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REVIEW

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Critical variables affecting the layering method of pelletization

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Abstract

The oral route of delivery is the most preferred route for administering most of the drugs. Pellets have gained importance since they offer numerous advantages like decreased dose dumping, improved patient compliance since dosing frequency is reduced, and ease of administering multiple chemically incompatible drugs immediately without the possibility of them interacting with each other. The critical variables related to process and equipment are identified and what impact they have on the quality of pellets formed is discussed. The position of the spray nozzle also affects the pellets and their yield. A complete guideline has been drawn which makes the process of pelletization using the Wurster method easier. The process variables affecting the pelletization process include inlet and product temperature, relative humidity, batch size; spray rate, and atomization air pressure and the equipment variables include column height, air distribution plate, a type of filter, and shaking interval. All these variables have a low, medium, or high impact on the process and they all together contribute to the quality of pellets formed. This review article focuses on critical process and equipment variables affecting the process of pelletization and the quality of pellets formed when using the Wurster equipment. The main objective is to review critical variables affecting the layering method of palletization and to sketch some basic problems encountered during pelletization and their troubleshooting.

Keywords Wurster, Pelletization, Process variables, Equipment variables, Guidelines for pelletization

Background

Because of advantages such as ease of administration and improved patient compliance, orally delivered medications are chosen over other dosage forms [1–3]. Parenterals do not offer patient compliance since it is invasive, therefore painful [4]. Oral dosage forms can further be categorized into single-unit dosage forms and multiple-unit dosage forms [5]. However, single-unit dosage forms possess more risk of dose dumping [6]. The advantages of multi-unit dose forms over other dosage forms are numerous. Better bioavailability, ease of coating, the ability to administer two incompatible medications simultaneously, a reduced dose dumping, and better dispersion are among the benefits [7].

Pelletization is a process of agglomeration that creates fine, free-flowing, semi-spherical units from fine powders or granules of bulk drugs and excipients, and it is the most suited method for multi-unit dosage forms where small particles, fine powders, and excipients accumulate to form smaller spheres of approximately 0.5mm-1.5mm [8]. The different techniques for pelletization are spray concealing [9], drug layering [10], cryopelletization [11], freeze pelletization [12], extrusion spheronization [13, 14], etc. Pellets are widely chosen for the oral route of administration in the form of tablets or capsules [15]. The layering method of pelletization is a process that is used in many industries to create pellets. It is a popular method for creating pellets for a variety of reasons, including its ability to produce high-quality pellets and the cost-efficiency it can bring to the production process.

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The Wurster process is used for precision application of a film coating onto particulate materials such as powders, crystals, or granules, and other solid ingredients with diameters ranging from 30 µm to several centimeters; this process helps in the formation of high-quality and uniform film coats [16]. The binder helps in the formation of functional layers on the core spheres until the desired size is achieved. In industry, solution/suspension layering using the Wurster process is widely accepted since it is a continuous process with minimal manual interruption and more reproducibility [17]. However, to create pellets using the layering method, there are a number of critical variables that need to be taken into account. In this article, the Wurster method of layering has been explored and some of the most important variables that need to be considered when using this method to create pellets are looked at. Through this discussion, how these variables affect the quality and cost-efficiency of pellets created using the Wurster layering method will be explained. By the end of the article, a better understanding of these variables and how they impact the process of creating pellets will be achieved.

Wurster technology—an overview

The Wurster processor is most commonly used for coating particles with sizes more than 100 microns [18]. In this process, the coating is done inside a hollow cylindrical chamber where the pellets move inside it and are fluidized because of high air velocity [19]. The spray gun helps in the coating of pellets and hot air helps in the simultaneous drying of the pellets that prevents agglomeration and allows uniform coating [20]. The features that make Wurster coater different from a fluid bed processor are the orifice plate (air distribution plate) and the cylindrical column [21, 22]. The movement of particles is well-organized to ensure a uniform coating of pellets; a high velocity of air near the nozzle aids in conveying the particles to the expansion chamber, where the velocity is lower, allowing the particles to fall back [23]. Here, the bubbling of particles is ensured by the air which flows through the periphery of the orifice plate. When the particles fall back, the high velocity of air creates suction due to which the particles fluidize again and this cycle continues until the entire coating is completed [24].

The top spray coater, bottom spray coater, and tangential spray coater are the three variations of Wurster equipment based on the position of the spray nozzle [25–27]. It is not only used for coating pellets but also for drying and granulation. In this, the pellets are fluidized and the coating solution is atomized with the help of an atomizer and are sprayed onto the pellets followed by drying [28, 29].

Powder granulation, taste masking, and protective coatings are all achieved with a top spray coater [32, 33]. The coating solution is sprayed against the airstream in this approach. As the particles move upwards, drying occurs [34].

The bottom spray coater is suitable for suspension coating of pellets, especially for control release substances [35]. An advantage offered by this is a complete coating of the surface by using less quantity of coating solution. The coating solution is sprayed from the bottom, and the pellets are fluidized with the force of heated air [36]. Once fluidized, they fall back on the plate and are sucked into the column, where the nozzle that will coat the pellets lies. The pellets again fall outside where the drying occurs [37].

A tangential spray coater is similar to a bottom spray coater but differs in having a motor driver rotor disc and is ideally used for pellet powder coating. The air passage allows the pellet placed on the turntables to roll meanwhile the coating solution is sprayed onto them. The rolling motion helps in providing a separation force, which prevents agglomeration [38, 39].

Variables involved in the coating of pellets using Wurster equipment: Process variables, equipment variables, and material variables are the three variables that together determine the quality of the pellets formed [17, 40]. Deviating from the optimal variables affects the final pellets; therefore, it is quite necessary to understand what impact each variable has.

Process variables

Process variables are an important factor when it comes to the layering method of pelletization. This method involves adding pellets one layer at a time, which requires precise process control in order for the pellets to achieve the desired size and shape. This process is facilitated by the use of a Wurster system, which is a specialized piece of equipment designed to disperse particles into layers. It is important to consider the different variables that come into play when setting up the Wurster system in order to ensure that the pellets are of the highest quality possible.

Inlet and product temperature and relative humidity

The temperature of the incoming air is a critical parameter to control because it affects the quality of the coatings generated. Spray drying occurs at high temperatures, whereas agglomeration occurs at low temperatures [41]. The optimum temperature allows the evaporation of the solvent gradually enough to permit for proper spray droplet spreading and polymer particle agglomerates, but rapidly enough to prevent agglomeration and drug migration into the liquid layer, resulting in uniformly coated pellets with smooth spherical surface [42]. When the air temperature is elevated, sprayed droplets dry quickly and do not agglomerate when impinged on the core particles. This results in rough, porous coats that lack the controlled drug-release properties that a functional coat requires (Figs. 1, 2, 3, 4, 5 and 6).

Due to high temperatures, atomized droplets may spray dry before reaching the core, resulting in coating material loss [18]. Spray-dried coating materials may become embedded in the film coatings, interrupting the film's continuity. However, when the temperature is too low, the drug takes longer to travel into the damp coat layers and evaporate. If the temperature is below the minimum film formation temperature, aggregation will not occur, resulting in distortion and porous films [43]. However, the temperature differs depending on the coating material [44] (Tables 1, 2, 3 and 4).

There are two types of coating solutions: aqueous and organic coating solutions, and the nature of the coating solution depends on the solubility of the materials to be added. A lower product temperature is required for organic coating because organic solvents evaporate at lower temperatures whereas aqueous solvent demands a higher product temperature [45]. Aqueous solvents do not easily evaporate as the organic solvent does, therefore there are water bridges formed between the pellets that lead to the formation of agglomerates, and hence high product temperature and low humidity are required. However, it should also be noted that the product temperature should always be higher than the minimum film-forming temperature of the polymer used in the solution/dispersion to produce continuous films [46]. Whenever the coating is aqueous, curing is required to ensure complete film formation and the airflow required is higher to ensure sufficient drying [47]. Whereas in the case of organic coating, the viscosity of the solution increases, and a gel-like phase is formed [48] and drying occurs at a comparatively lower temperature and bubbling type fluidization is required to reduce the development of static charges formed and to minimize attrition between the particles [49]. Lower moisture content leads to better drying even when the temperature is low, but it causes static charges between the particles that make them repel and move to a container's sides or stick to the column [50]. A higher moisture content leads to a drop in product temperature that causes condensation of water [51].

Batch size and spray rate

The batch size should be determined based on the capacity of the equipment in use. To determine the batch size, volume and bulk density need to be calculated. To achieve batch-to-batch homogeneity, batch size should be kept within the recommended occupancy. The batch size should be almost 20–25% of the working volume of the equipment [52]. This ensures adequate coating and drying of pellets with minimum losses [41]. If the bed load is more, it will require more fluidization pressure and superficial velocity. However, higher velocity leads to the formation of static charges. If the bed load is less, the

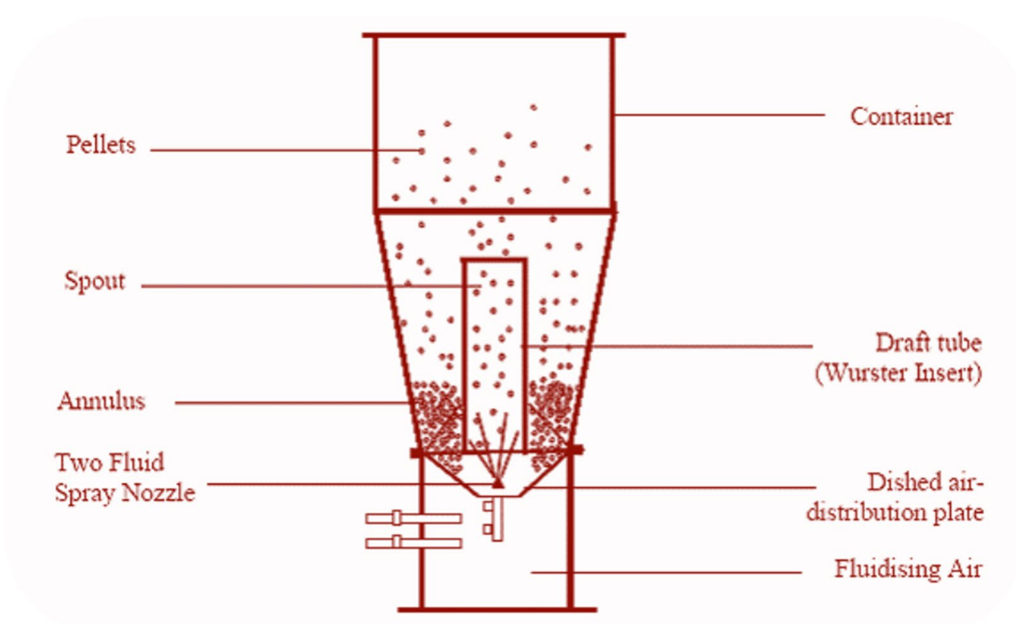

Fig. 1 Wurster coater–schematic representation [17]

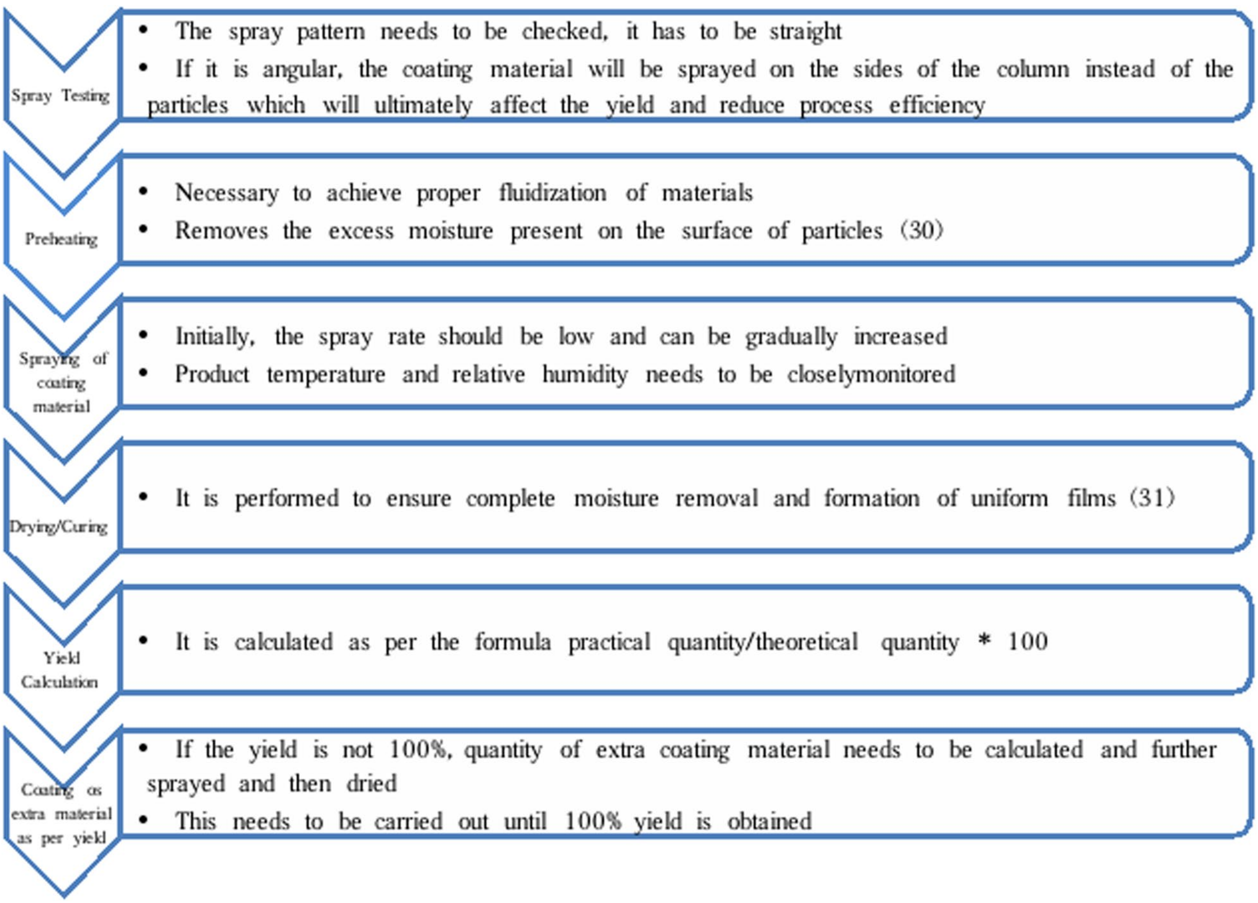

Fig. 2 Steps to be followed during the process of pelletization using Wurster equipment

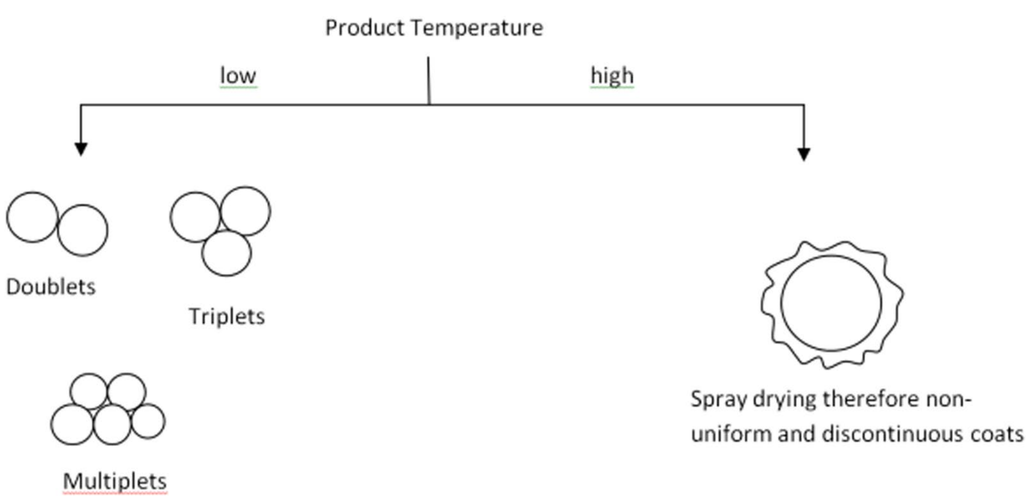

Fig. 3 Effect of product temperature on pellets [41]

fluidization pressure required is less [53]. The spray rate should be low when the batch size is less because a larger number of core pellets are not present and an increase in spray rate leads to spray material wastage since it sticks on the walls of the column [54]. The spray rate should always be increased gradually because initially the size of core pellets is too small and an increase in spray rate will lead to the formation of agglomerates. The spray rate can

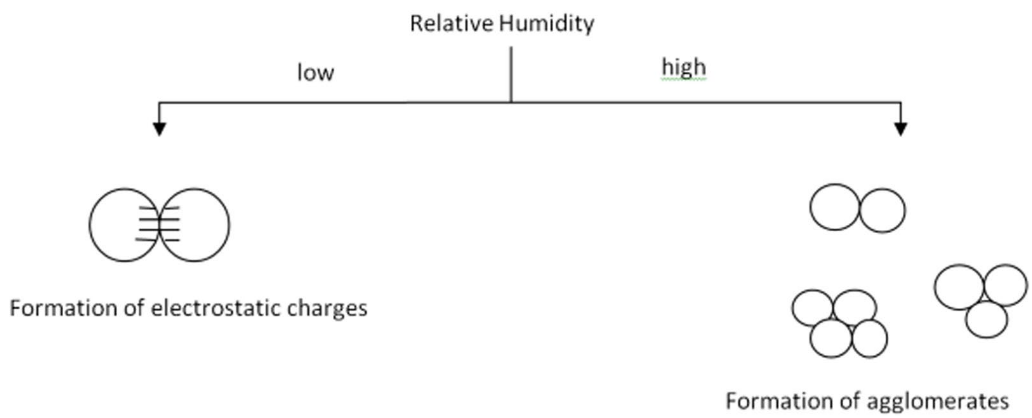

Fig. 4 Effect of relative humidity on pellets [50]

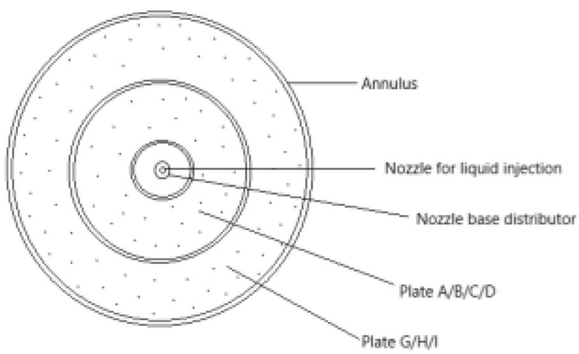

Fig. 5 Air distribution plates in commercial models

be increased once a sufficient amount of coating is performed [17]. As coating proceeds, the size of the pellet increases, and therefore the bed load, therefore air volume should also be increased to maintain a reasonable degree of fluidization [55].

Atomization air pressure

The droplet size of the coating material is also important and it depends on the size of the particles to be coated [56]. The droplet size can be controlled by determining the atomization pressure [57]. At higher atomization pressure, the droplet size is smaller and vice-versa [51]. For smaller particles, the droplet size needs to be small. High atomizing pressure results in attrition and production of fines [58].

By considering these variables, it is possible to optimize the layering method of pelletization and ensure that the final product meets the desired specifications.

When the coating material is sprayed, the moisture must be evaporated as well to avoid the formation of agglomerates [59]. The evaporation rate depends on the process air volume, inlet, and product temperature which are 30 °C and 24.20 °C, respectively [60]. As evaporation increases, relative humidity (60 to 70%) increases, which help dispel electrostatic charges [61].

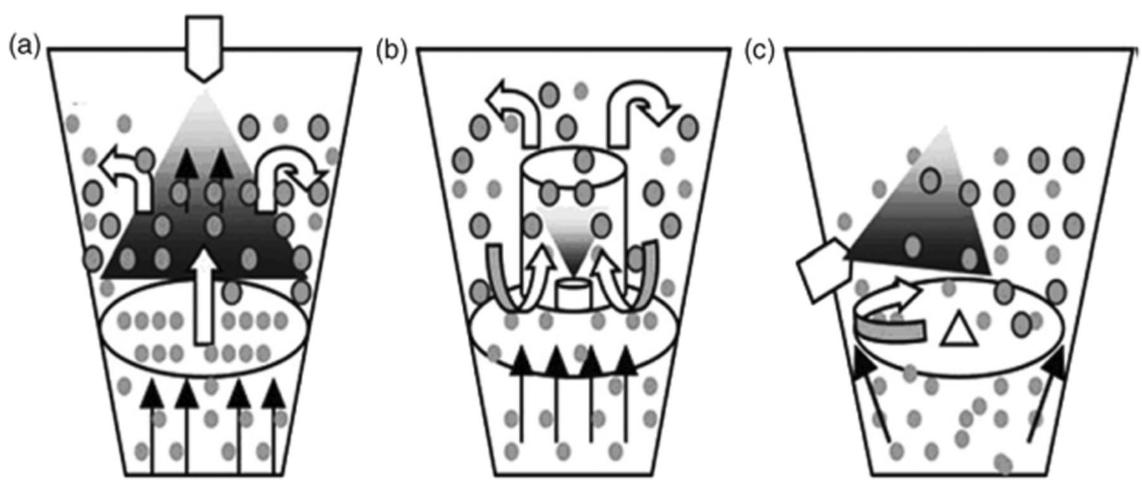

Fig. 6 **a** Top spray coater **b** Bottom spray coater **c** Tangential spray coater [30]

Table 1 Parameters were followed to prevent agglomeration

Parameter	Requirement	Reference
Inlet and product temperatures	Above the minimum film-forming temperature	[43]
Spray rate	Low, and can be increased gradually	[17]
Atomization pressure	High, but not too high that it produces fines	[58]

Table 2 The type of air distribution plate according to pellet size- lab scale and commercial scale [17]

Equipment	Pellet size in microns	Plate combination
6″ Wurster	< 500 Microns	A
	250 < < 1200 Micron	B
	600 < < 1800 Micron	C
	> 1200 Micron and Tablets	D
Commercial Models	< 300 Microns	A-I
	150 < < 800 Micron	B-I
	500 < < 1200 Microns	B-H
	700 < < 1400 Micron	C-H
	800 < < 1800 Micron	C-G
	> 1500 Micron and Tablets	D-G

Table 3 Major variables and effects on pelletization

Sr. No	Variables	Effects	References
1	Atomization	Mass/liquid ratio control droplet size	[17, 18, 52, 57, 58]
2	Blow speed	High airflow causes attrition and generates fines	
3	Inlet temperature	Premature drying	
4	Spray rate	Agglomeration	
5	Strength of the coating solution	Blockage of nozzles	
6	Size distribution	Flow properties	
7	Batch size	Fluidization	

However, the temperature should not be too high, which makes the zone of the coating so dry that it results in spray drying [60].

Equipment variables

The layering method of pelletization is a complex process that involves the use of specialized equipment. One of the most important pieces of equipments used in this process are Wurster fluid bed system, Extrusion screen, Extruder, Mixer. The fluid bed system is designed to create multiple layers of pellets that can be used for a variety of applications.

The Wurster system is incredibly precise and can produce pellets with precise sizes and shapes depending on the desired application. This precision is necessary for creating a good layer of pellets for layering. Without precise sizing and shape control, the layering process could fail, resulting in poor product quality.

Column height

To achieve proper fluidization, column height needs to be adjusted. Column height depends on the particle size. The larger the size of the particles, the larger the column height [17]. The number of pellets/particles drawn into the column depends on the column height. If the column height is less, fewer particles are drawn into the column but the amount of spray is the same, which leads to overwetting of particles, therefore formation agglomerates, and if the column height is more, more particles will be drawn into the column that will result in non-uniform and insufficient coating [62]. Suction pressure is needed to move particles from the annular zone to the coating tube and this effect is known as the Venturi effect [63]. An ideal column height (0.3–0.5 m) needs to be maintained to draw the maximum substrate in the column. Once the coating is done, drying needs to be carried out at a higher column height and decreased blower speed to ensure complete drying. Increasing the partition gap too many results in fluidization but a slight increase leads to dissociating clusters and achieving circulatory motion [21].

Air distribution plate

The air distribution plate is made of stainless steel and is porous. These pores help in the fluidization materials. As the column height depends on the particle size, similarly the selection of the air distribution plate also depends on the particle size. There are two types of pores: small and large. Small holes help in the bubbling of particles that are toward the periphery and the larger holes are present below the coating column that helps in the fluidization of particles [57].

Table 4 Troubleshooting in the process of pelletization

Problem	Remedy	Reference
Static charges on pellets	Increase the Relative humidity	[38, 39, 44]
Doublets/triplets/multiplets formed	Decrease the relative humidity	
Inability to increase the relative humidity	Provide external heating	
The increased number of fines produced	Reduce the blower speed	
Excessive wetting of the pellet	Decrease spray rate	
Defluidization of bed	Decrease spray rate	
Blockage of spray nozzle	Decrease the strength of the solution	

Filter bag and shaking interval

Since the particles are in a fluid motion, they travel to the upward chamber [52]. The fluidized bed processor has an automatic shaking mechanism to prevent filter obstruction. There are different types of filter bags like-bonnet filters, finger bags, cartridge filters, etc. [51]. The particle size of the core pellets is used to choose a filter bag. The ideal diameter of a filter bag is 720 mm. If the porosity of the filter bag is higher than ideal, the material loss will be substantial, and if it is lower than ideal, the filter bag will clog, resulting in process interruption and product yield. Differential pressure is used to check the filter bag's porosity. Filter bags with relatively smaller pores tend to clog easily with larger particles that reduces the yield and process efficiency [64]. The shaking of the bags is done at regular intervals [65]. The shaking can be synchronous or asynchronous. Asynchronous shaking is chosen for the pelletization process in which one bag is shaken and the other is functional that helps in the continuous process. Whereas in synchronous shaking, both the filter bags are shaken and the fluidization stops until the shaking is completed. The time for shaking can be adjusted depending on the material. Once the process is completed and the material needs to be unloaded, manual shaking is done to ensure no material is present in the filter bags that ensures better yield and helps in easy cleaning [56].

Process efficiency

The process efficiency needs to be calculated to know how much coating material is lost in the process. In some cases, the angle of the spray nozzle is such that the coating material gets sprayed on the walls of the column. Therefore, to prevent that an initial spray test needs to be performed to check that the spray material sprayed is straight and not angular.

The coating material required for each batch depends on the process efficiency/spray efficiency. By processing a few batches, the extra coating material required can be calculated and prepared for the other planned batches [54].

Selection of position of spray nozzle

(1) Top spray: The spray nozzle is on the top and it sprays the binder solution/drug solution downwards [66]. The top spray is used for drying wet granules/powder, granulation, and coating. The top spray is the most commonly used in granulation [56]. The variables that affect top spray granulation are-

a) Inlet air temperature
b) Fluidization air volume
c) Atomization air pressure
d) Rate of adding liquid [67]

Higher inlet temperature decreased the average particle size. An increase in the rate of liquid or binder addition helps in decreasing friability and therefore, comparatively larger particles are formed. Higher atomization air pressure reduces the particle size. However, top spray coating is not suitable where the quality and uniformity of the film thickness are desirable [68].

(2) Bottom spray: When the spray nozzle is at the bottom, heated air flows upward through the bottom. The bottom spray is most preferable for the coating process since it allows uniform coating on every material [61].

$$\text{Process efficiency is calculated by} = \frac{\text{Weight of coated pellets} - \text{Weight of uncoated pellets} \ast 100}{\text{Total solids present in the coating material sprayed}}$$

(3) Tangential spray: The nozzle here is placed on the side of the chamber. Three types of forces are provided- centrifugal force, lifting force, and gravity force that helps in homogenous granulation [69].

Material variable

The key formulation variables include composition, porosity, size, shape and density of the pellets; type and amount of polymer coating; nature, size and amount of excipients. Extrusion and spheronization method widely used for the preparation of pellets of various materials; natural extract, bacterial culture, drugs, etc., with immediate release, and modified release pattern.

Material variables are important because various the formulation of pellets for different purposes using various excipients to overcome the issues of solubility, stability and drug release properties etc.

Conclusion

The layering method of pelletization is an important tool in the pharmaceutical industry, as it allows for the production of well-defined particles with uniform shapes and sizes. In order for this process to be successful, there are several critical variables that must be taken into account. One such variable is the type of coating being used. Many different coatings can be used, and each one will provide different levels of protection and stability to the final pellet. Additionally, the physical properties of the coating, such as its viscosity, must be chosen appropriately in order to provide the desired result.

Another critical variable to consider when using the layering method of pelletization is the size of the pellets being produced. This is usually done through a process known as Wurster coating. Here, the pellets are sprayed with a coating solution, which is then dried either by air or in a vacuum. The size of the particles being sprayed will determine the size of the final pellet, and thus must be chosen accordingly. Additionally, the viscosity of the coating solution must be taken into account in order to ensure that the pellets are uniform in size.

Finally, the speed at which the pellets are produced must also be taken into account. If the process is too slow, then the particles may not be adequately coated and the pellets may lack uniformity. On the other hand, if the process speed is too fast, then the formation of the pellets may not be complete, leading to a lack of uniformity in the final product. Thus, the optimal speed must be chosen, taking into account the speed at which the coating solution is applied and the drying time.

All these variables contribute to the process efficiency. The effects of deviating from the optimal parameters have been discussed, which will help in the optimization of the variables. There are three positions where the spray nozzle can be placed; however, bottom spray seems promising in terms of the quality of pellets formed. These are the general guidelines mentioned in this article and these can vary depending on the molecule one is working on and the type of coating to be performed. Therefore, more lab studies must achieve the parameters for each molecule.

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References

1. Shahiwala A (2011) Formulation approaches for the enhancement of patient compliance to oral drug therapy. Expert Opin Drug Deliv 8(11):1521–1529. https://doi.org/10.1517/17425247.2011.628311
2. Sosnik A, Augustine R (2016) Challenges in oral drug delivery of antiretrovirals and the innovative strategies to overcome them. Adv Drug Deliv Rev 103:105–120. https://doi.org/10.1016/j.addr.2015.12.022
3. Fasano A (1998) Novel approaches for oral delivery of macromolecules. J Pharm Sci 87(11):1351–1356. https://doi.org/10.1021/js980076h
4. Lewis AL, Richard J (2015) Challenges in the delivery of peptide drugs: an industry perspective. Ther Deliv 6(2):149–63. https://doi.org/10.4155/tde.14.111
5. Aleksovski A, Dreu R, Gašperlin M, Planinšek O (2015) Mini-tablets: a contemporary system for oral drug delivery in targeted patient groups. Expert Opin Drug Deliv 12(1):65–84. https://doi.org/10.1517/17425247.2014.951633
6. Roy P, Shahiwala A (2009) Multiparticulate formulation approach to pulsatile drug delivery: current perspectives. J Control Release 134(2):74–80. https://doi.org/10.1016/j.jconrel.2008.11.011
7. Newton JM (2010) Gastric emptying of multi-particulate dosage forms. Int J Pharm 395(1–2):2–8. https://doi.org/10.1016/j.ijpharm.2010.04.047
8. Politis SN, Rekkas DM (2011) Pelletization processes for pharmaceutical applications: a patent review. Recent Pat Drug Deliv Formul 5(1):61–78. https://doi.org/10.2174/187221111794109493
9. Vergote GJ, Kiekens F, Vervaet C, Remon JP (2002) Wax beads as cushioning agents during the compression of coated diltiazem pellets. Eur J Pharm Sci 17(3):145–51. https://doi.org/10.1016/s0928-0987(02)00164-1

10. Zoubari G, Ali R, Dashevskiy A (2019) Water-insoluble polymers as binders for pellet drug layering: effect on drug release and performance upon compression. Int J Pharm. 569:118520. https://doi.org/10.1016/j.ijpharm.2019.118520
11. Byrne RS, Deasy PB (2005) Use of porous aluminosilicate pellets for drug delivery. J Microencapsul 22(4):423–437. https://doi.org/10.1080/02652040500100196
12. Shamma RN, Basalious EB, Shoukri R (2012) Development of novel sustained-release matrix pellets of betahistine dihydrochloride: effect of lipophilic surfactants and co-surfactants. Pharm Dev Technol 17(5):583–593. https://doi.org/10.3109/10837450.2011.557730
13. Steckel H, Mindermann-Nogly F (2004) Production of chitosan pellets by extrusion/spheronization. Eur J Pharm Biopharm 57(1):107–114. https://doi.org/10.1016/s0939-6411(03)00156-5
14. Loka NC, Saripella KK, Pinto CA, Neau SH (2018) Use of extrusion aids for successful production of Kollidon® CL-SF pellets by extrusion-spheronization. Drug Dev Ind Pharm 44(4):632–642. https://doi.org/10.1080/03639045.2017.1405975
15. Chen T, Li J, Chen T, Sun CC, Zheng Y (2017) Tablets of multi-unit pellet system for controlled drug delivery. J Control Release 262:222–231. https://doi.org/10.1016/j.jconrel.2017.07.043
16. Böhling P, Khinast JG, Jajcevic D, Davies C, Carmody A, Doshi P, Am Ende MT, Sarkar A (2019) Computational fluid dynamics-discrete element method modeling of an industrial-scale wurster coater. J Pharm Sci 108(1):538–550. https://doi.org/10.1016/j.xphs.2018.10.016
17. Sonar G, Rawat S (2015) Wurster technology: process variables involved and Scale-up science. Innovat Pharm Pharm Technol 1:100–109
18. Zhang R, Hoffmann T, Tsotsas E (2020) Novel technique for coating of fine particles using fluidized bed and aerosol atomizer. Processes 8(12):1525. https://doi.org/10.3390/pr8121525
19. Behzadi SS, Toegel S, Viernstein H (2008) Innovations in coating technology. Recent Pat Drug Deliv Formula 2(3):209–230. https://doi.org/10.2174/187221108786241633
20. Richard T, Xiu XC (2005) The scale-up of spray coating processes for granular solids and tablets. Powder Technol 150(2):78–85. https://doi.org/10.1016/j.powtec.2004.11.021z
21. Vipin S (2009) Fluidized bed processing for multiparticulates. Rasayan J Chem
22. Dixit R, Puthli S (2009) Fluidization technologies: aerodynamic principles and process engineering. J Pharm Sci 98(11):3933–3960
23. Mohylyuk V, Patel K, Scott N, Richardson C, Murnane D, Liu F (2019) Wurster fluidised bed coating of microparticles: towards scalable production of oral sustained-release liquid medicines for patients with swallowing difficulties. AAPS PharmSciTech 21(1):3. https://doi.org/10.1208/s12249-019-1534-5
24. Wang LK, Heng PWS, Liew CV (2010) Online monitoring of particle mass flow rate in bottom spray fluid bed coating—development and application. Int J Pharm 395(1–2):215–221. https://doi.org/10.1016/j.ijpharm.2010.05.044
25. Frey C (2014) Microencapsulation in the food industry. Fluid Bed Coating-Based Microencapsulation. https://doi.org/10.1016/B978-0-12-821683-5.00024-8
26. Heinrich S (2015) Mesoscale modeling in chemical engineering part I volume 46. multiscale analysis of a coating process in a Wurster fluidized bed apparatus. In: Advances in Chemical Engineering pp 83–135
27. Foroughi-Dahr M, Mostoufi N, Sotudeh-Gharebagh R, Chaouki J (2017) Particle coating in fluidized beds. In: Reference module in chemistry, molecular sciences, and chemical engineering, pp1–89
28. Pearnchob N, Bodmeier R (2003) Dry polymer powder coating and comparison with conventional liquid-based coatings for Eudragit® RS, ethylcellulose, and shellac. Eur J Pharm Biopharm 56(3):363–9
29. Hemati M, Cherif R, Saleh K, Pont V (2003) Fluidized bed coating and granulation: influence of process-related variables and physicochemical properties on the growth kinetics. Powder Technol 130(1–3):18–34. https://doi.org/10.1016/S00325910(02)00221-8
30. Tumuluru JS (2014) Effect of process variables on the density and durability of the pellets made from High moisture corn stover. Biosys Eng 119:44–57. https://doi.org/10.1016/j.biosystemseng.2013.11.012
31. Fries L, Antonyuk S, Heinrich S, Palzer S (2011) DEM–CFD modeling of a fluidized bed spray granulator. Chem Eng Sci. https://doi.org/10.1016/j.ces.2011.02.038
32. Joshi S, Petereit H-U (2013) Film coatings for taste masking and moisture protection. Int J Pharm 457(2):395–406. https://doi.org/10.1016/j.ijpharm.2013.10.021
33. Dewettinck K, Huyghebaert A (1999) Fluidized bed coating in food technology. Trends Food Sci Technol 10(4–5):168. https://doi.org/10.1016/S0924-2244(99)00041-2
34. Börner M, Peglow M, Tsotsas E (2013) Derivation of parameters for a two compartment population balance model of Wurster fluidised bed granulation. Powder Technol 238:122–131. https://doi.org/10.1016/j.powtec.2012.04.014
35. Werner SR, Jones JR, Paterson AH, Archer RH, Pearce DL (2007) Air-suspension particle coating in the food industry: part I — state of the art. Powder Technol 171(1):25–33. https://doi.org/10.1016/j.powtec.2006.08.014
36. Rajniak P, Mancinelli C, Chern RT, Stepanek F, Farber L, Hill BT (2007) Experimental study of wet granulation in fluidized bed: impact of the binder properties on the granule morphology. Int J Pharm 334(1–2):92–102. https://doi.org/10.1016/j.ijpharm.2006.10.040
37. Shelukar S, Ho J, Zega J, Roland E, Yeh N, Quiram D et al (2000) Identification and characterization of factorscontrolling tablet coating uniformity in a Wurster coating process. Powder Technol 110(1–2):29–36. https://doi.org/10.1016/S0032-5910(99)00265-X
38. Yang ST, Ghebre-Sellassie I (1990) The effect of product bed temperature on the microstructure of aquacoat-based controlled-release coatings. Int J Pharm 60(2):109–124. https://doi.org/10.1016/0378-5173(90)90296-G
39. Farag Y, Leopold CS (2011) Influence of the inlet air temperature in a fluid bed coating process on drug release from shellac-coated pellets. Drug Dev Ind Pharm 37(3):320–328. https://doi.org/10.3109/03639045.2010.512292
40. Krogars K, Heinämäki J, Vesalahti J, Marvola M, Antikainen O, Yliruusi J (2000) Extrusion–spheronization of pH-sensitive polymeric matrix pellets for possible colonic drug delivery. Int J Pharm 199(2):187–194. https://doi.org/10.1016/s0378-5173(00)00382-3
41. Tang ESK, Wang L, Liew CV, Chan LW, Heng PWS (2008) Drying efficiency and particle movement in coating—Impact on particle agglomeration and yield. Int J Pharm 350(1–2):172–180. https://doi.org/10.1016/j.ijpharm.2007.08.047
42. Yang Q, Yuan F, Xu L, Yan Q, Yang Y, Wu D et al (2019) An update of moisture barrier coating for drug delivery. Pharmaceutics 11(9):436. https://doi.org/10.3390/pharmaceutics11090436
43. Yang ST, Ghebre-Sellassie I (1990) The effect of product bed temperature on the microstructure of aquacoat-based controlled-release coatings. Int J Pharm 60(2):109–124
44. Gharsallaoui A, Roudaut G, Chambin O, Voilley A, Saurel R (2007) Applications of spray-drying in microencapsulation of food ingredients: an overview. Food Res Int 40(9):1107–1121
45. Thoma K, Bechtold K (1999) Influence of aqueous coatings on the stability of enteric-coated pellets and tablets. European J Pharm Biopharm 47(1):39–50. https://doi.org/10.1016/s0939-6411(98)00086-1
46. Tzika M, Alexandridou S, Kiparissides C (2003) Evaluation of the morphological and release characteristics of coated fertilizer granules produced in a Wurster fluidized bed. Powder Technol 132(1):16–24. https://doi.org/10.1016/S0032-5910(02)00345-5
47. Felton LA (2013) Mechanisms of polymeric film formation. Int J Pharm 457(2):423–427. https://doi.org/10.1016/j.ijpharm.2012.12.027.4
48. Dušek K, Dušková-Smrčková M (2000) Network structure formation during crosslinking of organic coating systems. Progress Polym Sci 25(9):1215–1260. https://doi.org/10.1016/S0079-6700(00)00028-9
49. Maurer S, Durán SR, Künstle M, Biollaz SMA (2015) Influence of interparticle forces on attrition and elutriation in bubbling fluidized beds. Powder Technol 291:473–486. https://doi.org/10.1016/j.powtec.2015.12.026
50. Salama F, Sowinski A, Atieh K, Mehrani P (2013) Investigation of electrostatic charge distribution within the reactor wall fouling and bulk regions of a gas-solid fluidized bed. J Electrostat 71(1):21–27. https://doi.org/10.1016/j.elstat.2012.11.002
51. Patel A, Patel A, Patel R, Dharamsi A (2019) Application of failure mode effect analysis in Wurster-based pelletization technology: a technical note. AAPS PharmSciTech. https://doi.org/10.1208/s12249-019-1516-7
52. Jones D (2009) Developing Solid Oral Dosage Forms. In: Development, Optimization, and Scale-up of Process Parameters

53. Akgün IS, Erkey C (2019) Investigation of hydrodynamic behavior of alginate aerogel particles in a laboratory scale Wurster fluidized bed. Molecules 24(16):2915. https://doi.org/10.3390/molecules24162915
54. Shah N, Mehta T, Aware R, Shetty V (2017) Investigation on influence of Wurster coating process parameters for the development of delayed release minitablets of Naproxen. Drug Dev Ind Pharm 43(12):1989–1998. https://doi.org/10.1080/03639045.2017.1357732
55. Morris J (2021) Mechanisms and mitigation of agglomeration during fluidized bed combustion of biomass. Fuel 250:452–473. https://doi.org/10.1016/j.fuel.2018.04.098
56. Jones D (1997) Air suspension coating for multiparticulates. Drug Dev Ind Pharm 20(20):3175–3206. https://doi.org/10.3109/03639049409041973
57. Juslin L, Antikainen O, Merkku P, Yliruusi J (1995) Droplet size measurement: I. Effect of three independent variables on droplet size distribution and spray angle from a pneumatic nozzle. Int J Pharm 123(2):247–256. https://doi.org/10.1016/0378-5173(95)00082-T
58. Dacanal GC, Menegalli FC (2010) Selection of operational parameters for the production of instant soy protein isolate by pulsed fluid bed agglomeration. Powder Technol 203(3):565–573. https://doi.org/10.1016/j.powtec.2010.06.023
59. Hemati M, Cherif R, Saleh K, Pont V (2003) Fluidized bed coating and granulation: influence of process-related variables and physicochemical properties on the growth kinetics. Powder Technol 130(1–3):18–34. https://doi.org/10.1016/S0032-5910(02)00221-8
60. Madlmeir S, Forgber T, Trogrlic M, Jajcevic D, Kape A, Contreras L, Carmody A, Liu P, Davies C, Sarkar A, Khinast JG (2022) Quantifying the coating yield by modeling heat and mass transfer in a Wurster fluidized bed coater. Chem Eng Sci. https://doi.org/10.1016/j.ces.2022.117505
61. Jones DM, Rajabi-Siahboomi AR (2017) Fluid bed technology, process robustness, and scale-up. In: Multiparticulate Drug Delivery. https://doi.org/10.1007/978-1-4939-7012-4_4
62. Chan LW, Tang ES, Heng PW (2006) Comparative study of the fluid dynamics of bottom spray fluid bed coaters. AAPS PharmSciTech 7(2):E45–E53. https://doi.org/10.1208/pt070237
63. Akgün IS, Erkey C (2019) Investigation of hydrodynamic behavior of alginate aerogel particles in a laboratory scale Wurster fluidized bed. Molecules. https://doi.org/10.3390/molecules24162915
64. R Dumpala, C Patil (2020) A review on pellets and pelletization techniques. Int J Trend in Innovat Res
65. Naidu VR, Deshpande RS, Syed MR, Deoghare P, Singh D, Wakte PS (2016) PAT-based control of fluid bed coating process using NIR spectroscopy to monitor the cellulose coating on pharmaceutical pellets. AAPS PharmSciTech 18(6):2045–2054. https://doi.org/10.1208/s12249-016-0680-2
66. Ronsse F, Pieters JG, Dewettinck K (2007) Combined population balance and thermodynamic modelling of the batch top-spray fluidised bed coating process. Part I—Model development and validation. J Food Eng 78(1):296–307. https://doi.org/10.1016/j.jfoodeng.2005.09.030
67. Davies WL, Gloor WT (1971) Batch production of pharmaceutical granulations in a fluidized bed I: effects of process variables on physical properties of final granulation. J Pharm Sci 60(12):1869–1874. https://doi.org/10.1002/jps.2600601224
68. Srivastava S, Mishra G (2010) Fluid bed technology: overview and parameters for process selection. Int J Pharm Sci Drug Res 2(4):236–246
69. Yamamoto K (2017) Process development, optimization, and scale-up. In: Developing solid oral dosage forms. https://doi.org/10.1016/B978-0-12-802447-8.00029-7

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