

See discussions, stats, and author profiles for this publication at: <https://www.researchgate.net/publication/260025445>

Fluidized Bed Systems: A Review

Chapter · January 2007

CITATIONS

2

READS

12,013

10 authors, including:



Mukesh Gohel

Anand Pharmacy College

163 PUBLICATIONS 3,021 CITATIONS

[SEE PROFILE](#)



Lalji Baldaniya

Faculty of Pharmacy, Marwadi University, Rajkot

34 PUBLICATIONS 67 CITATIONS

[SEE PROFILE](#)



Bhavesh Subhashchandra Barot

K.B. Institute of Pharmaceutical Education and Research

28 PUBLICATIONS 305 CITATIONS

[SEE PROFILE](#)



Punit Parejiya

49 PUBLICATIONS 367 CITATIONS

[SEE PROFILE](#)

Some of the authors of this publication are also working on these related projects:



HEPATIPROTECTION [View project](#)



Formulation, Optimization and Evaluation of Extended Release Tablet of Pregabalin [View project](#)

2002	Asif and Ibrahim	FBS		Proposed models to predict axial distribution of particles with different size in fluidized bed.
2002	Tanfara and colleagues	FBD,FBG	Types of gas flow	They used electrical capacitance tomography to generate contour plots of a fluidized bed cross sectional area and the wide distribution of placebo granules revealed two different types of gas flow such as annular and Centralized.
2004	J.Ylirussi and Eetu Rasanen et al ⁽⁴⁾	FBS		They worked on characterization of fluidization behavior using a novel multichamber micro scale fluid bed.
2005	A.Bajaj and R.Meshram ⁽⁵⁾	FBC		They carried out solid dispersion and enteric coating of pancreatin enzyme using fluidized bed system.

FBC = Fluidized bed coater, FBD = [Fluidized bed dryer](#), FBG = Fluidized bed granulator

2. Concept Of Fluidization ^(1, 7- 9)

2.1. Introduction ^(7- 9)

Many important industrial processes rely upon intimate contact between a fluid (liquid or gas) and a granular material · ⁽⁸⁾ In early applications, the fluid flowed through a static bed of granules supported on a grid. provided the material is suitable, great improvement in mixing and contact is achieved if the granule size is properly matched to the upward velocity of the fluid. The particles of material will be

supported by the drag forces and the bed is said to be "**fluidized**".⁽⁸⁾ The fluidized beds show following liquid or fluid like properties^(7,9)

- Lighter objects float on top of the bed (*i.e.*, objects less dense than the bulk density of the bed),
- The surface stays horizontal even in tilted beds,
- The solids can flow through an opening in the vessel just like a liquid,
- The beds have a "static" pressure head due to gravity.
- Levels between two similar fluidized beds equalize their static pressure heads.
- It has a zero angle of repose.⁽⁷⁾
- Assumes the shape of vessel that contains it.⁽⁷⁾

A gas-fluidized bed may have the appearance of a boiling liquid. It has bubbles, which rise and appear to burst. The bubbles result in vigorous mixing and a generally horizontal free surface.⁽⁸⁾ The motion of the bed varies with the fluid flow rate. At high velocities, particles may become entrained and transported by the fluid.⁽⁴⁾

2.2 Principle Of Fluidization⁽⁷⁾

The principle of operation of fluidized systems are based on the fact that if a gas is allowed to flow through a bed of particulate solids at velocity greater than the settling velocity of the particles and less than the terminal velocity for pneumatic conveying and equal to the minimum velocity of fluidization (V_{mf}), the solids get partially suspended in the stream of upward moving gas. The gas stream negates the gravitational pull due to weight of particles to enable the suspended state of the solid.

The resultant mixture of solids and gas behave like a liquid and thus rightly solids are called Fluidized. The solid particles are continually caught up in eddies and fall back in a random boiling motion so that each fluidized particle is surrounded by the gas stream for efficient drying or granulation or coating purpose. In the process of fluidization there occurs an intense mixing between the solids or gas resulting in uniform condition of temperature, composition and particle size distribution throughout the bed.

2.3 Theory Of Fluidization^(1, 8, 9)

2.3.1 Phenomenon of Fluidization

Stages of fluidization:- The stages of fluidization is mostly based on the fluid velocity passing through the particle bed. According to **Ridgeway** and **Quinn**⁽¹⁾ the stages of fluidization can be summarized as follows.

- 1) Static bed
- 2) Expanded bed
- 3) Mobile bed
- 4) Bubble formation
- 5) Pneumatic transport

2.3.2 Role of Fluidization velocity⁽⁹⁾

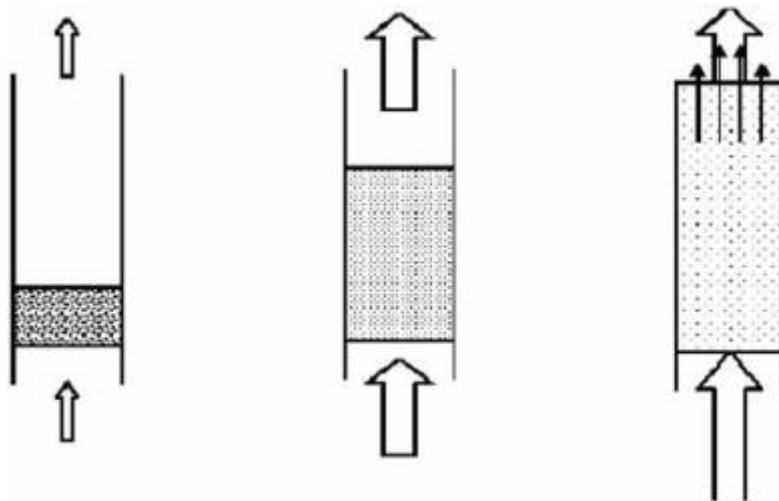
A mass of finely divided solids is transformed into a fluidized bed by lifting action of gas passing through it. Thus three stages can be identified in the process of fluidizing a bed of solids basing on the velocity of gas flow through it. They include

- 1) Fixed bed or Static Bed
- 2) Expanded bed or particulate fluidization.
- 3) Mobilized bed

- 1) When a fluid is pumped upward through a bed of fine solid particles at a **very low flow rate** the fluid percolates through the void spaces (pores) without disturbing the bed. This is known as a **fixed bed process**.⁽⁹⁾
- 2) If the upward **flow rate is very large** the bed mobilizes pneumatically and may be swept out of the process vessel. This is known as **Mobilized bed process**.⁽⁹⁾
- 3) At an **intermediate flow rate** the bed expands. This is known as an **expanded bed**.⁽⁹⁾
- 4) After mobile bed formation if velocity is further increased the bed expands considerably with increase in voidage and **bubble formation**⁽¹⁾ occurs.
- 5) If further increase in velocity of air occurs, eventually the lifting force of passing air blows particle out of the bed altogether leading to **Pneumatic transport**.⁽¹⁾

In the fixed bed the particles are in direct contact with each other, supporting each other's weight. In the expanded bed the particles have a mean free distance between particles and the particles are supported by the drag force of the fluid. The expanded bed has the properties of a fluid and is also called a fluidized bed.

As shown in Figure below, the velocity of the fluid through the bed opposite to the direction of gravity determines whether the bed is fixed, expanded, or is swept out. This led to the development of the concept of minimum fluidization velocity (V_{mf}) at which the bed just begins to fluidize. Thus the primary concern is to measure and optimize the V_{mf} for efficient fluidization.



(a) Slow flow rate (b) Intermediate flow rate (c) High flow rate

Fixed bed Fluidized bed Mobilized bed

$$V_0 < V_{mf} \quad V_{mf} \leq V_0 < U_t \quad V_0 \geq U_t$$

Figure -1. Fixed, Fluidized, and Mobilized beds. ⁽⁹⁾

The **fixed bed (a)** occurs when the approach velocity or superficial velocity, (V_0), is much smaller than the minimized fluidization velocity, (V_{mf}). The **fluidized bed (b)** occurs when the approach velocity is intermediate between the minimum fluidization velocity and the terminal velocity. The pneumatically **mobilized bed (c)** occurs when the approach velocity is much greater than the particle terminal velocity, (U_t)

Status of approach fluid velocity (V_0)	Type of bed formed
$V_0 < V_{mf}$	Fixed Bed
$V_{mf} \geq V_0 < U_t$	Fluidized Bed
$V_0 \geq U_t$	Mobilized Bed

2.3.3 Determination of Minimum velocity of fluidization (V_{mf}) ⁽⁸⁾

The determination of minimum velocity of fluidization plays a vital role in efficient operation of a fluidized bed system. Basing on the nature of size distribution of a solid bed V_{mf} calculation differs.

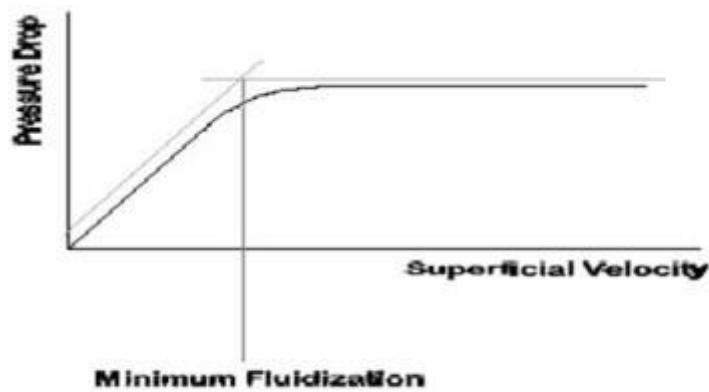


Figure- 2 (a). Pressure drop with decreasing superficial velocity ⁽⁸⁾

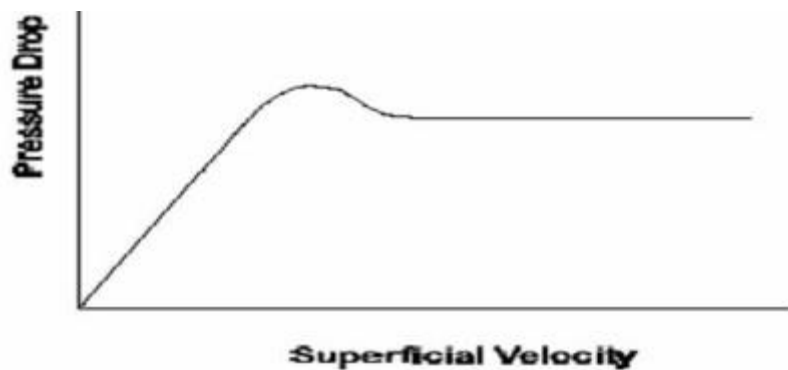


Figure -2 (b) .Pressure drop with increasing superficial velocity ⁽⁸⁾

e.g. if the solid bed contains solids of uniform density V_{mf} calculation is done basing on the equation developed by Ergun ⁽⁸⁾

If the solid bed is having wide size distribution of particles (i.e. bed contains solids with differing densities) V_{mf} determination is analogous to measurement of boiling point of a liquid mixture, the boiling point of mixture is not fixed but varies with composition. Also V_{mf} can be determined using average particle size of the bed.

2.3.4 Role of pressure drop in Fluidization ^(8,9)

When a fluid flows through a bed of particles in a tube, it will exert a drag force upon the particles resulting in a pressure drop across the bed. As the fluid's approach velocity is increased, pressure drop is magnified.

In an unrestrained bed with fluid flowing upwardly through it, a condition will be reached where, with increasing fluid velocity, the drag forces will cause the bed to expand. This expansion allows the particles to offer less resistance to the fluid flow. When the drag force is sufficient to support the weight of the particles in the bed, the bed is said to be **fluidized**. The fluid/solid system shows fluid-like properties, and the bed can be made to flow from one vessel to another.

The pressure drop across the bed, Δp , then remains constant (even with further increase in the fluid velocity) and equal to the effective weight of the bed per unit area

$$\Delta p = \frac{m}{\rho_p S_b} (\rho_p - \rho_f) g$$

m - mass of particles
 ρ_p - density of particles
 S_b - cross-sectional area of the bed
 ρ_f - fluid density
 g - gravitational acceleration

When the unit is operated at pressures comparable to atmospheric, therefore p_c is negligible compared with p_p . As the gas velocity, V_0 , is raised beyond that required to bring the bed to a fluidized condition, i.e. beyond the minimum fluidization velocity V_{mf} , the bed will begin to bubble. This condition is called aggregative **fluidization**.⁽⁸⁾ If the gas velocity were increased excessively, the bubbles would grow so large that they would nearly or completely fill the cross-section of the tube pushing slugs of particles forming a **slugging bed**.⁽⁸⁾

If the fluid were more dense, (e.g. a gas at the high static pressure of a liquid), or if the particles were finer (20 to 100 μm) and less dense ($<1400 \text{ kg m}^{-3}$), the bed would be able to sustain a degree of stable expansion, also known as **particulate fluidization**.⁽⁸⁾ The bed would remain stable until the V_{mf} had been exceeded by a factor of 2 or 3. In contrast, when using gas to fluidize a bed, the bed would collapse and reinitiate bubbling with further increase in gas velocity. A liquid fluidized bed usually continues to expand stably with increasing velocity resulting in a non-bubbling fluidized condition known as **quiescent bed**.⁽⁸⁾

With finer, less dense and cohesive powders, it is very difficult to fluidize the bed at all, because the interparticle forces are then greater than the gravitational ones. The particles tend to stick together, and the gas passes through the bed by blowing channels through it.

3. Parameters To Be Controlled In Fluid Bed Systems ^(1, 10, 11)

The parameters that affect the final product processed through fluidized bed systems can be enumerated as below.

3.1 Apparatus Parameters

- 1) Air distribution plate Position of the air distribution plate influences the airflow pattern inside the body.
- 2) Shape of instrument body Annular base gives better product and fluidization.
- 3) Nozzle height in case of coater and granulator. It plays vital role as in coating, the atomized coating solution should not get dried before reaching the tablet surface.
- 4) Positive and negative pressure operation

3.2 Process Parameters

3.2.1. In Drying Process

The following inlet air parameters are critical, and applicable in all processes of drying, granulation and coating.

1) Temperature

As the inlet air temperature increases the rate of drying increases and *vice versa*. This approach to increase the rate of drying can not be used always because some materials are harmed by high temperature, e.g. Ibuprofen liquefies above 60°C temperature of inlet air should be optimized without any impact on product quality. If temperature is high, it leads to blistering. If temperature is low, soft spot can be formed.

2) Humidity

Humidity in the inlet air should be as low as possible and ideally dehumidified air should be used for faster drying rate because as the humidity of inlet air decreases the rate of drying increases.

3) Air flow rate

Air flow rate should be controlled properly in order to get efficient use of drying air. As the air flow rate increases, the rate of drying increases but the cost of drying also increases. If drying air is allowed for sufficient time to remain in contact with the drying material, proper heat transfer and mass transfer takes place and thus drying cost decreases. Air flow rate should not be too fast or too slow but optimized to have efficient drying.

3.2.2. In Granulation Process.

Related To Spray Nozzle

1) Nozzle position in relation to material height.

Nozzle position is determined on bases of bed height and it should be placed suitably for better contact of binder with the powder to be granulated.

2) Spray rate.

It should be optimized otherwise poor wetting/agglomeration of the product will take place hindering the fluidization and quality granule formation.

3) Spray pressure.

It is important for proper atomization of binder solution.

Miscellaneous

1) Pressure drop across exhaust filters.

2) Outlet gas temperature.

The above two parameters give indication of the efficiency of the fluidization process. System's level of efficiency can be drawn from measuring these two parameters.

3.2.3. In Coating Process

Related To Spray Nozzle

1) Distance of spray nozzle.

Efficiency of coating depends on the quality of the coating solution. The coating solution should not get dried before reaching the fluidized substances viz. tablet, particles, and granule surface.

2) Droplet size.

Quality of the coat depends on the droplet size. So it should neither be too big nor be too small.

3) Spray rate.

Flow rate should not be too fast or too slow, but should be of optimized rate for efficient coating.

4) Spray pressure.

Atomization of coating solution depends on the spray pressure, thus for proper atomization droplet size should be optimum.

Miscellaneous

1) Moisture content in processing compartment. Moisture should not be present in case of hygroscopic materials.

2) Method used for coating should be chosen on basis of the purpose for which it is used. e.g. SR, ER, etc.

3) Time of drying should be determined on bases of the product and quality of the coat desired.

3.3. Product Parameters.

3.3.1. In Drying Process.

1) Initial moisture content of material.

It should not be high otherwise it increases drying time.

2) Batch size.

It should be small and optimized based on feasibility.

3.3.2. In Granulation Process.

1) Granulating agent.

Type of granulating agent is based on selection of solvent to be used in binder solution. This solvent should be preferably aqueous as organic may cause explosions. Binder solution used to granulate the material should be used in optimum concentration so as to obtain good quality of granules. Temperature of granulating agent should not be high otherwise it will be dry before reaching to the powder surface.

2) Starting material.

Fluidization of starting material should be optimized for better contact with the granulating agent. If the starting material hydrophobic, hydrophilic granulating agent is to be used for better contact and granulation of material.

3.3.3. In Coating Process.

1) Coating agent.

Selection of coating agent should be done according to type of coating required e.g. Enteric coating, Sugar coating, etc. Solvent should be selected according to the properties of the coating agent. If solvent is volatile, it should be checked for inflammability. Concentration of granulating agent should be optimized for uniform spreading and droplet formation. Temperature of the coating agent should not be so high that coating solution get dried before reaching to the tablet surface.

2) Starting material.

Shape of tablets greatly affects the coating process. In case of powder coating the particles shape and density affects the coating process.

4. Classification Of Fluidized Bed Systems ⁽¹⁾

4.1. According To Process Applications ⁽¹⁾

4.1.1. Drying

The fluidized bed dryers available for use in the Pharmaceutical industry are of two types,

1) Batch type Vertical [Fluid Bed Dryer](#) with Granulating option.

I.Reverse turning bed type

II.Rotating discharge type

2) Continuous type Horizontal Vibrating Conveyor [Fluid Bed Dryer](#).

4.1.2. Granulation

The fluidized bed dryers available for use in the Pharmaceutical industry are of two types,

1) Top Spray Fluid Bed Granulator,

2) Rotating disk Fluid Bed Granulator with Dryer option.

4.1.3. Coating

The fluidized bed dryers available for use in the Pharmaceutical industry are of three types,

1. Top Spray Pellet with Particle Coating option,

2. Fluid Bed Bottom Spray Pellet with Particle Coating option,

3. Fluid Bed Roto Processor with Drug Loading & Coating option.

4. Huttlin Kugel Fluid Bed Coater

4.2. According To Principle

1) Spiral Granulator,

2) Bottom spray coating,

3) Tangential spray roto processor.



Figure - 3 Classification according to principle

5. Equipments For Fluidized Bed Systems ^(8,12-17)

5.1 [Fluidized Bed Dryer](#)

5.1.1 Introduction

Fluid bed drying is most widely used technique for drying pharmaceutical powders and granulation. The direct contact between particles and air/gas is possible in fluid bed system. Here any type of inert gas or

air is used. They can be designed in either batch or continuous type fluid bed dryer. Various innovations in fluid bed drying are discussed in section 7.

The fluid bed drying operates under the principle of direct drying where direct contact between a heated gas/air and the product occur to effect heat and mass transfer. The hot air/gas used for drying can be generated by either steam coils or a combustion furnace. The holes in the perforated plate are covered with caps that prevent material from entering the plenum when the dryer is not in operation. The fan equipped in the upper part of the apparatus induce fluidizing air stream.

Hot air is fed in the material layer at rest from the bottom of gas straightening valve (e.g. perforated plate). The velocity of air is adjusted by means of a damper. When the velocity of hot air accelerates a bit, particle groups gradually come to make active movements gradually resulting in hot air pressure loss due to the material layers comes to be in proportion to the weight of material particles on the unit area of the straightening vane. With further accelerating the velocity of hot air, the particle groups undergo vigorous movement to mix with gas in all directions, resulting in suspension state.

If all the particles are fully supported by air/gas then a bed may be fluidized well. The solid become partially suspended in gas stream when the velocity of gas is greater than the settling velocity of the particles and less than the velocity for pneumatic conveying. The solids in this state are said to be fluidized and the resultant mixture of solids and gas/air behaves like a liquid. The angle of repose of gas-solid mixture is zero and it assumes the shape of the vessel that contains it. In fluid bed drying uniform conditions of temperature, composition and particle size distribution is achieved throughout the bed because of complete mixing between the solids and gas is obtained.

When the material layer approaches to a certain flow velocity (i.e. minimum air velocity for fluidization), it makes a minimal expansion causing particles moving and leading to minimum fluidization.

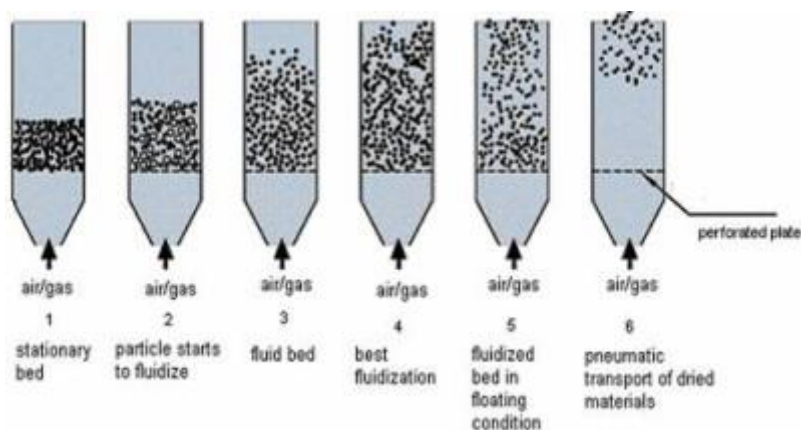


Figure- 4. Various steps in fluid bed drying. ⁽¹²⁾

The material later expands to 1.2 to 1.6 times in height that was at resting position. ¹ Product height in the fluid bed reaches between 100 to 500 mm (average 300 mm) depending on the application. The material layer behaves as it is liquid and shows an appearance as it is boiling. This state is termed as “fluid state”. This type of fluid bed can be formed within a certain range of flow velocity depending upon particle size, specific gravity and other properties of the material.

Uniform processing conditions are obtained by passing hot air (or other inert gas) through a material layer under controlled velocity conditions to create a fluidized state. Air is filtered after drying in multicyclones and /or bag filters. However, the use of bag filter is troublesome if the dryer is often used for different products because careful cleaning of the dryer is required.

The dry product overflows an adjustable weir plate and is discharged continuously through a rotary air lock. In fluid bed drying, airflow need not be the only source of heat. Heat can also be effectively introduced by heating surfaces (panels or tubes) immersed in fluidized layer. ⁽¹⁴⁾

Fluid bed dryer can also be constructed with an integral cooling system thus avoiding the need for a separate cooler in those applications that require one. In fluid bed cooling usually ambient or conditioned air is used. Another option is cooling surfaces immersed in the fluidized layer. Conditioning of the air may be required to obtain sufficient product cooling in an economically sized plant and to prevent pick up of volatiles including moistures. ⁽¹⁴⁾

Fluid bed dryer is suitable for powders granules, agglomerates and pellets, having average particle size normally between 50 and 5000 micron.

The material containing very fine, light powder (low density) or highly elongated particles may require vibration for successful fluid bed drying. ⁽¹⁴⁾

Most fluid bed dryers are single pass system where the process gas passes through the bed only at once and is exhausted to atmosphere. Depending on the economic feasibility of the operation, some systems can be designed for recirculation or recuperation. The larger particles that fall out of bed are introduced back into the bed or propelled along the length of dryer by vibrating action. Vibrating systems decrease power requirements for fluidization and thus reduce operating cost. ⁽¹⁵⁾

In indirect fluid bed processing, a tube or series of plates are incorporated into the drying chamber. They are arranged in such a way that products remain in intimately contact with the heated surface. The heat energy is transferred by means of conduction. Here steam is used as a source of energy. The cost of operation is low because steam is low cost energy source. ⁽¹⁵⁾

A fluid bed dryer is capable to use almost any heat source. As the temperature of the process gas is increased, the volume of air required is small and the unit required is also small. ⁽¹⁵⁾

With the correct design, fluid bed dryers can withstand at extremely high temperatures, providing the potential for calcining. Incorporation of refractory lining the box, drying chamber or expansion chamber is required with these designs. With independent control of airflow and temperature, the dryer can be divided into several different zones. This design is useful for sensitive products or where altering the inlet temperature can benefit the process. The advantage of this design is that drying can take place at the maximum desirable rate in each stage by maintaining efficiency and preventing damage to the heat sensitive materials. The width of dryer ranges from 12 to 57 inches and length ranges from 10 to 50 feet. The bed depth is about 3 inches. Dryer capacity is dependent only on retention time produced by speed of conveying, which generally ranges from 5 to 25 feet per minute.

The fluid bed dryer can be operated in either open or closed cycles. Using a solvent recovery system & an inlet gas like nitrogen as the drying medium, the operation of the fluid bed dryer can be carried out in a closed cycle. A cyclone or febric collector, and a condenser to remove the solvent clean vent gases. The cooled, saturated gases can be heated and utilized further. ⁽¹⁶⁾

5.1.3 Types Of Fluid Bed Dryer ^(8,17)

(1) Batch Type Vertical Fluid Bed Dryer With Granulating Option.

In batch-type dryer, the drying chamber is equipped in such a way that it can be removed from unit to permit charging and dumping. The dryer is capable of drying 5 kg to 200 kg material with an average drying time of about 20 to 40 min.

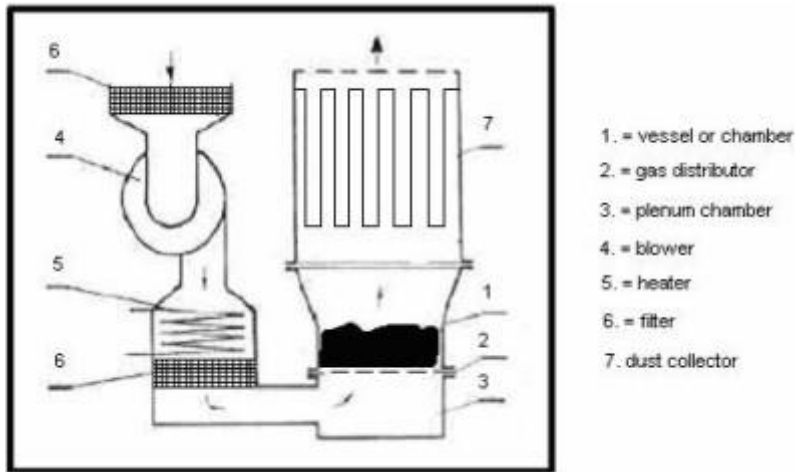


Figure-5. Batch fluidized bed dryer ⁽⁶⁾

I. Reverse Turning Bed Type ⁽¹⁷⁾

In this equipment, by turning the gas dispersion plate (the reverse turning bed) in 90° direction with the control motor, all the dried material can be discharged at once.

II. Rotating Discharge Type ⁽¹⁷⁾

Dried material is discharged by opening the discharge gate equipped at the side of the Dryer. As the perforated plate is used as the gas dispersion plate, the gas inside the equipment whirls and pushes the dried material out from the discharge gate.

Characteristics Of Batch Type Fluidized Bed Dryer ⁽¹⁷⁾

The residence period of the dried material can be controlled which results in uniform drying. It is most suitable in case where an accurate control of the residence period is required at the decreasing rate drying zone. Small destruction of particle occurs therefore suitable for granular or crystallized material.

Easy operation can be achieved by an automatic control of material feeding, drying discharging etc. When multiple stage system is adopted, the exhaust gas heat can be used efficiently.

(2) Continuous Type Horizontal Vibrating Conveyor Fluid Bed Dryer. ⁽¹⁷⁾

The dried material is moved to a next drying chamber through a gap at the bottom of the partition plate and after finally dried, the material is discharged over the overflow gate. For large volumes of materials, a continuous dryer is more suitable than a batch type. The continuous Fluid bed dryer which is suitable for pharmaceutical use is horizontal vibrating conveyor dryer shown in figure-7.

The heated air enters the chamber below the vibrating conveying deck. The air then passes through perforated conveying surface and enters into the wet bed of material and causes fluidization of the particles.

Due to vibrating movement of the conveyor, a fluidized bed of uniform density and thickness is maintained in any given drying zone.

Residence time in any drying zone is dependent on

- (1) Length of the zone
- (2) The frequency and the amplitude of the vibration
- (3) Use of dams

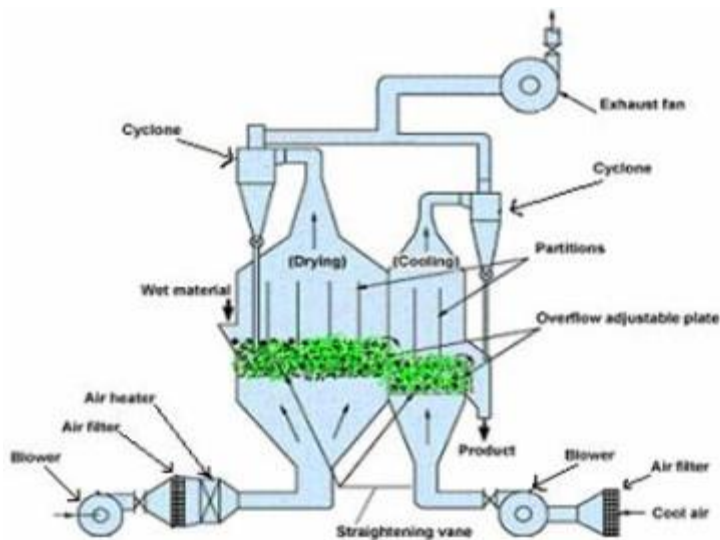


Figure –6. Horizontal multiple chambers fluidized bed drying and cooling system ⁽¹²⁾

Heat Transfer Unit Built In Continuous Fluidized Bed Dryer ⁽¹⁷⁾

Heat transfer units such as tube or plate, are built inside the equipment. These unit supplies 60-80 % heat necessary for drying. Thus the quantity of hot air is decreased, reducing the power consumption and operating cost. The equipment becomes compact. The auxiliary equipment can also be miniaturized.

Characteristics Of Continuous Fluidized Bed Dryer ⁽¹⁷⁾

- (1) The materials with relative high moisture content can also be dried.
- (2) At and after a second drying chamber, piston flow ability can be achieved by arranging numbers of the partition plates as per the required residence period. The perforated plate at the fixed direction ensures easy discharging.
- (3) Small destruction of particles, so suitable for granules or crystalline materials.

In multiple zones fluid bed dryers, heating and cooling occurs in same unit. Each zone has independent control for temperature, dewpoint and velocity of air/gas. By adjusting the weir height for each zone, residence time can vary up to four fold in the unit.

5.2 Fluidized Bed Granulator ^(1, 14, 18, 19)

5.2.1 Introduction ⁽¹⁹⁾

The basic concept in granulation (also known as agglomeration) involves suspending particulates in an air stream and spraying a liquid from the top on to the fluidized bed. Particles in the path of the spray get slightly wetted and become tacky. The tacky particles collide with other particles and adhere to them to form a granule.

There are two different mode of fluid bed granulation:

- 1) Dry stage
- 2) Wet stage

In the **dry stage granulation** , the granulating solution is applied at a rate less than or equal to the evaporation rate so that the particles are wetted slightly to become tacky and stick to each other. Thus the particles remain “dry” through the entire process.

In the **wet stage granulation** , the granulating solution is applied at the rate higher than evaporation rate until the particles build up enough moisture to granulate so that particles are wetted significantly before they become tacky enough to stick to each other.

Dry stage granulation is more common than wet stage granulation which allows for denser products.

Three Techniques Are Used For Granulation ⁽¹⁾

1. If the powder materials are soluble in the solvent (usually water), during drying crystalline bridge form & hold the granules together (recrystallization).
2. If the powder material insoluble in the solvent or stronger binder is required, a binding agent is used for granulation (as hardening agent).
3. To build agglomerate starting with a substrate and adding alternate layer of binder and active material until a desired size of granules form (as known as layering).

5.2.2. Instrumentation And Operation

Instrumentation ⁽¹⁴⁾

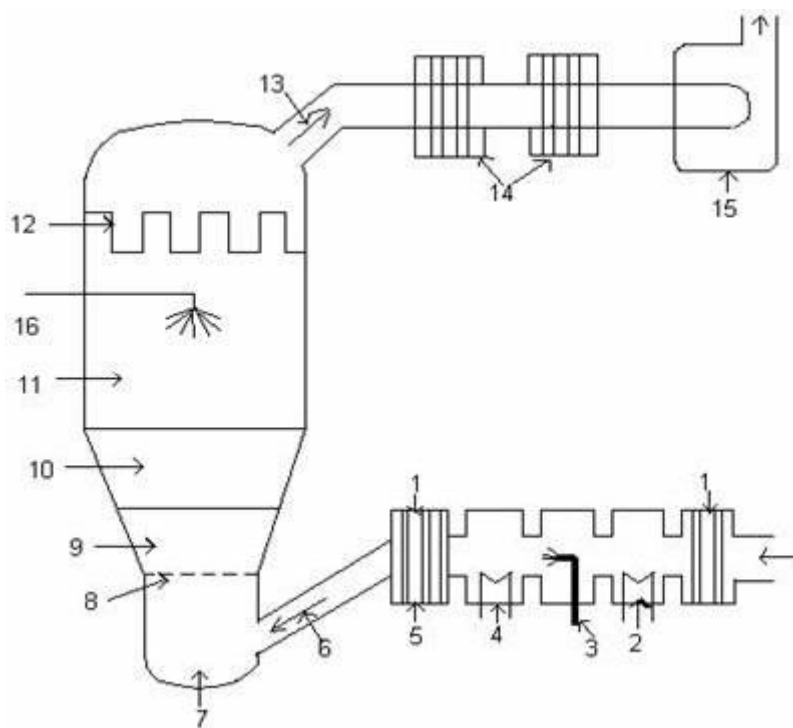


Figure-7. Fluid bed granulator

1. Inlet air filter
2. Condenser
3. Humidifier
4. Inlet air Heater
5. HEPA filter
6. Inlet air
7. Inlet air plenum
8. Gas distributor plate

9. Product container
10. Conical expansion zone
11. Filter housing
12. Product filter
13. Outlet air
14. HEPA filter
15. Fan
16. Spray gun

Operation

A suction fan mounted at the top portion generates the airflow necessary for fluidization of powders. The air used for fluidization is heated to the desired temperature by an air heater. The liquid granulating agent is pumped from its container & sprayed as a fine mist through a spray head onto the fluidized powder. The wetted particles undergo agglomeration through particle contacts. After appropriate agglomeration is achieved, the spray operation is discontinued and the material is dried and discharged from unit.

5.2.3. Principle Of Granulation ⁽¹⁸⁾

The powder is fluidized by the hot air in fluid bed granulator. The binding liquid such as solution, suspension is sprayed on the fluidized powder to build liquid bridges among them to form agglomerates.

The liquid bridge that serve to hold the particle together in two ways (1) by surface tension at the air liquid interface (2) by hydrostatic suction.

The liquid bridges are dried by the hot fluid air to stick the powder together. While the liquid sprayed continuously, the particles grow bigger to a desire granule size. The process is carried out continuously. Finally it forms ideal, uniform and porous granules.

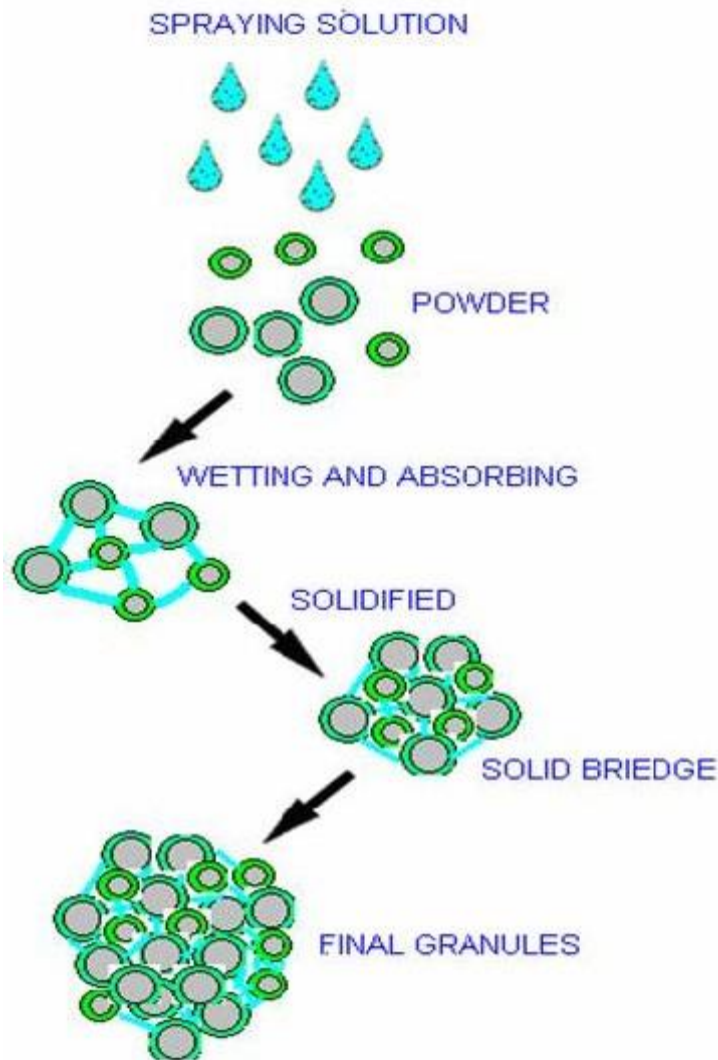


Figure-8. Principle of granulation process

5.2.4. Types Of Fluidized Bed Granulator ⁽¹⁾

1) Top Spray Fluid Bed Granulator

The recrystallization and hardening binder technology are generally carried out in the top spray granulator. In this equipment spray nozzle located at the top the base of the product container is equipped with a fine – mesh retention screen to allow small particle size. Spray nozzle to permit positioning above the static bed in the lengthened expansion chamber. The granulator is operated by fluidizing the bed of powder & spraying the granulating solution at the controlled rate. Proper agglomeration achieved, the liquid spray is cut off and the material allows drying to the desired moisture content.

2) Rotating Disk Fluid Bed Granulator With Dryer Option

Layering technology carried out by rotating disk granulator and coater. The technique have been extended to coating operation and combined with an expansion chamber to form the rotating disk granulator & coater fluid bed device.

The rotating disk can be moved up or down to create a variable slit opening between the outer perimeter of the disk and the side wall of the container.

This allows independent control of air velocity over air volume, air is drawn into the product container through the slit under negative pressure. At the same time the disk rotate at varying speed & product move under centrifugal force to the outer positions where it is lifted by the fluidizing air stream into the expansion chamber. As the material fall to the center of the rotating disk and repeat the processes. This fluidization pattern also described as a spiraling helix or rope like pattern around the inside the rotor chamber.

The motion of fluidization of the particle controlled by the forces like fluidization, centrifugal force and gravity.

Spray nozzle immersed in the bed of fluidization and spray applied in tangential fashion with respect to the particle flow.

Pellet production by the layering technique, in this process started with seed material (smaller as diameter 250 mm). The solution or suspension of the drug and binder can be applied to the seed material in several layers. Drugs can apply as a dry powder fed into the bed at a controlled rate. So that bed expands both horizontal and vertical, layers up to 1000% at starting weight can be applied. The resulting pellets formed are uniform and subsequently coated for controlled release.

In the layering technique dry powder can be fed into the wet bed resulting in the build up the layers of the powder on to the particle substrate. At the end of the coating process the liquid spray is cut off and the material in the product chamber is dried by increasing the fluidizing air volume and temperature.

5.2.5. Common Problem In Fluid Bed Granulation ⁽¹⁸⁾

1) Excessive fine

- In sufficient quantity of binder
- High fluidized velocity or air flow
- Weak binder or low concentration of spraying liquid
- Inlet temperature too high
- Binder spray rate is too low
- High atomization air pressure
- Fine droplet size of the binder.

2) Excessive coarse granulation

- Binder spray rate too high
- Inlet air temperature too low
- Low fluidization velocity or air flow
- Stronger binder or higher concentration of spraying liquid.
- Nozzle position too low

3) Final moisture inconsistency

- Improper fluidization
- Temperature probe out of calibration
- Humidity of outside air

4) Poor fluidization

- Air velocity is low
- Processor fan does not have adequate pressure drop
- Air distributor not cleaned properly
- Too much product in the product container
- Incorrect air distribution plate
- Exhaust filter porosity too small
- Exhaust is blocked

5) Finished product non uniformity

- Insufficient filter shaking
- Product homogeneity before granulation is not adequate
- Lumps in raw materials
- Spraying time is insufficient

6) Low yield

- Filter bag is not shaken at the end of the process
- Material sticks to the expansion chambers as a result of static charge
- Wrong porosity exhaust filter
- Air distributor with coarser screen opening

In the system, a granulating solution or solvent is sprayed into or onto the bed of suspended particles. The rate of addition of binder or solvent, conc. of binder, spray rate, distance between spray nozzle & fluid bed, temperature of air, volume & moisture content of the air all play important roles in the quality & performance of the final product.

In general fluid bed granulation yields less dense particles than conventional methods.

5.3 Fluidized Bed Coater ^(1, 8, 20)

5.3.1 Introduction ⁽¹⁾

Pharmaceutical dosage forms like tablets, powders, granules and pellets are often coated with polymeric material to mask objectionable taste or odor, protect an unstable ingredient, separate incompatible ingredients, improve appearance for enteric coating and sustained release coating. So many methods are used for applying coating to the core material including fluidized bed coating.

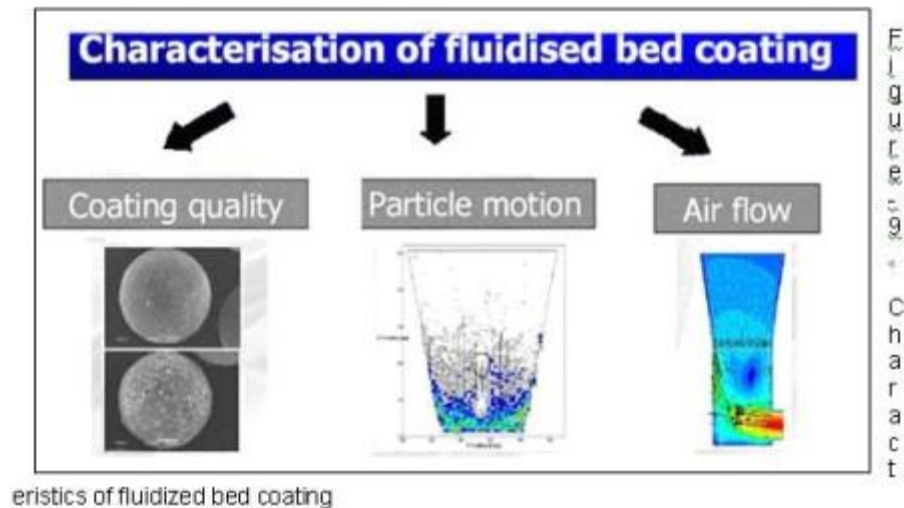


Figure-9. Characteristics of fluidized bed coating

5.3.2. Instrumentation And Operation ⁽¹⁾

1) Incoming Air

It should be direct contact with the product and be free from air born dust , oily particles ,other impurities. The air should be filtered through both coarse and fine dust filters and also from HEPA filters if required. Cooling with cool water or refrigeration agents or passing through adsorptive agents should dehumidify it.

2) Product Container

The product container should be made up of high quality polished stainless steel having suitable shape and size. The bottom part should hold a screen of the correct size required to catch the product. It may also be equipped with discharge pneumatic devices, choppers to break lumps of granules during processing, special film-coating partitions and nozzles to spray fluid from below.

(3) Filter Bag Housing

The filter bag & housing are very important parts of fluidized bed equipment. Manufacturers patent the no, design, size, shape and other characteristics of filter bag housing. The filter shaking device and filter below off device are used for cleaning the filters.

(4) Spray Device

This device used to distribute the firmly atomized and homogenized granulating or coating liquid on to the fluidized product. One fluid nozzles, which atomize liquid by its own pressure against the nozzle tip, and two fluid nozzles where high-pressure air is introduced at the nozzle tip to break the liquid into fine droplets. The latter one is most widely used since it places, much finer droplets.

Different types of pumps are employed to move the liquid and atomized air to the nozzles.

5.3.3. Types Of Fluidized Bed Coater ^(1, 8, 20)

(1) Top Spray Pellet With Particle Coating Option,

This is known as down-spray coating

Features:

The expansion chamber is lengthened allowing powder to remain fluidized longer and to move with a higher velocity so that agglomeration is minimized. The expansion chamber is conical shaped allowing

uniform deceleration of the air stream. The filter housing is larger. Its design allows to shake the fines back into the bed without interrupting fluidization, this reduces tendencies of agglomeration. The nozzle is kept low in the expansion chamber, so that coating materials impinge on the fluidized particles a short distance from the nozzle, this reduces droplet spray – drying and provides for longer subsequent drying of the coated particles.

Top spray coater is used

To apply aqueous and organic solvent based film coating

§ Controlled –release coating

§ Hot melts on granules & small particles

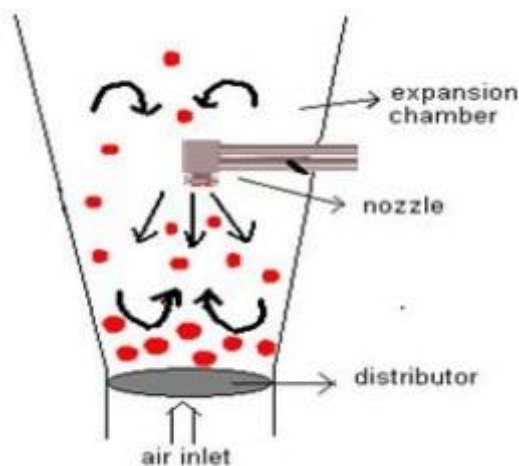


Figure-10. Top spray coating

2) Fluid Bed Bottom Spray Pellet With Particle Coating Option,

This coater employs a cylindrical product container with a perforated plates. In the container, there is a second cylinder (coating partition), which is raised slightly above the perforated plate.

Centrally, in the plate below this partition, there is a nozzle used to dispense the coating solution. The perforated plate is designed with large holes in the area under the coating partition & smaller holes in the remainder of the plate, excluding the one ring, of larger holes at the perimeter. Bottom-spray coating provides a highly organized particle flow & high quality reproducible film so this system is used extensively for sustained release coating. This process is capable of handling solvents, Aqueous Solutions, emulsions, suspension, films & hot melts. It is used for coating small particles, pellets & tablet with batch size from a few hundred gm to 600 kg.

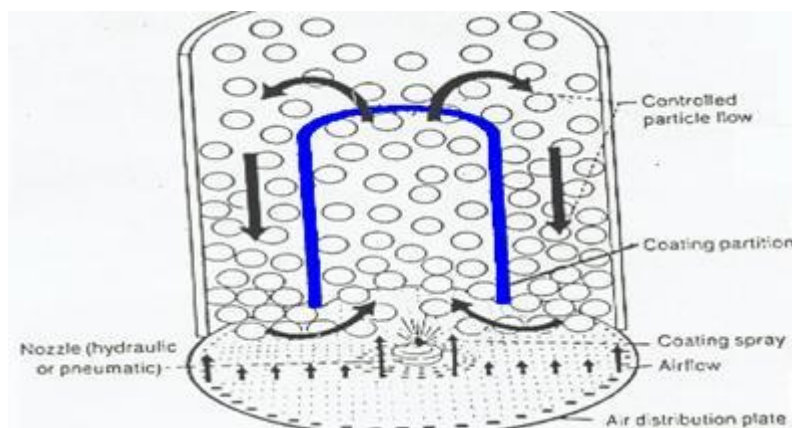


Figure-11.Wurster process

3) Fluid Bed Roto Processor With Drug Loading & Coating Option.

This is the technique in which fluid bed system utilizes rotating disk to add centrifugal force to the forces of fluidization and gravity and offers very rapid mixing.

The particles cycling time in tangential spray fluidized bed equipment is very rapid so the films are uniform in thickness.

Rotoprocessor insert (Tangential spray insert)

Principle of operation

The principle of operation is that tangential nozzles are fixed on the rotating plate such as to do different operation using the same insert. The rotating plate is a specially designed perforated plate such that the powder does not fall down and at the same time air can come through the plate creating fluidized effect in the processor.

The uniformity is well and the wastage is the minimum as the spray nozzle is embedded within the bed.

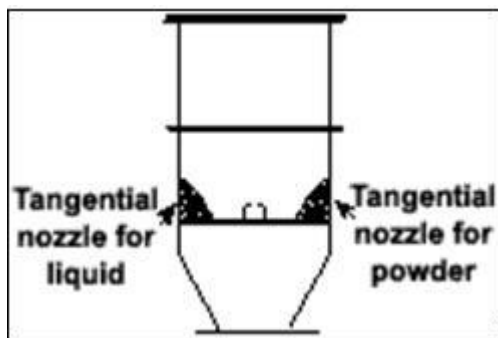


Figure-12. Rotoprocessor

Operations possible:-

Tangential coating

Tangential granulation

Pellet formation

Pellet formation, Pellet drug loading on dummy beads.

Concave tablet coating.

Spray application systems:-

1) High pressure, air less

2) Low pressure, air atomized

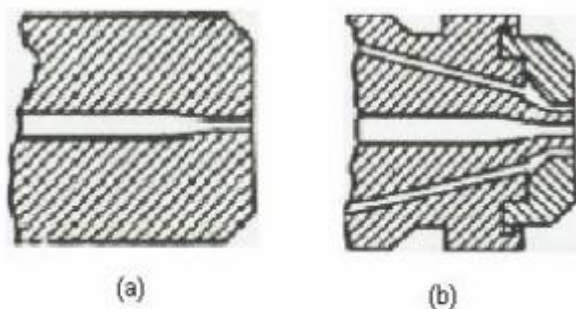


Figure-13. Spray application systems

4) Huttlin Kugel Coater:-

It does not consist of a central processor. The product container of kugel coater is spherical. Fluidized air is introduced by tube that passes down the center of the product container. A series of spray nozzles are also located at the bottom of the product container in such a way that fluidizing air creates a balloon effect to keep the product being coated away from the spray nozzles. Addition of multiple spray nozzles intended to maximize uniformity of distribution of coating.

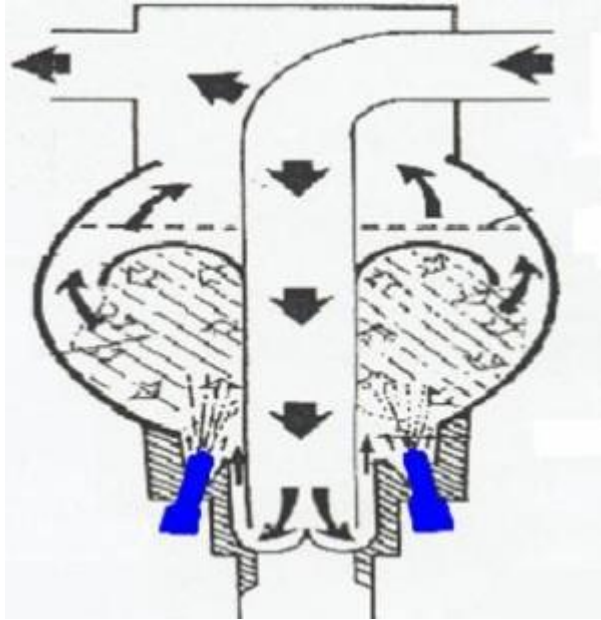


Figure-14. Huttlin kugel coater

5.3.4. Design Features ⁽¹⁾

1) GMP

As per GMP regulations the products prepared for human use meet certain minimum quality standards. A surface of container should be made up of high quality polished stainless steel. Joints should be perfectly welded with a highly polished finish. Components should be easily dismantled and neat.

2) Safety requirement

In case of fluidized coater vast of amount of heated air is used and when this air mixes with solvent and dust, an explosive mixture can result. Adequate safety devices are required to prevent destruction of the machinery and injury to the operating staff.

In case of an explosive (pressure of 9 to 12 bar) horizontal and vertical pressure, sufficient panels of relief doors are needed. Explosion proof and waterproof motors and electrical switches are common features of advanced technology.

3) Solvent recovery

The coating done in fluidized bed system, the complete solvent removal is not possible, the exhaust gases containing organic solvents vapors of toxic materials must not be automatically vented into the atmosphere.

These gases should not be treated by solvent recovery system for filtration device to decrease the emission to the minimum amount allowed by law and to prevent environmental pollution.

5.3.5. Influence Of The Spray Nozzle ⁽²⁰⁾

Nozzle position:

Low vs. high

(121 vs. 168 mm above distributor)

Nozzle pressure:

Maintenance vs. 2 vs. 3 vs. 4 bars

Coating:

Sodium caseinate vs.

Gelatin hydrolysate

Spray rate:

5 – 7.3 g/min

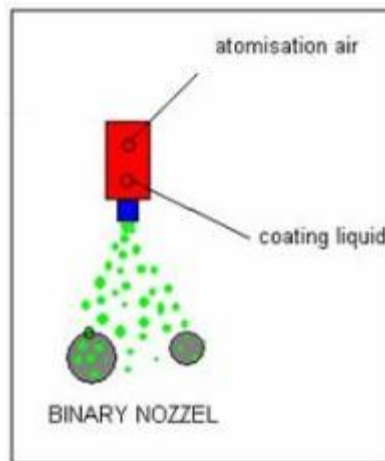


Figure-15. Influence of the spray nozzle

Coating liquid dry matter:

5 – 15 wt%

5.3.6. Particle Motion Visualization ⁽²⁰⁾

- Optical : Behavior along the wall
- Probes: e.g. Fiber optical, capacitance, inductance

Invasive technique: local motion disturbance

- PIV, LDA: Transparent equipment/materials required
- MRI: Material do not contain metal parts
- Tomography: e.g. Capacitance poor resolution, blurred results
- Tracer techniques: Non-invasive technique. Real-time recording is possible High temporal and spatial resolution. e.g. Positron emission particle tracking (PEPT)

6. Advantages, Disadvantages And Applications Of Fluidized Bed Systems ^(8, 9)**6.1. Advantages**

1. Liquid like behavior, easy to control
2. Rapid mixing, uniform temperature and concentrations.
3. Resists rapid temperature changes, hence responds slowly to changes in operating conditions and avoids temperature runaway with exothermic reactions.
4. Applicable for large or small scale operations.
5. Heat and mass transfer rates are high, requiring smaller surfaces.
6. Continuous operation.
7. Ease of process control due to stable conditions.

6.2. Disadvantages

1. Bubbling beds of fine particles are difficult to predict and are less efficient.
2. Particle comminution (breakup) is common.
3. Pipe and vessel walls erode due to collisions by particles.
4. Non-uniform flow patterns (difficult to predict).

5. Size and type of particles, which can be handled by this technique, are limited.
6. Due to the complexity of fluidized bed behavior, there are often difficulties in attempting to scale-up from smaller scale to industrial units.

6.3 Applications ^(8,9)

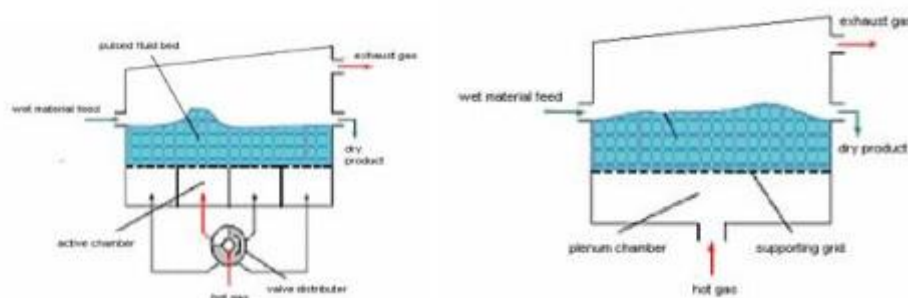
Degree of application decides importance of process. Fluid bed systems are widely applied in non-pharmaceutical fields in comparison to their use in pharmaceutical fields as there are numerous apparatus, process and product parameters that affect the quality of final pharmaceutical product. Also in pharmaceutical field each formulation presents its own individual development problems that had led to fluidized systems not reaching its full potential in pharmaceutical production:

1. Fluidized bed dryers are used in drying of various materials such as powders, tablets, granules, coals, fertilizers, plastic materials.
2. This process is being used in granulation of pharmaceutical powders.
3. Fluidized bed coaters are used widely for coating of powders, granules, tablets, pellets, beads held in suspension by column of air.
4. The three types (Top spray, Bottom spray, Tangential spray) are mainly used for aqueous or organic solvent-based polymer film coatings.
5. Top-spray fluidized bed coating is used for taste masking, enteric release and barrier films on particles/tablets. Bottom spray coating is used for sustained release and enteric release and Tangential spray coating is used for SR and enteric coating products.

7. Innovations In Fluidized Bed Systems ^(14, 20-24)

7.1. Pulsed Fluid Bed Dryer ^(23, 24)

In pulsed fluid bed dryer, at a given time period, the fluidizing gas flows through a fraction of grid surface area and is then redirected to consecutive sections in fast succession (the gas plenum chamber is divided into several sections). While in conventional fluid bed dryer, the fluidizing gas flows through the entire surface area of grid surface.



A. Pulsed fluid bed B. Conventional fluid bed

Figure-16. Comparison between conventional and pulsed fluid bed dryer.^(23, 24)

Advantages of pulsed fluid bed over conventional fluid bed.

- For easy fluidization for irregularly shaped particles such as fibers, flakes, needles
- For fluidization of material having a wide particle size distribution
- For fluidization of bed of particles with 30 to 50% less air
- It operates with improved fluidization uniformity (reduced channelling)
- For fluidization of fragile particles

7.2. Fluidized Spray Dryer (14)

The Fluidized Spray Dryer FSD™ is one of the most successful designs of spray dryers, combining fluidization and spray drying technologies, enabling the size and structure of particles to be easily controlled. Therefore, the FSD™ is often used as a spray dryer agglomerator or spray dryer granulator.

Another important feature which makes this concept ideal for producing heat sensitive products in dried form.

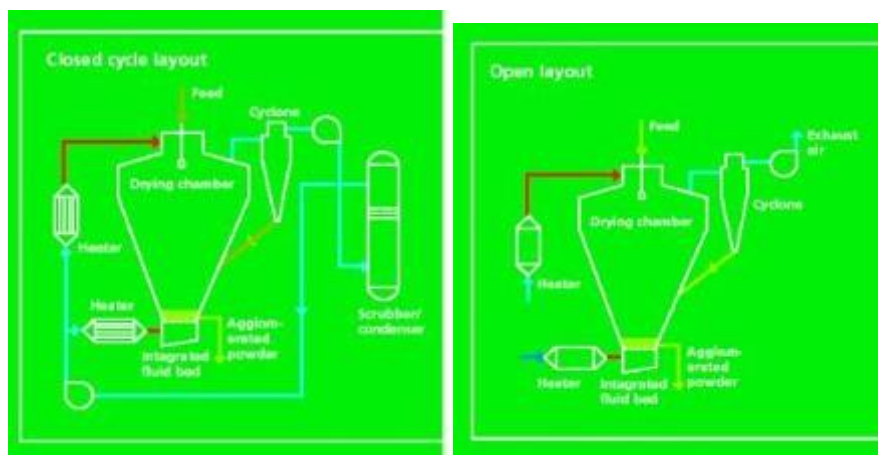


Figure-17. System layout (14)

Advantages

- Produces free flowing powders in agglomerated or granulated form.
- Produce powders having a very low content of small particles (dustless).
- Many thermoplastic and hygroscopic products those are problematic in other designs can be dried.
- Ideal for heat sensitive products as particle temperatures are kept low throughout the drying process.
- Drying is completed at low outlet drying temperatures, giving high energy utilization efficiencies.

7.3. Precision Granulation (21, 22)

Fluid Bed Granulation and High Shear Granulation are presently the most important wet granulation techniques employed in the pharmaceutical industry. Precision Granulation™, a new bottom spray method, is evaluated for comparison with the conventional granulation methods.

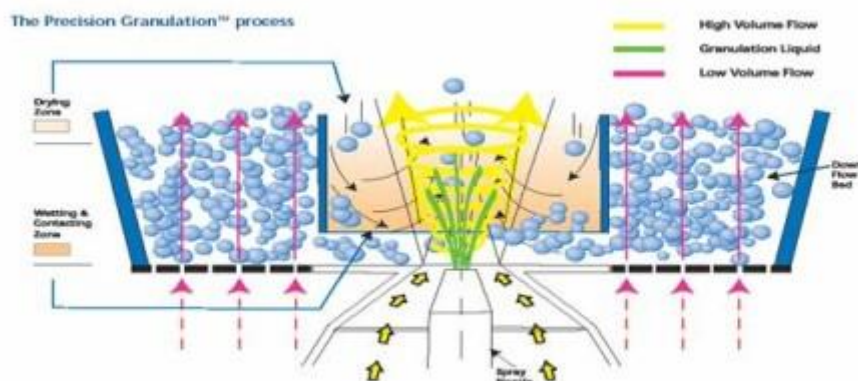


Figure-18. Precision granulation process (21, 22)

The objective of this study was to compare Precision Granulation™ (PG) with Top Spray Fluid Bed Granulation (TS-FBG) and High Shear Granulation (HSG) for tabletting.

Finally they conclude with:

PG produced good quality granules with adequate flow and strength for tableting. The quality of these tablets was comparable to those of tablets prepared from TS-FBG and HSG

Porosity, strength, bulk density and tapped density of PG granules were intermediate to those of HSG and TS-FBG granules. PG granules had the lowest Carr index and Hausner ratio values. For equivalent tablet weight and hardness, PG tablet batches showed faster disintegration times.

Preliminary studies with the two grades of lactose and powdered sugar suggested that PG can offer an alternative to existing methods for investigating granulation of "difficult-to-granulate" materials.

Real Time Process Determination TM (RTPD) is a software program that can be integrated with the granulator controls system for enhancing process monitoring and control.

7.4. Multi Function Fluid-Bed Granulator and Coater ⁽²⁰⁾

Vanguard's VPL Series Fluid Bed Granulators and Coaters have multi-functional systems. The top spray system is the third generation of the top spray granulator. It is more efficient than most common fluid bed granulators in the industry. This type of advanced series equipment integrates three fluid bed processes including the top-spray granulating, bottom spray coating, and tangent spray pelleting and coating such that it achieves both economical and technological advantages in solid dose processing and other applications.

Features:

- High efficient dryer
- Granulator meeting different requirement
- Bottom spray coating system
- Tangent spray rotor system for powder layering, pelleting, coating
- Intelligent control system
- 2 bar shock resistant as standard

8. References

1. Swarbrick J, Boylan J.C, "Fluid bed dryer, granulator and coaters,**Encyclopedia of pharmaceutical technology** , Marcel Dekker INC, New York , Volume- 6,171-173, 1992
2. Othomer D.F,"Background,History and Future of Fluid bed systems",**Fluidization** , Reinhold publishing corporation, New York , 102-115 ,1956
3. Banks, Michael, Aulton, Michael E, "Fluidized bed granulation - A Chronology" , **Drug development and industrial pharmacy** , , 17(11), 1437-1463, 1991
4. Ylirussi J., Rasanen E, Rantanen J., Mannerman J.P "The characterization of Fluidization Behavior Using a Novel Multichamber Microscale Fluid Bed",**Journal of Pharmaceutical Sciences** , , 93(3), 780-791,2004
5. Meshram.R, Bajaj .A, "Solid dispersion and enteric coating of pancreatin enzyme using fluidized bed coating and other techniques" **Indian Drugs** , ,42(12), 792-796,2005
6. Vazquez .E.R, "Optimization of drying end point measurement for the automation of Fluidized bed dryer using FT-IR Spectroscopy" **M.Sc Thesis** , , University of Puerto Rico , Mayaguez Campus, 17, 2004
7. Lachman L, Lieberman H.A, Kanig J.L, Third edition "Granulation" , **The Theory and practice of industrial pharmacy**,Verghese Publishing House, Bombay, 58-59, 1991
8. www.engr.pitt.edu/chemical/undergrad/lab-manuals

9. www.engineering.uakron.edu/chem/fclty/chase/solids/solids note 5.
10. Aulton M.E., second Edition "Granulation", **Pharmaceutics "The science of dosage form design**, Churchill Livingstone , Edinburgh , 373, 2002
11. Ansel C., Allen L.V., Popovich N.G., eighth edition "Tablets", **Pharmaceutical dosage form and Drug delivery system**, B.I Publications , India , 193 and 243 , 2005
12. www.kurimoto.co.jp
13. www.bepex.com
14. www.niroinc.com
15. www.drytecheng.com
16. www.swensontechnology.com
17. www.nara-m.co.jp
18. www.pharmaceutical-equipment.com
19. www.umangpharmatech.com
20. www.fte.ugent.be
21. 21. Walter K.T., A Process for Granulation of a Particulate Material. **European Patent** 1064990 (2001).
22. Liew C.V., Walter K.T, Wigmore A.J, Brzezczko A.W. and Heng P.W.S, Precision Granulation™ as an Alternative Granulation Method, **Poster Presented at 2002 AAPS Meeting and Exposition**, Toronto (Nov 2002).
23. Worldwide patented technology: CA2236290; DE69813207; EP0979140; GB2324744; US5918569, WO98/48932.
24. Technology licensed to Aeroglide Inc., P.O. Box 29505 , Raleigh , North Carolina 27626-0505 U.S.A. ;