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A REVIEW ON FLUIDIZED BED PROCESSOR

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ABSTRACT

One potential instrument for creating innovative trends and implications in the field of formulation and development with enhanced medicinal efficacy is fluidised bed processing technology. The fluidised bed processor is used for granulation, stacking, drying, and coating. It is currently dominating thes industry because to its innovative tactics and the latest trends and developments. The most recent and promising development in pharmaceutics granulation technology is the fluidised bed granulation process. Fluidised bed granulation is a crucial method in pharmaceutics that enhances the powder's solubility and dissolution while also improving the powder's powder characteristics for creating pharmaceutical dosage forms. Granules of superior quality were produced by comprehending and managing the crucial process factors. The principles of fluidised bed processors and fluidised bed granulation are reviewed in this article, along with comprehensive details on the current technology, benefits, and troubleshooting techniques.

KEYWORDS: Granulation, Fluidization, Particle growth, Drying and Fluidized bed granulation.

INTRODUCTION

Granulation is an essential unit activity in the manufacturing of pharmaceutical dosage forms, especially in the filling of capsules and the fabrication of tablets. This process involves the transformation of either fine or coarse particles into larger aggregates referred to as granules. Granulation usually starts when the powder ingredients and the active pharmaceutical ingredient are first pre-blended or dry mixed, which allows for a consistent dispersion of all ingredients in the combination. These granules are mostly made as intermediates, meant to be mixed with other components before tablet compaction and capsule filling, although they can be packaged directly as a dosage form.[1-4]

The granulation process uses a granulation fluid, which is composed of dry powder ingredients combined with a liquid. Often, binders are made by combining dry particles like powders and sometimes crystals with granulation fluid, also known as the binder solution. To guarantee that the granulating solution is distributed evenly and to encourage particle interactions, this combination is added to the dry components. Inter-particle forces are essential to the creation of the granules and sustain their stability.[5-7,29]

Objective of granulation[1,2,7,8,15-18]

1. To enhance the density of the, blend thereby reducing the volume occupied per unit weight, which facilitates improved storage and transportation.
2. To make metering and volumetric dispensing possible.
3. To enhance the visual appeal of the formulation.
4. To increase the product's dispersibility.
5. To minimize dust generation during the granulation process.
6. To decrease the risk of exposure to toxic substances and mitigate process-related hazards.
7. To achieve a spherical granule shape, which enhances the flow properties of the powder.
8. To ensure the presence of sufficient fines that can fill the voids between granules, promoting better compaction.
9. To preserve a tight distribution of particle sizes, guarantee content homogeneity, and make volumetric dispensing easier.
10. To determine the proper hardness, moisture content, and compression properties in order to avoid breakage and dust production during manufacturing.
11. When powders are extremely fine and fluffy, they can pose significant challenges in processing. These powders may not:

- Remain blended consistently
- Compress adequately in the tablet press

Granulation of Fundamentals[1,2,7,8]

Granulation is a physical process used to turn grains, pellets, and small powder particles into huge agglomerates. The main tool used in this process is a granulation fluid, which is mixed with the granulating solution and can be either a dry binder or a binder solution. The dry powder mixture is combined with these granulating fluids. When the dry powder blend and the granulating fluid are combined, agglomerates are created. Continuous mixing promotes the development of bridges or contacts between particles and results in uniform dispersion. The forces that exist between the particles create stable granules.

Fluidized bed processor[7-16,27]

Catalytic cracking techniques served as the initial setting for the development of the fluidised solids concept. Developments in standard oil have been greatly aided by the fluidisation process. The fluid bed technique was developed as a result of groundbreaking studies on the flow properties of solid particles suspended in gases by professors E.R. Gilliland and W.K. Lewis. Although the idea was first presented by Dale Wruster in 1960, the fundamental principle of fluidised solids was first applied in an industrial context for non-pharmaceutical uses in 1930. By applying a coating solution over a bed of tablets with a stream of heated air in 1953, Wrester invented the tablet coating technique, which is today known as the Wruster process. The granulation of powders was then developed by Dr. Dale Wurster in 1960. There was a notable uptick in fluid bed process development, use, and commercialization in the 1980s.

Fluid bed processing offers several advantages, including

- Reduced processing stages
- Lower cost
- Decreased processing time

This modern technology encompasses various procedures, such as

- Coating
- Granulation
- Drying of powdered materials
- Drug layering

In the pharmaceutical industry, the most widely recognized fluid bed coating method

- Bottom Spray (Wurster) process

Principle of fluidized bed processor[8,10,27]

A bed of solid particles or a layer of powdered material makes up the fluid bed. The particles are raised and suspended in the air stream by the introduction of hot air at high pressure through an air distribution plate at the bottom. The fluidisation process is the term used to describe this occurrence. Then, using spray nozzles, a granulating or coating solution is sprayed to coat the particles or form granules, respectively. At the same time, the heated air causes the coated particles or granules to dry.

The concept of fluidization[8,10,27,28]

Fluid bed processing can be executed through various methods, including:

1. **Top spray:** Ideal for uniform granulation and pelletization.
2. **Bottom spray:** Employs a Wurster coating unit for spray application.
3. **Tangential spray:** Another configuration option.

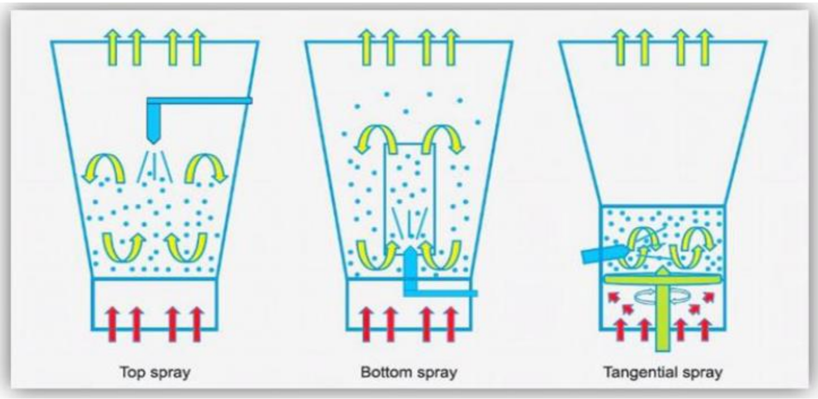
Characteristics of a fluidized bed

A fluidized bed exhibits the following characteristics:

- Particle Behavior
- Flowability
- Pressure Head
- Angle of Repose

Fluid bed processor designs: The three fluid bed processor designs are distinguished by the placement of their spray nozzle:

a. Top Spray Configuration: The spray nozzle is positioned at the top of the fluid bed granulation equipment.
b. Bottom Spray: The equipment's spray nozzle is situated at the bottom, often using a Wurster coating unit.
c. Tangential Spray: Spray nozzle is located tangentially to the equipment, providing a unique spray pattern.



Concept of fluidization

FBP Parts and their Functions

Sr. No	Parts	Function
1	Nozzle	The granulating or coating solution's droplet size and dispersion.
2	Plate for air distribution	the way that fluidised air is distributed between the inner and exterior parts.
3	Draft tube /plenum	Air is introduced, ensuring presser is balanced for a more uniform disribution.
4	Cylinder	Particles are drawn through the gap in the partition.
5	Filter bags	Filter bags are utilized for the ongoing process of fluidization.
6	Expansion chamber	To facilitate the continuous movement of the particles.

Fluidized bed granulation[8,10,13-20]

Through constant mixing in the presence of a granulating fluid, small solid particles are transformed into bigger aggregates during the granulation process. This procedure is lengthy and multi-step, which might have a number of drawbacks. However, These challenges could be solved by employing innovative methods like fluidised bed granulation and drying in the fluidized bed processor. FBG, often referred to as agglomeration, is one of the most widely used processes for creating solid pharmaceutical products. The pharmaceutical sector favours the fluidised bed granulator (FBG) because of its efficiency and cost-effectiveness as a one-pot process. There are a number of methods for creating agglomerates, such as high shear granulation, pneumatic dry granulation, and drum granulation, in addition to fluidised bed granulation. Because it can provide complete mixing, high mass and heat rates, and the preservation of a somewhat constant temperature throughout the bed, this method is frequently used.

Fine droplets of the granulating solution are applied to the fluidised particles' surface during the fluidised bed granulation process. Liquid bridges are created when the particles get moist and clash with one another; these bridges then solidify. The solvent present evaporates when the fluidizing air heats these particles enough. As a result of the particles sticking together, agglomerates or granules are created. Solid dispersions have recently been prepared using the fluidised bed granulation process. Because it can overcome many of the drawbacks and restrictions of traditional multi-step granulation and solid dispersion production processes, this approach has attracted interest as a manufacturing process.

Principle of fluidized bed granulation process[8,9,13,25-29]

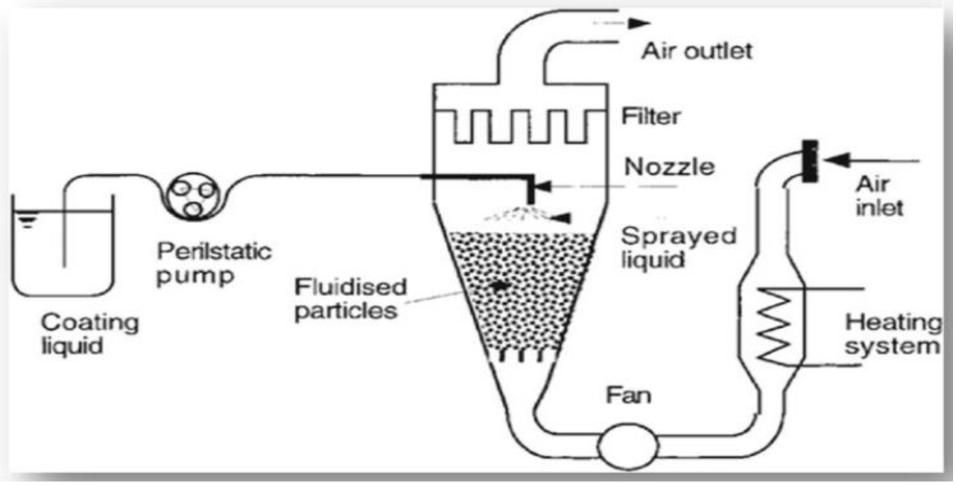
Fluid bed equipment may be used to efficiently carry out a continuous production line in the tablet manufacturing industry that includes many processes including coating, drying, and granulation. Fluid bed granulation is the process of applying a binder solution, suspension, or dispersion to a physical combination, also called a powder bed, in which particles are suspended in an air stream. When the granulating or binder solution moistens these particles, collisions between them cause liquid bridges to develop, which eventually results in the production of granules. There are two ways in which particles adhere to these liquid bridges:

1. The interface's surface tension
2. The use of hydrostatic suction

Numerous factors can affect the bed's moisture content and the granule microstructure, such as the size of the primary particles, the fluidizing air velocity, the binder solution's concentration and spray rate, and the production methods used. These factors could slow down the rate at which granules shatter. The solidification of liquid bridges results in the creation of clusters of solid particles, such as granules or agglomerates, even though fluid bed granulation is known to increase the solubility and dissolution rates of drugs that are poorly water-soluble. In the fluidised bed granulation process, particles are wetted and dried while dry excipients are continuously pre-blended. Consequently, the influencing elements may make the fluidised bed granulation process challenging. Particles adhere to one another and form enormous lumps during the process of wet quenching, which occurs when substantial portions of the bed defluidize as a result of an excess or uneven distribution of the granulating solution. We call this dry quenching. However, if particle development is too great, the fluidisation velocity may exceed the operating velocity and the The square of the particle diameter will determine the minimum fluidisation velocity.

Granulators[8]

By raising the granulating solution's volume and the mixer's mechanical action, each granule's density is increased. Thus, the density and strength of the agglomerates or granules may be efficiently controlled by adjusting the amount of binder, granulating solution, and degree of mechanical activity. Granulators are the name of the equipment made specifically for this technique. The term "shear" refers to the degree of mechanical force that the granulators apply, and these granulators can be classified as low shear, medium shear, or high shear. A low-shear granulator mixes powders and binding solutions with the least amount of mechanical effort possible.

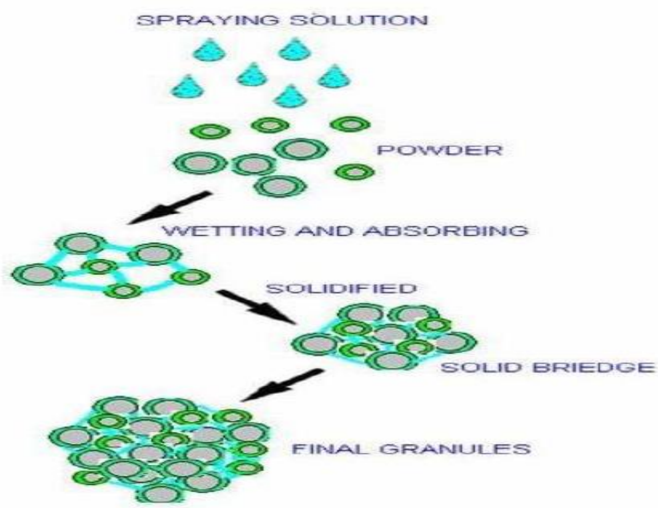


Fluidized bed granulators

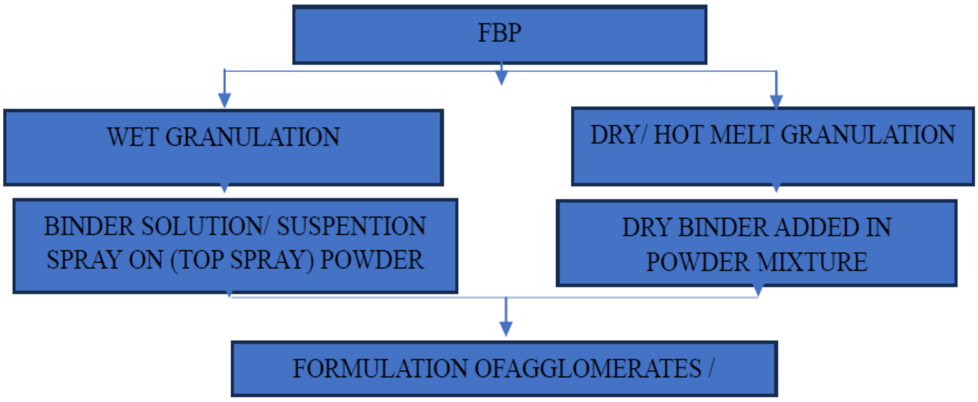
Fluidized bed granulation[8,13,25]

A common method for creating porous granules is fluidised bed granulation, a kind of low shear granulation. In order to create weak linkages, a granulating solution is atomised onto the powders while a significant airflow is used to elevate the powders inside a vessel. Fluidised bed granulators, in contrast to high shear granulators, rely on the properties of the powders and the binder solution to form loosely bound agglomerates rather than using mechanical energy. It is crucial to remember that light grains cannot be produced by high shear granulators.

Fluidised bed granulation steps



Fluidised bed granulation allows for both Dry and Wet granulation processes.



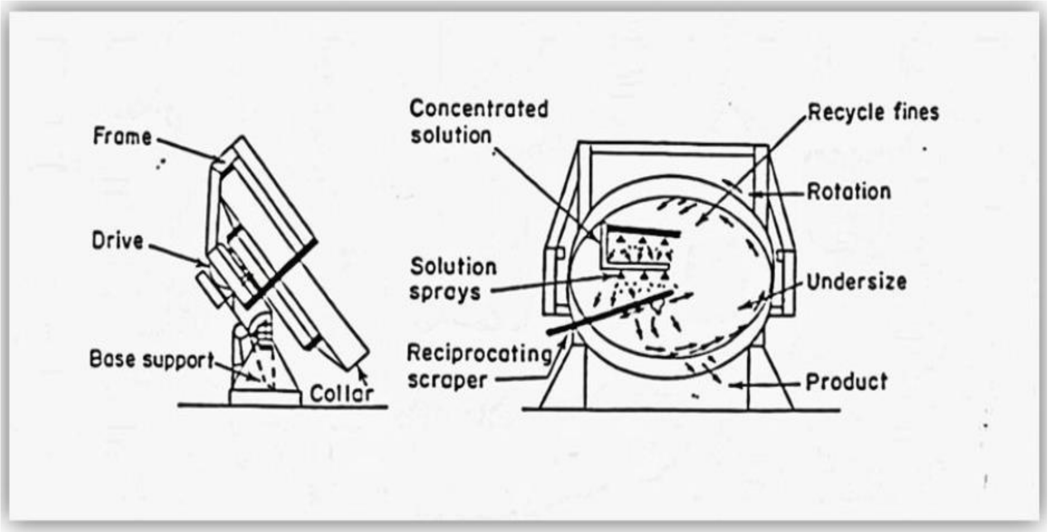
Types of fluidised bed processor

1) Top spray fluid bed granulator uses two technologies

Recrystallisation and hardening binder. To let in tiny particles, the device has a thin mesh retention screen and a spray nozzle on top. The product container receives the powder from the base of the device. In this process, the nozzle spray is positioned above the powder bed, within an expanded chamber. A binding agent is sprayed onto the powder bed at a controlled rate, facilitating the formation of granules. Once optimal moisture levels and agglomeration are achieved, the liquid spray is halted, and the granules are dried to complete the process.

2) A revolving disc granulator for fluid beds

Rotating Disc Granulator with Dryer Option the revolving disc and coater were carried by layering technology Granulator Because coating technology extends the granulation process, To produce a revolving disc granulator and coater fluid bed device, the unit is connected to an expansion chamber. A changeable slit aperture will develop between the side wall of the container and the outside perimeter of the spinning disc as it goes up or down. Independent control of air velocity over air volume is made possible by the negative pressure that pulls air through the slit and into the product container. By fluidizing the chamber, the product travels to the outside location air stream under centrifugal force as the disc rotates at a different speed as it is lifted into the expansion. The operations are repeatedly repeated as the material falls to the centre of the revolving disc. The fluidizing patterns inside the rotor chamber are characterised as spiralling helices or rope-like patterns. A number of forces, including fluidisation, gravity, and centrifugal force, regulate the particle's fluidisation motion. The fluidisation bed contains the spray nozzle, which applies tangential spray to the particles. When making pallets, the layering technique can be used. The process commences with seed particles of a predetermined size, typically 250 mm in diameter. Multiple layers of medication and binder solutions or suspensions can be applied sequentially, allowing for precise control over the final product's characteristics. The active pharmaceutical ingredient can be introduced as a dry powder feed at a controlled rate, facilitating uniform growth of the particle bed in both vertical and horizontal directions. Through this process, it is possible to achieve weight gains of up to 1000% relative to the starting material, resulting in uniformly coated and layered pellets with tailored release profiles.



Rotating disk fluid bed granulator

Factors Influencing and Managing The Fluidised Bed System[8–12, 18–25, 30]

Numerous parameters affect the end product that is processed by the fluidised bed processor.

1. **Apparatus parameters**

- Operation of positive and negative pressure
- Instrument Body Shape: The Annular Shape Base Provides Better Fluidisation and Products
- Nozzle height: This is an important factor in the coating and granulation processes. Before the atomised coating solution reaches the tablet surface, it shouldn't dry out.
- Air distribution plate: This component's placement within the body influences the airflow pattern.

2. Process parameters

During the drying process

Critical inlet air characteristics apply to all processes, including coating, drying, and granulation.

1. Temperature Control: Higher inlet air temperatures accelerate drying, but may damage sensitive materials. Finding the ideal temperature balance is crucial, as seen with Ibuprofen's optimal temperature range above 60°C.
2. Humidity Management: Dehumidified air enhances drying rates. As humidity increases, drying rates decrease, emphasizing the importance of minimizing inlet air humidity.
3. Air Flow Regulation: Balancing air blow rates is vital. While higher rates increase drying costs, optimal rates facilitate efficient heat and mass transfer, reducing costs and ensuring effective drying.

In granulation process

Regarding the Spray Nozzle:

Three critical factors require careful consideration to achieve optimal fluidized bed granulation:

1. **Nozzle placement:** Positioning the nozzle correctly is vital to ensure effective mixing of the material and binder solution, with the nozzle typically located at the top of the fluidized bed.

2. **Spray rate optimization:** Adjusting the spray rate is essential to prevent inadequate wetting and unwanted product clumping, which can disrupt fluidization and compromise granule quality.

3. **Spray pressure calibration:** Precise control of spray pressure is necessary to produce high-quality granules, highlighting the importance of careful optimization in this process.

Miscellaneous

- **Exhaust gas temperature:** The temperature of the outlet gas is an important parameter to monitor.
- **Pressure drop across exhaust filters:** Tracking the pressure drop across exhaust filters helps ensure proper filtration and process efficiency.

3. **Product parameters**

In drying process

- **Initial moisture content:** A higher initial moisture content of the drying material can lead to longer drying times, which should be taken into account during process planning.
- **Optimal batch size:** To ensure efficient drying, batch sizes should be minimized and optimized based on feasibility studies, taking into account factors such as equipment capacity and material handling constraints.

In granulation process

- **Granulating agent selection:** Choosing the right granulating agent is crucial for successful granulation. The selection should be based on the solvent used in the binder solution. Aqueous solvents are generally preferred, while organic solvents can pose explosion risks. The solvent concentration should be optimized to produce high-quality granules. If the solvent temperature is too high, the binder solution may dry out before reaching the powder material.
- **Starting material considerations:** To ensure effective contact between the starting materials and the granulating agent, fluidization should be optimized. For hydrophobic starting materials, a hydrophilic granulating agent can facilitate better contact and granulation. This consideration is essential for achieving optimal granule formation and quality.

Frequent issues occur in fluidised bed granulation[8,10-15,18,22,25]

1) Excessive fine

1. Inadequate Binder Quantity: Insufficient binder can lead to poor granule formation and excessive fines.
2. Excessive Air Flow or Fluidization Velocity: High air flow or fluidization velocity can disrupt granule formation and generate excessive fines.
3. Low Binder Spray Rate: A binder spray rate that is too low can result in inadequate binder distribution and excessive fines.
4. High Atomization Air Pressure: Excessive atomization air pressure can lead to overly fine droplets, contributing to excessive fines.
5. Weak or Dilute Binder Solution: Using a binder with low binding strength or a binder solution with low concentration can lead to poor granule formation and excessive fines.

6. High Inlet Temperature: Elevated inlet temperatures can cause premature drying of the binder, leading to excessive fines.

2) Excessive coarse granulation

1) High binder spray rate: Excessive binder can cause particles to stick together, forming large, coarse granules.
2) Low inlet air temperature: Insufficient heat can slow down the drying process, allowing particles to clump together and form large granules.
3) Low fluidization velocity or air flow: Inadequate air flow can prevent particles from being properly separated, leading to the formation of large granules.
4) Incorrect nozzle position: If the nozzle is positioned too low, the binder spray may not be evenly Stronger Binder or Higher Concentration of Spraying Liquid: distributed, causing particles to clump together and form large granules.
5) Using a binder that is too strong or a spraying liquid with too high a concentration can cause particles to stick together excessively, forming large, coarse granules.

3) Final moisture inconsistency

- **Temperature probe malfunction:** A temperature probe that is out of calibration can provide inaccurate readings, leading to improper process control and potentially affecting granule quality.
- **Inadequate fluidization:** Improper fluidization can disrupt the granulation process, causing uneven particle distribution, poor binder dispersion, and ultimately affecting the quality of the final product.
- **External environmental factors:** External factors such as high outside air humidity can influence the granulation process, potentially leading to issues with particle size, shape, and quality.

4) Fluidization is poor

- **Insufficient air velocity:** Low air velocity can impede proper fluidization, leading to uneven particle distribution and poor granule formation.
- **Inadequate fan pressure:** If the processor fan lacks sufficient pressure drop, it may struggle to maintain optimal air flow, compromising the fluidization process.
- **Poor maintenance of air distributor:** Failure to properly clean the air distributor can lead to clogging and reduced air flow, negatively impacting fluidization.

- **Overfilled product container:** Exceeding the recommended product quantity in the container can disrupt air flow and fluidization, causing processing issues.
- **Incorrect air distribution plate:** Using an incorrect air distribution plate can lead to uneven air flow and poor fluidization, affecting granule quality.
- **Blocked exhaust:** A blocked exhaust can prevent proper air flow and pressure release, causing processing issues and potentially damaging equipment
- **Inadequate exhaust porosity:** If the exhaust porosity is too small, it can restrict air flow and pressure release, leading to processing issues and equipment damage. Porosity of exhaust is small

5) Finished product non uniformity

- **Inadequate spraying time:** Insufficient spraying time can lead to uneven binder distribution, resulting in poor granule formation and inconsistent quality.
- **Presence of lumps in raw materials:** Lumps in the raw materials can disrupt the granulation process, causing uneven particle size and shape, and ultimately affecting the final product's quality.
- **Inadequate filter shaking:** Failing to shake the filters sufficiently can lead to clogging and reduced air flow, negatively impacting the granulation process and product quality.
- **Inadequate product homogeneity:** If the product is not adequately mixed and homogenized before granulation, it can lead to inconsistent particle size, shape, and quality, ultimately affecting the final product's performance and characteristics

6) Low yield

- **Incomplete filter maintenance:** Failing to shake the filter bag at the end of the process can lead to residual powder accumulation and affect future batches.
- **Material buildup in expansion chambers:** Material sticking to expansion chambers can disrupt airflow, reduce efficiency, and impact product quality.
- **Incorrect exhaust filter porosity:** Using an exhaust filter with the wrong porosity can compromise airflow, pressure, and overall process performance.

Advantages of fluidized bed granulation

1. Improved Compressibility: Enhances tablet formation by increasing powder compressibility.
2. Scalability: Suitable for both large-scale and small-scale operations.
3. Continuous Operation: Allows for uninterrupted processing, increasing efficiency.

4. Time and Cost Efficiency: Streamlines production, reducing processing time and costs.
5. Minimized Product Loss: Reduces waste and optimizes product yield.
6. Enhanced Operator and Environmental Safety: Decreases dust formation, promoting a safer working environment.
7. Improved Housekeeping and Worker Safety: Encourages a cleaner, more organized workspace, reducing accidents.
8. Labor Cost Savings: Automates certain processes, reducing manual labor requirements.

Disadvantages of fluidized bed granulation

9. Labor-Intensive Cleaning: Cleaning processes can be time-consuming and require significant manual effort.
10. Equipment Erosion: Particle collisions can erode internal components, pipes, and vessel walls.
11. Catalyst Particle Attrition: Particles may break down or degrade during processing.
12. Risk of Product Degradation: Excessive heat during hot melt granulation can damage the product.

CONCLUSION

The flow characteristics of powders are adversely affected by extremely tiny and small particles. and won't compress in the die cavity or remain mixed. to manufacture tablets. They need to be granulated in order to solve this issue; granulation is used to enhance the powders' functional qualities. The powder particles cling to one another and form clusters during the granulation process, which results in an increase in particle size. Several agglomeration techniques can be used, depending on the granules' end-use characteristics. The industry makes extensive use of the fluidised bed granulation process because it yields granules with great uniformity and porosity. To resolve any issues that may arise, provide the intended results, and comprehend the method by which the parameters influencing The granulation process and granule characteristics, such as the mixing rate, binder property, moisture content, inlet air temperature, etc., are thoroughly examined and managed.

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