on the core particles. This forms discontinuous coats which are rough and porous and will not impart the desired controlled release properties of a functional coat (Fukumori, 1994). The high temperatures may also cause spray drying of atomized droplets before they reach the cores, resulting in loss of coating material and thinner coats. Spray dried coating materials may also be embedded in the film coats, disrupting the continuity (Oliveira et al., 1997; Ronsse et al., 2007). On the other hand, when the temperature is too low, a longer time is required for coat drying and this allows soluble drug to migrate from the cores into the moistened coat layer. The dissolved drug reduces the surface tension of the liquid layer, lowering the capillary forces required for deformation and coalescence of spray droplets. Drug embedded in the resultant coat may dissolve on contact with dissolution media, resulting in a porous and more permeable coat. If the temperature is lower than the minimum film formation temperature, coalescing would not occur, resulting in discontinuous porous films (Oliveira et al., 1997). In methacrylic acid based coating, at higher temperature spray gun choked frequently due to film formation of low glass transition coating dispersion. So it recommendated that run the methacrylic acid based coating below 30°C product temperature. While in aqueous ethyl cellulose based coating required minimum 45°C product temperature due to high glass transition temperature of ethyl cellulose polymer.

Air distribution plate (ADP)-Suitable ADP has to be selected to get consistent fluidization at minimum attrition. The fluidization volume affects particle velocity; the smaller particle requires lesser air volume to attain certain height than the bigger particles. The air velocity and differential pressure at the air distribution plate must be almost same. Therefore, when deal with the smaller particle, use plate with lesser opening area to create the resistance at the ADP to have better distribution of the air (Shetty, 2010; Qiu Y et al., 2009). There are some recommendations for plate selection based on size of pellets or power

Equipment	Pellet size in micron	Plate combination
6" Wurster	< 500 Micron	A
	250 << 1200 Micron	B
	600 << 1800 Micron	C
	> 1200 Micron and Tablet	D
For commercial models	< 300 Micron	A-I
	150 << 800 Micron	B-I
	500 << 1200 Micron	
	700 << 1400 Micron	B-H
	800 << 1800 Micro	C-H
	> 1500 Micron and Tablets	C-G

Table 1: Guidelines for plate selection with respect to the final particle size

Filter bags -A filter bag is used to prevent loss of material and to allow air to pass through. If the porosity is higher than optimal, the loss of material will be high. If the porosity is lower than optimal, the filter will clog and processing will be interrupted which impact on the product yield. A filter bag is selected based on particle size of material and previous experience.

Dew point-In addition to the temperature, humidity of the inlet drying air also affects the drying of coated particles. The relationship between temperature and relative humidity or moisture content of air at different atmospheric pressures may be derived from psychometric charts (Shallcross, 1997). The humidity of air may vary from season to season or day to day. The changes in dew point of air changes the evaporating efficiency of that air. Lower humidity in the inlet air will enhance the drying capacity of air even at low temperature but it will cause excessive static charge in the product. To eliminate static charge and process variability, the required specific and absolute level must be set at the initial stage of development itself. Too high absolute humidity will result in a depression in air temperature below dew point, which will cause the condensation of water either on to machine or product substrate surface. It is not recommended to keep high moisture for a water soluble substrate at initial stage. The humidity can be increased after the initial coating because the static charge develops only once the pellets are coated with polymers (McGinity, 2002). To maintain same environment in Wurster chamber during particle coating in lab scale or commercial batches, run the process at dew point mode. The dew point is scale independent factor.

2. Substrate Flow

Drug-layering or film-coating process starts with a substrate whose surface is essentially dry. The interface with the liquid (or spray pattern) takes place in a finite or "microenvironment." While the drying capacity of process air is an important consideration, maximizing the interface between the moving substrate particles and the atomized droplets – or "coating zone" – is of paramount importance. Setup and process parameters should be focused on maximizing the substrate concentration (the number of particles) and their velocity through the coating zone. A high "mass flow" will permit a high spray rate and a higher utilization of the available drying capacity. Coating takes place on the surface of the substrate, and there is little if any penetration of the comparatively dry core by water or solvent. In film-coating process, there is no reservoir of water to keep the surface of the substrate saturated with moisture.

Column height-Appropriate adjustment of the partition gap ensures proper substrate circulation through the spray zone and up the partition column (Christensen and Bertelsen, 1997). The height of column changed based on the particle properties like size, shape, flow and bulk density. It was recognized as an important factor in determining the success of coating small substrates and was found to affect the drug release profile of coated pellets (Porter and Ghebre-Sellassie, 1994). This was due to the pellets flow into the column and the exposure of pellets to the coating droplets in the spray zone (Fitzpatrick et al., 2003; Shelukar et al., 2000). The slow and slugged form flow of particles through column leads to increased in agglomerates which column gap is too more and insufficient pressure differential created to draw particles in column. When gap is too small, less pellets draw in the column and coating material loss and chances of over wetting. Adjust the column height such a that maximum pellets comes in column. Frequently change in column height is not recommended. The recommended gap for 6" Wurster is 15-25 mm and for 18" Wurster is 40-50 mm.

Air volume -Air volume is responsible for the circulation and drying of substrates during coating. Insufficient airflow may not provide sufficient drying air to circulate the substrates and remove the moisture from the deposited sprayed droplets during coating and consequently result in a high degree of agglomeration. However, excessively high airflow rates can increase attrition conditions causing erosion of friable cores or stress cracks in coats and may also augment the spray drying effect. For functional coats, this can result in loss of the desired release properties (Cole, 1995, Qiu Y et al., 2009). The suitable airflow rate is unique for each coating equipment and also depends on product characteristics such as particle density, size, and shape (Christensen and Bertelsen, 1997). For nonaqueous coating a bubbling type of fluidization in down bed is suggested to minimize the generation of static charge and particle friction, whereas for aqueous coating more rigorous fluidization is needed to have more drying efficiency.

3. Droplet Size-

A discussion on spraying is incomplete without a dialogue on nozzle maintenance and testing. In any coating application, the spray nozzle is the single most critical component. Its performance dictates droplet size control, the quality of the applied film, and the reproducibility of the resultant product properties. These include agglomeration, appearance, potency, film-coating efficiency, and drug release characteristics. In retrospective process troubleshooting, spray nozzle performance is often the root cause of batch failures. Droplet size is governed by several factors, including the atomizing air pressure and volume, the liquid spray rate and liquid properties such as the surface tension and viscosity. In general, irrespective of the process technique used, droplet size should be small relative to the particle size of product to be coated. Pneumatic nozzles are typically used in fluidized bed equipment. The qualified operating range for atomizing pressure is usually from about 1 bar (about 15 psi) to as much as 6 bar (nearly 90 psi). Irrespective of nozzle design, the lower the atomizing air pressure, the lower the atomizing air volume. Higher pressure and air volume will result in a higher atomization air velocity, peaking at supersonic speed (about 300 m/s), increasing kinetic energy at the interface between the spray pattern and the slower moving substrate. This would increase the potential for attrition or erosion of the substrate

When coating small particles using a fluidized bed, a somewhat higher atomization air pressure and volume may be necessary to achieve small droplet size and to avoid or minimize agglomeration. There is some risk, however, that the high shear associated with pressures in the 3–6 bar (45–90 psi) range, depending on the type and size of the spray nozzle, may cause breakage of fragile core material. This is especially true for production-sized nozzles that use significant quantities of compressed air to accommodate high spray rates.

Spray rate In Wurster binary nozzle are used. The droplet formation, spreading, coalescence and evaporation happen almost simultaneously during the process. The spray rate depends on the core particles as well as the solution properties. The evaporation occurs by atomization air used for the formation of spray mist which results in increase in the droplets viscosity. In case of solvent coating, sometime excessive atomization pressure leads to spray drying portion of spray. The spray rate has to be adjusted according to drying efficiency, tackiness of solution. To coat smaller particles we need to keep the droplet size small either by increasing the atomization pressure or by decreasing spray rate to avoid agglomeration. At the beginning of coating the spray rate must be kept low to avoid solubilizing the core, seepage of the drug or coating polymer in to other layer. Once the initial barrier formed, the spray rate can be increased up to the optimum level. It is known that as the particle becomes bigger it can take up more droplets without agglomerating. When the particle enlargement is too high we may require increasing the spray rate in a regular interval (Swarbrick and Boylan, 1992). High spray rates increase the propensity for agglomeration and result in formation of less uniform coats, while low spray rates increase the coat uniformity (Singh et al., 1996). Low spray rates also enable smaller spray droplets to be formed which would reduce agglomeration, especially when coating smaller substrates (Jones and Percel, 1994). However, if the spray rate is too low, fast drying of the droplets could prevent coalescence of polymer particles, resulting in poorly formed coats (Heng et al., 1999).

Atomization air pressure- Pneumatic nozzles are commonly used for spraying of coating materials in air suspension processes. These nozzles make use of air pressure to shear the coating materials into atomized droplets. Higher atomizing air pressures result in smaller spray droplets (Wan et al., 1995) and are required to prevent agglomeration, especially when coating smaller substrates (Hemati et al., 2003). When the atomizing pressure is too high, the spray droplets can be propelled away too quickly and this does not promote droplet-core contact. High atomizing air pressure also increases the attrition of cores and can produce more fines. On the other hand, low atomizing pressure causes the formation of coarse spray droplets, which dry slowly and encourage the formation of liquid bridges between the cores, leading to increased agglomeration of the substrates being coated (Heng et al., 1999). There is an important consideration in larger capacity equipment, where there may be significant drying capacity, and the rate limiting factor is the inability of the nozzle to atomize liquid (to a satisfactory droplet size) at the rate at which the process air may remove the resultant water vapor. The only possibility for taking advantage of the increased drying capacity is to enlarge the nozzle i.e. use more compressed air at the same pressure. A process that has excessive drying capacity, but is limited by droplet size, will result in unnecessarily hindered productivity. Upgrading to the HS nozzle, which uses substantially more compressed air at the same atomization air pressures (approximately three times the volume of the 940 series nozzle), will result in a dramatic improvement in drying capacity utilization.

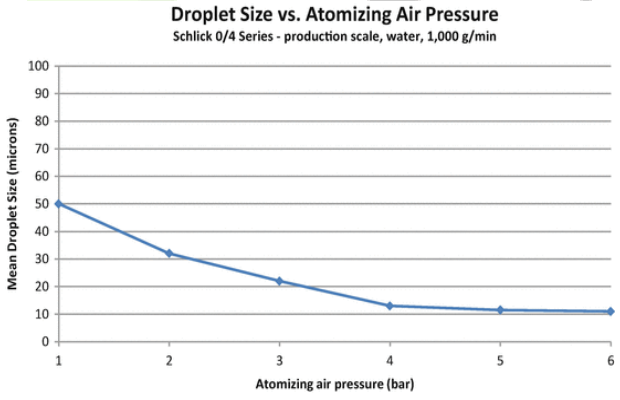

Fig No.2 Relationship between Droplet size and atomizing air pressure

Nozzle tip diameter- For the selection of nozzle, smaller the nozzle insert, more consistent will be spray. However smaller nozzle insert may cause nozzle choking. To avoid agglomeration in wurster coater the coating fluid is to be atomized more finely than in pan coater for tablets. It is necessary that the nozzle used in capable of atomizing the coating fluid even if the coating fluid delivery rate is increased. Large droplets of coating fluid generated by low performance nozzle does not distribute evenly over the material to be coated and do not dry quickly as smaller droplets. Very small droplets may dry quickly. Some droplets may contact tablets or beads surface but may dry before getting spread, it will result in to the irregular surface on core material. To maintain uniform atomization when spray rate exceeds the capacity of nozzle large droplets of coating fluid appears along with small droplets, large droplets results in to the formation of agglomerates. To avoid agglomeration multiple unit nozzles should be used (Harlan, 2004).

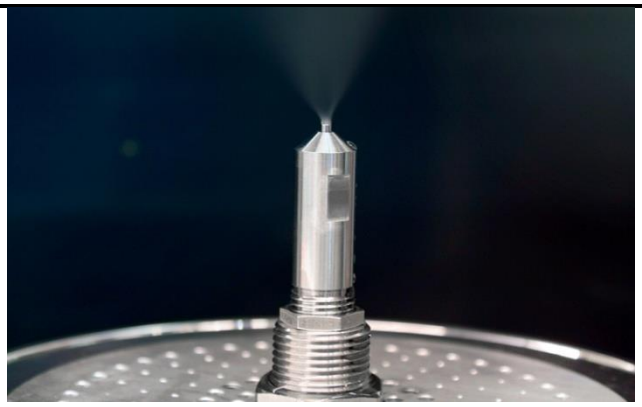

Fig No.3 Multiple unit nozzles

4. Liquid Properties-

In a water-based drug-layering or film-coating process, the incidence of agglomeration for multiparticulates may be related to what is referred to as an "exit air relative humidity threshold." As the spray rate is increased and the process air temperature elevated to accommodate the moisture (holding the product temperature at the same value), the relative humidity of the process air moves toward saturation. The closer the air is to being saturated, the lower the driving forces to remove the surface moisture. In other words, the air begins to lose its ability to draw the moisture from the film or the applied layer, whose affinity for moisture will eventually dominate. At this threshold, there may be sufficient surface moisture to cause liquid bridges to form between particles, resulting in the formation of soft agglomerates. It is important to find this limit as it will aid in identifying an upper limit for the operating range for spray rate at a given product temperature. The surface tension and viscosity of the coating liquid also play a key role in product performance. Irrespective of the product stage, drug layering, seal coating, final modified release coating, for all water-based coating formulations, identifying the exit air relative humidity threshold yields a key insight into the process conditions at which there is a potential for agglomeration or collapse of the down bed.

Coating solution/suspension nature Coating solution/suspension should have enough solid content to easy spraying. If the viscosity of coating liquid is more it will affect on droplet size and change the pellets surface. The ideal coating liquid velocity should not be more than 250 MPa.s

Drying/curing time-

The polymers dissolved in organic solvent increased the solution viscosity. During film formation, gel like phase create during solvent evaporation and polymer film formed (Muschert S, 2008). While in aqueous dispersions, film formation is more complicated (Fukumori, 1994). Surfactants, anti tacking agent and plasticizers are used aqueous dispersion to improve film nature and coating process. Plasticizers are used to reduce minimum film formation temperature (MFT) of polymers having high glass transition temperature (Tg) (Wheatley, 1997). In aqueous dispersions base coating, polymer particles come into contact with each other and form coalescence during drying (Paeratakul O, 1993).

Scale up process

The process parameters in the fluid beds are controllable precisely, which ensures easier optimization and reproducibility of the product quality. There are some wrong concepts related to Wurster based scale up process. There are number of articles available about Wurster processing, optimization and scale up. Mehta showed little correlation between load sizes; spray rate and process time, with total spraying time increasing at every scale over five different size chambers, both single and multiple nozzles (Mehta, 1988). Other published studies, which confirm reproducibility of coating applied also, demonstrate a processing time increase of 5x and 3.1x for two different products scaled from small scale to manufacturing scale (3kg to180kg).

Still question arises - "What would be the scaling up factor and consideration for reproducibility of the product quality in Wurster coating?''. The industry, which needs to scale up newly developed products from laboratory or research to manufacturing scale, must be aware of the proper designing for scaling up factor. Currently FDA is focusing on the Quality by Design (QbD) concept where in one has to build the finished product quality attributes in the design itself. USFDA also demanding for scientific approach for scale activity based on development batches. In one of the USFDA's guide to inspections report pre/post approval issues explained the expectations of regulatory authority on scale up activity said - it is important that the development and scale-up of the process be well documented so that a link between the bio/clinical batches and the commercial process can be established (USFDA, 1994).

Before attempt for successful scale up, key variables and their effect on the output should be identified during lab scale. If the scale up activity starts at the stage of development itself then it will be very easy to scale up and scale out the formulation. Wurster process has 'n' number of variables. Some of them are easy to establish e.g. batch size, spray liquid viscosity, concentration, spray assembly setting, base plate, column height and dew point etc. Perform some trials to fix some dependent variables like air volume, atomization air pressure, spray rate, product temperature etc. It is easy to understand the variables in small scale and it requires less time and cost. Finally apply design of experiments (DoE) to fix up most critical parameters as per regulatory requirement. To minimize the number of trials further one can use statistical software like Design-Expert software (Stat-Ease, Inc., Minneapolis, MN). From the output of the statistical analysis fix up the ranges for the parameter and validate the process to check the reproducibility and freeze the parameter. Once these variables are frozen, we are left with only one unknown factor - "mass effect" due to increase in the batch weight from lab scale to commercial scale. Once the parameters are studied then it will be easier to compensate the mass effect by doing minor changes in the predicted parameter in pilot and commercial level. After freezing the parameters at lab model next step is predicting the parameter for scale up. Since, at least 3 successful reproducible development batches done then next step is to setup parameters for pilot batch also have single Wurster. The development of the product is normally done 6"wurster with the batch size 0.5 to 2 kg. The wurster column and spray nozzle is small. Overall coating zone is small. The recommended pilot model is 18"wurster where the wurster column and base plate are much larger. From the lab to pilot although there is single spray nozzle but the nozzle is much bigger and can permit higher spray rate. The batch depth and mass flow density increases. Overall, the coating zone increases from lab to pilot scale. The overall coating zone will remain same in pilot and commercial scale except the height of the wurster column. Therefore, base area of wurster column plays important role in

efficient coating. All process parameters should be proportional to the base area of wurster column compared with lab model column. All the process variables again show their significance in scale up model also. Nevertheless, once the effect of variables are studied and understood in lab model it will make the analysis much easier. Just like the variables remaining same in pilot scale also, the same process control will apply. Only the unknown factor will be the mass effect. As in the lab scale, one has to follow sequential approach to set the parameter for the scale up. Linear scale up from lab scale to pilot scale assumed that the occupancy are the same and the distribution plate in each piece of equipment is geometrically similar. Additionally, ratios of air volume to plate area and spray rate to air volume maintained. The scale up factor from Pam GPCG 1.1 to Pam FBE 125C is approximately 9-fold based on vendor recommendation. This scale up factor is applicable for air volume, spray rate and atomization air pressure. The variables considered during successful scale up batch in Wurster are discussed below.

Batch size

First step to design pilot scale up after deciding equipment is defining the batch size. The process parameter may change slightly depending on the batch size due to mass effect. Set and validate the process for any change in the batch size. Keep the batch size within the recommended occupancy. e.g. For Pam GPCG 1.1, the working volume is 2.4 liter, where as Pam FBE 125 it is 84 liter, i.e. 35 times. If pilot scale up planned in FBE 125C then batch size should be 35 times of batch size taken in GPCG 1.1 (Table 2). Working volume of batch at initial and final stage should be in 20 to 100% for non functional coating and 20 to 80% for functional coating limit.

Air volume

Fluidization pattern during processing is depending on air volume. The air volume of scale up batch decided based on optimized lab scale batch. From lab to pilot scale the face velocity must be kept same. To maintain the same velocity one must know the base plate area under column of lab and pilot equipment. It is expressed in the term of fluidization air volume. Following equation can be used to calculate the Airflow. $V2 = V1 \times A2 / A1$

Where, V1 =Air flow at Lab model, V2 =Air flow for scale up model, A1 = Base area of wurster column for lab model, A2 = Base area of wurster column for pilot model.

Spray rate and atomization air pressure

The increase in the spray rate shall be always in the line of increase in the drying capacity rather than the batch size. The spray rate for a product is typically a key variable, from several perspectives. The first is economic-long processes result in high manufacturing costs. Lengthy processes also increase the likelihood of problems during the process, particularly nozzle port clogging. The spray rate is increased in related to increase in inlet air volume. Drying capacity is critical component consider in scale up activity. The drying capacity, batch size, core material and droplet size of coating liquid in coating zone are the rate limiting factors. Being said the inlet air humidity and temperature will remain same for the scale up model, the drying efficiency is increased only it terms of air volume. The spray rate can be increased in the same fold increase in the inlet air volume. spray nozzle with HS Wurster has benefits over conventional coating gun. The droplet size is large near the tip of spray gun which formed agglomerated while by accommodating HS Wurster, material not comes in contact with coating gun and spray rate can increased more. Following equation used to calculate to predict the spray rate in pilot model.

$S2 = S1 \times V2 / V1$

We can also say that $S2 = S1 \times A2/A1$ Where, V1 =Air flow at lab model V2 =Air low for scale up model, S1 =Spray rate in Lab model, S2 =Spray rate in pilot model

The increase in the spray rate must be compensated with the increase in the atomization air pressure to maintain the droplet size of the spray mist. To keep the droplet size same both in lab as well as pilot model one has to keep the spray rate to atomization air volume same. Normally atomization air volume should restrict them maximum pressure up to 4 to 5 bar. Higher the atomization air pressure the mechanical stress on the core will be high due to higher velocity. If someone uses higher air pressure in lab model then during the scale up either the spray rate needs to be reduced or the spray gun with higher capacity like HS gun can be used. Any deviation in the spray rate from the scale up factor of airflow shall be compensated by either increasing or reducing the inlet air temperature.

Mass effects

Mass effect can't predict based on batch performance in small scale equipment. The best scale up of Wurster process is from 6" lab model to 18" industrial scale model. In 6" Wurster, bed height not more than 200 mm and material fluidized up to 125 cm or less height. In the 18" Wurster, bed height is up to 600 mm, and fluidization height up to 2 meters. Scale up from
18" to 32" or more capacity Wurster is simpler due to bed height is almost same.

Theoretical parameters

Since product temperature and dew point are most critical factors that have an impact on the product movement as well as release profile, during scaling up these parameters should be kept constant. There may be some deviation in the results from lab scale even after maintaining the parameters as per the scale up calculations due to mass effect. One or the other parameter may have to be changed marginally to achieve desired release profile. The scale up activity starts with preliminary trials with predicted parameter, analyze the results, and take action if required to match the profile. If all the parameter and their effect on the release were understood in the lab scale, it will be easier to analyze the analytical results and vary the parameters to get desired profile. Process validation is recommended to check the robustness of the process before filing the parameters or planning the scale out activity.

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