

Multi Unit Particulates Systems (MUPS): A Novel Pellets for Oral Dosage Forms

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INTRODUCTION:

Pelletization is an agglomeration process that converts fine powders or granules of bulk drugs and excipients into small, free flowing, spherical or semi spherical units, referred to as pellets¹. Pellets range in size, typically, between 0.5 – 1.5 mm, though other sizes could be prepared. Pellets can be prepared by many methods, the compaction and drug-layering techniques being the most widely used today. Regardless of which manufacturing process is used, pellets have to meet the following requirements.

- (1) They should be near spherical and have a smooth surface; both considered optimum characteristics for subsequent film coating.
- (2) The particle size range should be as narrow as possible. The optimum size of pellets for pharmaceutical use is considered to be between 600 and 1000 μm .
- (3) The pellets should contain as much as possible of the active ingredient to keep the size of the final dosage form within reasonable limits.

Pellets are for pharmaceutical purposes and are produced primarily for the purpose of oral controlled-release dosage forms having gastro resistant or sustained-release properties or the capability of site-specific drug delivery. For such purposes, coated pellets are administered in the form of hard gelatin capsules or disintegrating tablets that quickly liberate their contents of pellets in the stomach.

As drug-delivery systems become more sophisticated, the role of pellets in the design and development of dosage forms is increasing. Formulation of drugs in multiple-unit dosage forms, such as coated pellets filled in capsules or compressed into tablets, offers flexibility as to target-release properties. The safety and efficacy of the formulation is higher than that of other dosage forms.

Pellets provide high degree of flexibility during the design and development of oral dosage forms. They can be divided into desired dose strengths without formulation or process changes, and can also be blended to deliver incompatible bioactive agents simultaneously or particles with different release profiles at the same site or at different sites within the gastrointestinal tract.

In addition, pellets have numerous therapeutic advantages over traditional single units, such as tablets and powder-filled capsules. Taken orally, pellets generally disperse freely in the gastrointestinal tract, and consequently maximize the drug absorption, minimize local irritation of the mucosa by certain irritant drugs because of the small quantity of drug available in a single pellet, and reduce inter and inpatient variability².

As the advantages of pellets over single units became clear, the pharmaceutical industry as a whole started to devote resources to conduct research in pellet technology and, whenever possible, acquire advanced equipment suitable for the manufacture of pellets.

Pellets may be manufactured by using different methods according to the application and the choice of producer. The methods used for Pelletization are essentially the same as the granulation methods. The most widely used processes are extrusion and spherization and solution or suspension layering, and powder layering. Other processes with limited application in the development of pharmaceutical pelletized products include globulation, balling, and compression.

ADVANTAGES OF PELLETS:

- They can be divided in to desired dosage strength without process or formulation changes.
- When pellets containing the active ingredient are in the form of suspension, capsules, or disintegrating tablets, they offer significant therapeutic advantages over single unit dosage forms³⁻⁵.
- They can also be blended to deliver incompatible bioactive agents.
- They can also be used to provide different release profile at the same or different sites in the gastrointestinal tract.
- Pellets offer high degree of flexibility in the design and development of oral dosage form like suspension, sachet, tablet and capsule⁶⁻⁸.

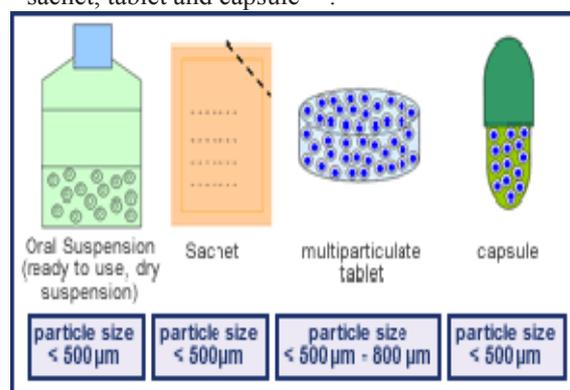


Figure No-1: Flexibility of pellets in development of dosage form.

- Pellets disperse freely in gastro intestinal tract (GIT), maximize drug absorption, and minimize local irritation of the mucosa by certain irritant drugs.
- **Improved flow characteristics:** Spheres have excellent flow properties, which can be used in

automated processes or in processes where exact dosing is required, e.g. tableting, moulding operations, capsule filling, and packaging.

- **Coating:** Coating of granules is often applied for stabilizing active ingredients in the granule or to control the release of these active ingredients. Typical applications in the pharmaceutical industry are the controlled release medicines. The easiest shape to coat is the sphere due to the absence of edges. It is also the most economical one to coat as no extra coating material is required to fill irregularities in the surface of the granules⁹⁻¹¹.
- **Packing of beds and columns¹²:** In certain processes, porous beds or columns are used as chemical reactors. Spherical particles allow the reproduction of beds with always the same void volume, surface area and permeability. Calculations and predictions of the process characteristics also become easier when round particles are used as many equations are based on flows around symmetrical bodies.
- **Density increase:** Both the true and the bulk density of granules are increased by spheronising. This can improve the process and the packaging.
- **Marketing:** For consumer products, spheronising is sometimes only applied for improved product appearance and marketing reasons.
- **Hardness and friability:** Hardness and friability depend on the internal cohesive forces and surface characteristics. Spheronization increases the hardness and reduces the friability of granules. This will reduce the amount of fines generated during handling or transportation.

DISADVANTAGES OF PELLETS¹³:

- Dosing by volume rather than number and splitting into single dose units as required.
- Involves capsule filling which can increase the costs or tableting which destroy film coatings on the pellets.
- The size of pellets varies from formulation to formulation but usually lies between 1 to 2 mm.

DESIRABLE PROPERTIES OF PELLETS:^{14,15}

- **Uncoated pellets:**
 - Uniform spherical shape,
 - Uniform size,
 - Good flow properties,
 - Reproducible packing,
 - High strength,
 - Low friability, Low dust,
 - Smooth surface,
 - Ease of coating.
- **Once coated:**
 - Maintain all of the above properties,
 - Have desired drug release characteristics.

THEORY OF PELLET FORMATION AND GROWTH¹⁶:

One of the most significant properties of pellets is their ability to withstand the mechanical forces that act on them during the manufacturing process and the subsequent conditioning and/or coating and handling. If the pellets lack

sufficient mechanical strength, they may disintegrate completely or wear down in size due to frictional forces. The ability to withstand the mechanical forces becomes pronounced during a coating operation, particularly in fluid bed equipment where pellets are in constant motion and rub against each other and against the walls of the instrument. It is absolutely essential, therefore, that pellets possess sufficient strength to overcome any appreciable abrasion during agitation¹⁷. The role that pellet strength plays during the development of high-quality products has been well recognized. There are number of procedures to evaluate and various theoretical and mathematical expressions designed to explain the strength of pellets, mechanism of pellet formation and growth and the fundamental bonding forces that determine the strength of pellets during any pelletization process^{18,19}.

Bonding forces

The strength of pellets depends on the physical forces that bond the primary particles together. Initially, mechanical forces, such as tumbling, kneading, agitating, extruding, rolling, and compressing are needed to bring individual particles in contact with one another; these physical forces are also responsible for the inherent strength of other types of agglomerated particles.

i) Attraction between solid particles

Attractive forces are short-range forces that cause solid particles to adhere to each other only if they are brought close together; their effectiveness diminishes dramatically as the size of the particles or interparticular-distance increases. Therefore, the significance of attractive forces in the overall mechanism of agglomerate bonding is not only play a crucial role in the binding of the final product but they initially hold and orient the particles in a contact region long enough for stronger forces to take over.

ii) Interfacial forces and capillary pressure in movable liquid surfaces

In any wet agglomeration process, it is the liquid phase in the system that initially generates the cohesive forces between particles. Therefore, the amount and type of solvent present at any given time is very critical in determining the strength of the final product (Figure 1.8). The solvent could be added prior to or during the agglomeration step. When the solvent is added initially, part of the void space in a randomly packed material is filled with the liquid to form discrete lens-like rings at the contact and coordination points between particles forming the agglomerates. During the agglomeration process, when the ratio of the liquid to the void volume is low and air is the continuous phase, is known as the pendular state (Fig 7 A) Mutual attraction of particles is brought about by the surface tension of the liquid and the negative suction pressure generated at the liquid bridges. The forces that bond the particles are, therefore, derived from the interfacial tension at the liquid-gas interface. The capillary state is reached when all the void space within the agglomerate is completely filled with the liquid (Fig 7 C). The quantity of liquid, however, is not sufficient enough to surround the agglomerate. Since the liquid extends up to the edges of the pores at the surface, a concave meniscus, which creates a negative capillary pressure, develops at the surface of the agglomerate and gives rise to bonding forces.

Capillary pressure and interfacial forces create strong bonds between particles, which disappear once the liquid evaporates. In between the pendular and capillary states exists an intermediate state known as funicular state (Fig 7 B). In the funicular state, as in the pendular state, liquid bridges containing gas and pores filled with liquid are present and the cohesive strength of the agglomerate is attributed to the bonding forces exerted by the pendular bridges and capillary suction pressure. In the droplet state liquid completely envelopes the agglomerates (Fig 2 D) and the primary particles are held together only by the surface tension of the droplet. There is no interparticle capillary bonding and the concave surfaces observed with the capillary state are replaced by the convex surfaces of the liquid droplets. Thus, the strength of the droplet is dependent only on the surface tension of the liquid used.

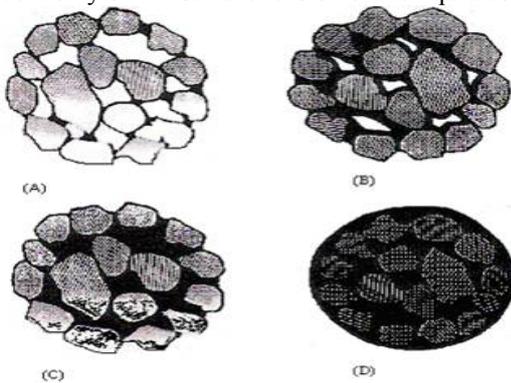


Figure No-2 Liquid saturation in a spherical assembly of particles.
 (A) Pendular state (B) Funicular state (C) Capillary state (D) Droplet state

iii) Adhesional and Cohesional forces

Many viscous binders harden during the agglomeration process and form solid bridges (Figure 3). Thin-adsorption layers are also immobile and can form strong bonds between adjacent particles by either smoothing out surface roughness or increasing the interparticle contact area or by decreasing the effective interparticle distance and allowing the intermolecular attractive forces to participate in the bonding mechanism (Fig 8 A). The areas of contact of adsorption layers increase appreciably when the solid particles are subjected to a high pressure like compression and produce high bonding forces.

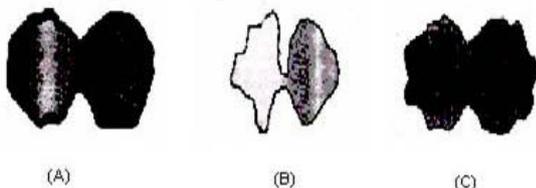


Figure No-3: Formal representation of A) Thin adsorption layer B) Solid bridges C) Mechanical interlocking

iv) Solid bridges

The above methods described the forces that initially bond the primary particles together; it is the solid bridges that largely determine the strength of the final cured or dried product, formed by different mechanisms (Fig. 8 B) such as:-

- 1. Crystallization of the dissolved substances:** As the dissolving medium evaporates, the dissolved substance may be identical to the bonded particles in nature or it may be the solid component of the binding liquid.
- 2. Hardening:** Binders are commonly used in the form of solutions to agglomerate primary particles. Upon curing, these binders harden and form bridges that owe their strength to the properties of the binder substance itself, the forces of adhesion between the binder and particles and /or the physicochemical characteristics of the particles forming the agglomerate.
- 3. Melting:** Substances that melts on the input of energy tend to solidify when cooled, and invariably form strong, solid bridges between particles. The strength and extent of the bridges formed can be either small or large depending on the chemical composition of the molten material and the other constituent of the agglomerate.

4. Sintering and chemical reaction: Formation of solid bridge by this mechanism is not common in the pharmaceutical industry.

The most common solid-bonding mechanisms that are usually encountered during the manufacture of drug pellets are hardening of binders, crystallization of solutes during the curing or drying stage of the pelletization process and melting and subsequent cooling of pellet components that may occur during compression, extrusion or spray congealing.

v) Mechanical Interlocking

Mechanical Interlocking of particles may occur during the agitation and compression of fibrous, flat-shaped and bulky particles (Fig 3 C). It is probably a minor contributor to pellet strength. However, it can provide sufficient mechanical strength.

ELEMENTARY GROWTH MECHANISMS²⁰

It is essential that the fundamental mechanisms of pellet formation and growth are clearly understood in order to optimize any pelletization process. On the basis of various theories, techniques and experimental reports, a formal representation of the elementary growth mechanisms of pellet formation is shown in (Fig 9). These mechanism known as nucleation, coalescence, abrasion transfer and layering, are believed to constitute a complete set of elementary events, which, directly or indirectly influence the growth and formation of pellets during manufacture.

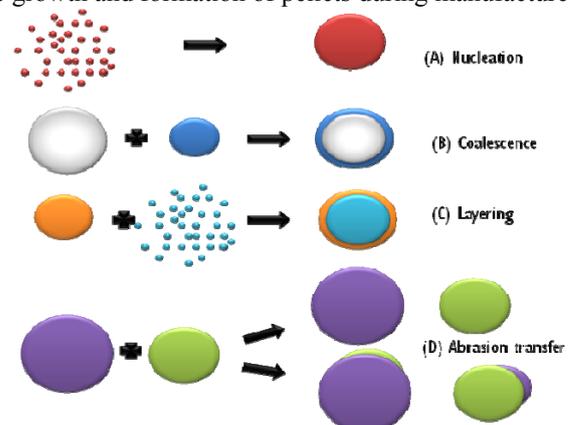


Figure No-4: Pellet growth mechanisms

i) Nucleation

It is a growth mechanism in which primary particles are drawn together to form three-phase air-water-solid nuclei (Fig 4 A), the particles are held together by liquid bridges, which are pendular in nature. The liquid is either added to the primary particles at once in a carefully controlled manner or sprayed slowly onto a mass of dry powder to produce moist nuclei. An important feature of nucleation is that both the mass and nature of the nuclei in the system changes as a function of time.

ii) Coalescence

The formation of large sized particles following random collision of well-formed nuclei is known as coalescence (Fig 9 B). Successful collisions occur only if the nuclei have a slight excess of surface moisture, if it is not so, the nuclei cannot deform and coalesce easily unless subjected to significant mechanical pressure. In coalescence, the total mass of the system does not change, although the number of nuclei is progressively reduced.

iii) Layering

Layering is a growth mechanism that describes the successive deposition of materials on already formed nuclei (Fig 9 C). The material deposited over the nuclei may be dry or moist and the growth rate is always slow, since a small amount of material is added to the growing nuclei at any given time. Although the number of particles remains same, the particle size increases uniformly as a function of time, thereby increasing the total mass in the system.

iv) Abrasion transfer

Abrasion transfer involves the transfer of material from one particle to another without any preference in either direction (Fig 9 D). It is therefore, apparent that the situation does not result in a change in the total number or mass of the particles. The particles, however, undergo a continuous change in size as long as the conditions that lead to the transfer of material persist.

v) Size reduction

There are three size reduction mechanisms that have an indirect effect on the elementary growth mechanisms, particularly layering, and to some extent coalescence. Well-formed particles may undergo size reduction due to attrition, breakage and shatter. If the particles have sufficient surface plasticity, however, they may coalesce to form larger particles upon collision.

PELLET FORMATION AND GROWTH:

Depending on the type of equipment and process selected for pellet formation and growth may occur in a number of ways. The following methods describe the systematic formation of pellets during the various pelletization processes in terms of the bonding forces and the elementary growth mechanisms.

i) Balling

This technique is not popular in the pharmaceutical industry as a pelletization process, probably due to the constraints of particle size distribution and content uniformity. Work in this area is expected to continue. It is appropriate, therefore, to examine the various phases of pellet growth in a drum, pan, or disc pelletizer. The first phase, known as the nucleation region, involves the random collision and subsequent coalescence of the primary

particles to provide well-formed nuclei. The sizes of the nuclei depend on the sizes of the primary particles, the moisture content, the viscosity of the binding liquid, and the wettability of the substance. Followed by the transition region where particles collide with each other and coalesce in a preferential molten, or where smaller particles are crushed and layered on large particles. This mechanism in this region is, therefore, size dependent; fines that are produced through attrition or crushing are picked up by large pellets. Production of fines and subsequent coalescence and layering continues until a time is reached when the number of favorable collisions declines rapidly, thereby leading to a reduction in the rate of growth of the pellets. At this point, the third phase, known as the ball growth region, is reached. In this region surface abrasion becomes marked; as a result, layering becomes the predominant mechanism of growth i.e., spherical agglomeration (Figure 5) or emulsion solvent diffusion (Figure 6). During the process, the tumbling action in the pelletizers allows the particles to re-orientate themselves and form dense pellets of appreciable strength. The strength of the uncured pellets is directly related to the surface tension of the binding liquid which in turn affects the suction potential that develops into the pellets.

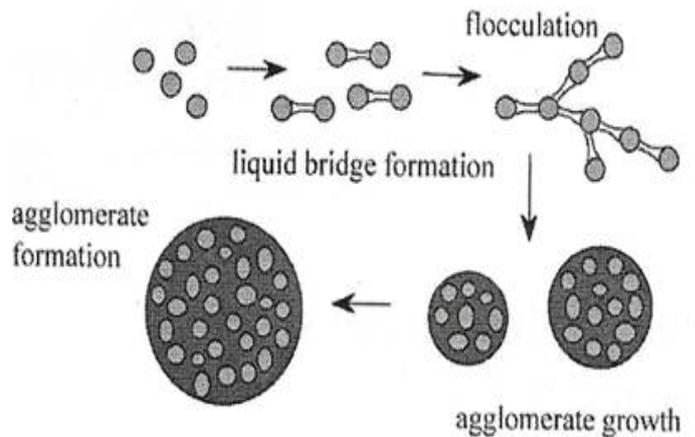


Figure No-5: Pellet growth mechanisms- (spherical agglomeration)

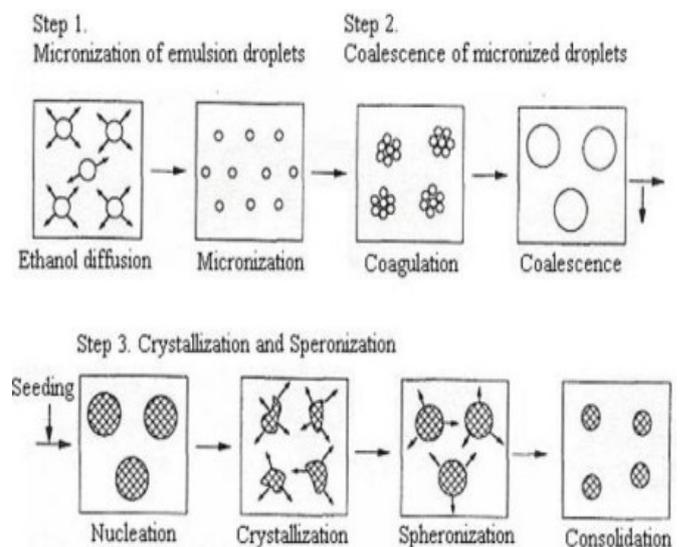


Figure No-6: Pellet growth mechanisms- (emulsion solvent diffusion)

ii) Drug Layering

Pelletization by layering involves the deposition of successive layers of drug moieties from solution, suspension, or dry powder of preformed nuclei, which may be crystals or granules of the same material or inert starter seeds.

In solution/suspension layering, the drug particles are dissolved or suspended in the binding liquid; a hardening binder may or may not be added in the binding liquid. Once this formulation is sprayed, the droplets, which owe their existence to the surface tension of the liquid, spread out on the nuclei, and drying follows. Spreading depends on the droplet wetting characteristics, the wettability of the material, and the thermodynamics. As the liquid evaporates, the dissolved substances crystallize out. On further evaporation, these crystals and the particles they are initially suspended in the binding liquid are drawn toward each other and toward the starter seeds by capillary forces. This leads to the formation of solid bridges among the particles. Strength of the solid bond depends on the properties of the binder, other additives in the formulation and the active ingredient. This phenomenon of spraying and drying and the subsequent formation of solid bridges are repeated until the desired size of pellet is achieved. In powder layering, liquid saturation is low and irrespective of

the solubility of the active in the binding liquid, complete dissolution does not occur. Typically, a binder solution is first sprayed onto the nuclei, followed by the addition of powder. The moist nuclei tumble in the rotating pan or disc, pick up powder particles, and form layers of small particles that adhere to each other and the nuclei by means of capillary forces developed in the liquid phase. As additional binding liquid is sprayed, layering of more powder on the nuclei continues until the desired pellet sizes are achieved. On drying, the binder and other dissolved substances crystallize out and the liquid bridges are partially replaced by solid bridges.

iii) Compaction (Extrusion-Spheronization)

Compaction is a form of pressure agglomeration, in which drug particles or granules are forced together with or without formulation aids by a mechanical force to generate pellets of well defined shapes and sizes. The pelletization process can be subdivided into compression and extrusion. In the first stage of compression, particles that are pretreated through the blending or wet granulation followed by drying, rearranges themselves to form a closely packed mass, during this process, particles retain most of their properties.

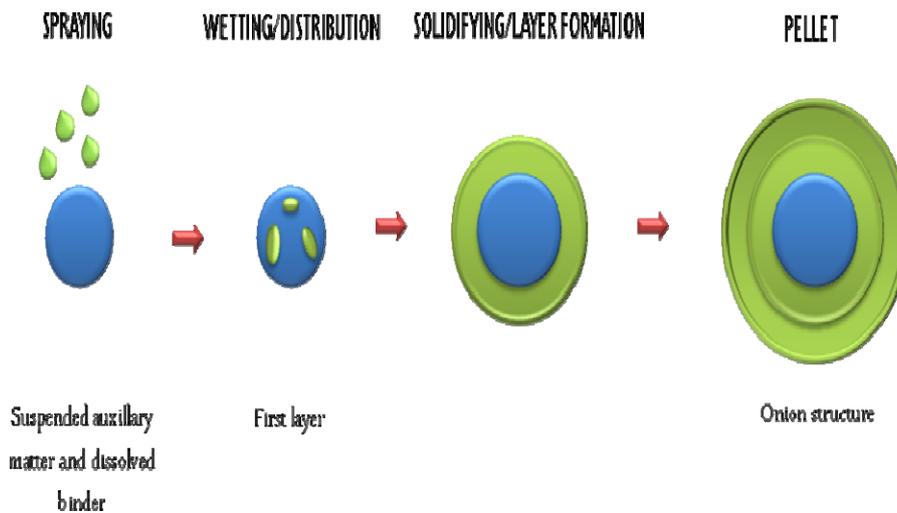


Figure No-7: Scheme of steps involved in pelletizing by layering. Steps of the Suspension and Solution Layering.

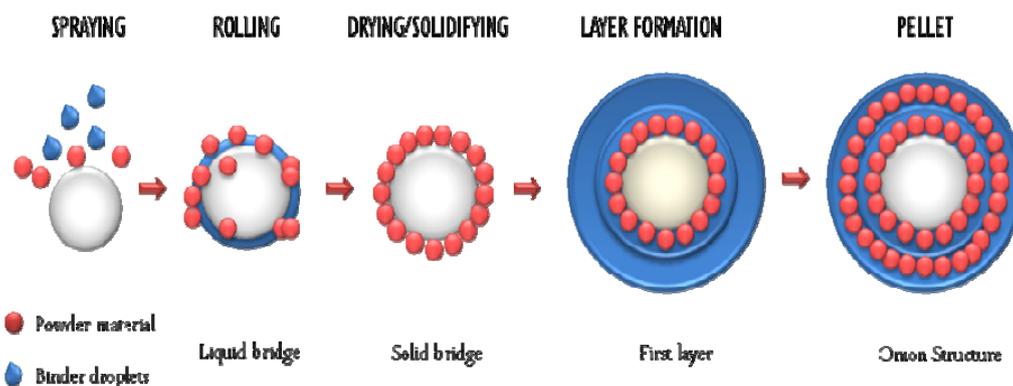


Figure No-8: Scheme of stage involved in pelletization by Suspension or Solution layering.

At high pressures, increased interparticle contact is observed. Mechanical interlocking is the only bonding mechanism that does not involve any forces and is expected to contribute very little to the physical strength of the pellet. On cooling, the molten material forms very strong solid bridges, tapped moisture, albeit insignificant may also contribute to bonding through capillary forces. In the second stage, the granulation is then put into the extruder to produce high-density extrudates. These extrudates are bonded together by capillary forces, solid bridges formed due to loss of moisture, mechanical interlocking and to some extent, molecular forces. These extrudates are finally converted to pellets on spheronization. During the process, the moisture is forced out from the pellet interior into the outside and imparts plasticity to the pellet surface. The surface plasticity, coupled with the concurrent tumbling of the particles in the spheronizer, allows the formation of spherical pellets.

iv) Globulation

It is a process where hot melts, solutions, or suspensions are atomized to generate spherical particles or pellets. In globulation, atomization produces solid particles directly from the liquid phase through evaporation or cooling and subsequent solidification of hot melts, solution and suspension. During spray drying, the atomized droplets are contacted by a hot gas stream and evaporation of the liquid is initiated, which involves simultaneous heat- and mass transfer and depends on the temperature, humidity, and transport properties of the air surrounding the droplet. As more and more liquid evaporates, surface saturation conditions are reached and formation of solid begins. These particles are initially held together by capillary forces developed by the liquid phase and are gradually replaced by solid bridges. Continuation of the process leads to the formation of a porous layer or crust on the surface of the

droplets and thickness of the crust increases through both evaporation and subsequent crystallization of the dissolved material that may include active drug, hardening binder or any other excipients which have solubility in the binding liquid. The rate controlling mechanism is the diffusion of the liquid through the expanding crust, followed by convective transport from the surface of the shell. In cross-linking technique, the polymer is rigidized by chemical reaction with the cross linking agents such as aldehydes, calcium chloride, etc.

During spray congealing, the atomized droplets are cooled below the melting point of the vehicle. The particles are held together by solid bonds formed from the congealed melts. Due to the absence of solvent evaporation during most spray congealing processes, the particles are generally nonporous and strong and remain intact upon agitation. The processing conditions play a very significant role in the development of good quality pellets, it is the physical forces that first bond the primary particles together and initiate the pelletization process. The propensity and strength of these physical forces depend to a large extent, upon the physicochemical properties of the formulation components. Therefore the physical forces coupled with the elementary growth mechanisms ultimately determine the strength and performance of pellets and should be taken into account during the design and development of pellet dosage forms.

PELLETIZATION TECHNIQUES²¹⁻²³:

The preparation of spherical agglomerates can be approached by several techniques which can be subdivided into the basic types of systems shown in below figure.

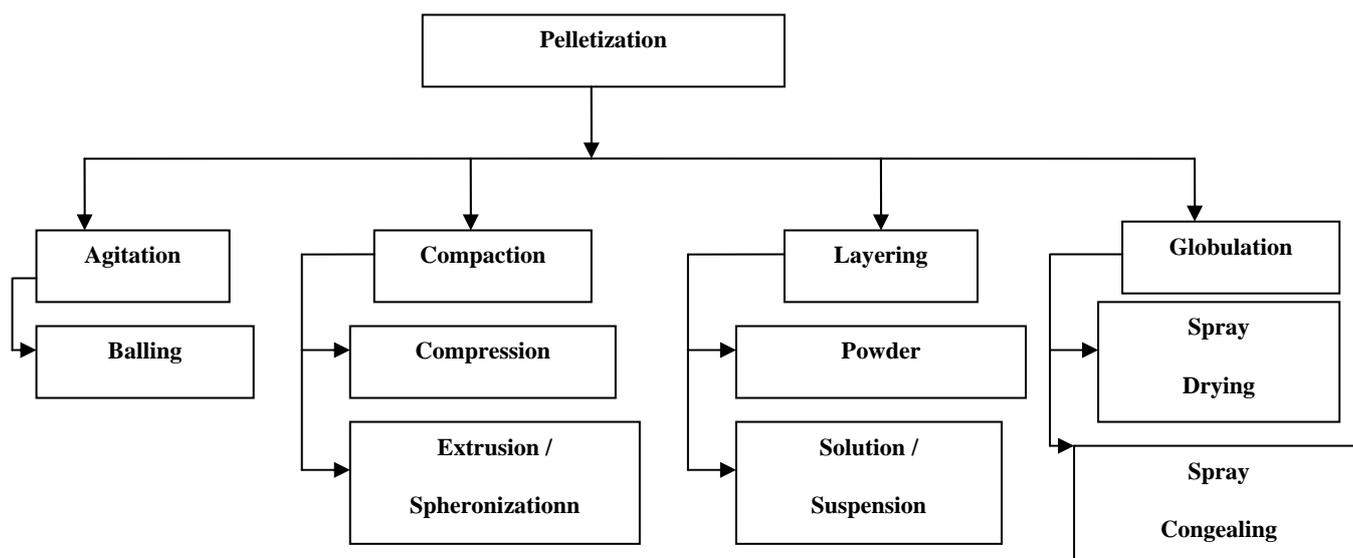


Figure No -9: Techniques of Pelletization

FLUID BED COATING FOR LAYERING OF PELLETS

24,25.

- Innovative processes for coating the products.
- Film coating; lipid hot melt coating, Coating of granules, pellets, tablets.
- Specific manipulation of the particle surface characteristics. Protection of the product against moisture, light and air.
- Specific manipulation of the way in which the particle dissolves the decomposition or the release of active ingredients.
- Process advantages: Uniform, continuous product coating. Aqueous or organic coatings can be applied. Coating and drying take place in one machine. In terms of total Containment, the coating process and the filling and emptying of the machine can be carried out in complete isolation and without product spreading into the environment.

PRINCIPLE OF OPERATION OF FLUID BED COATING²⁵:

With fluid bed coating, particles are fluidized and the coating fluid sprayed on and dried. Small droplets and a low viscosity of the spray medium ensure an even product coating. Glatt offers Batch Fluid Bed Systems in different batch sizes with:

- Top Spray Coating
- Bottom Spray Coating (Wurster Coating)
- Tangential Spray Coating (Rotor Pellet Coating)

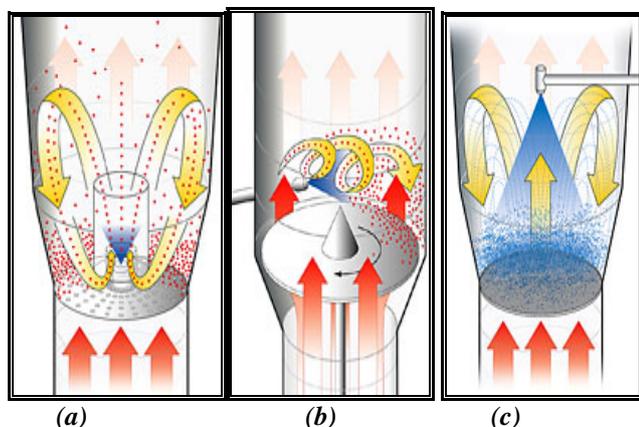


Figure No-10: (a) Principle of Bottom sprays batch fluid coating. (b) Principle of Tangential spray batch fluid coating. (c) Principle of Top spray batch fluid coating.

A.) Top spray coating:

This process is used for general coatings right up to enteric coating. With top spray coating in the fluid bed (batch and continuous), particles are fluidized in the flow of heated air, which is introduced into the product container via a base plate. The coating liquid is sprayed into the fluid bed from above against the air flow (countercurrent) by means of a nozzle. Drying takes place as the particles continue to move upwards in the airflow. Small droplets and a low viscosity of the spray medium ensure that the distribution is uniform. Coating in the continuous fluid bed is particularly suitable for protective coatings/color coatings where the product throughput rates are high. The product is continuously fed

into one side of the machine and is transported onwards via the sieve bottom by means of the air flow. Depending on the application, the system is sub-divided into pre-heating zones, spray zones and drying zones. The dry, coated particles are continuously extracted.

B.) Bottom spray coating (Wurster coating):

This process is particularly suitable for a controlled release of active ingredients. In the Wurster process, a complete sealing of the surface can be achieved with a low usage of coating substance. The spray nozzle is fitted in the base plate resulting in a spray pattern that is concurrent with the air feed. By using a Wurster cylinder and a base plate with different perforations, the particles to be coated are accelerated inside the Wurster tube and fed through the spray cone concurrently. As the particles continue traveling upwards, they dry and fall outside the Wurster tube back towards the base plate. They are guided from the outside back to the inside of the tube where they are once again accelerated by the spray. This produces an extremely even film. Particles of different sizes are evenly coated.

Bottom spray coating (Continuous fluid bed):

Particularly suitable for protective coatings/color coatings where the product throughput rates are high. The product is continuously fed into one side of the machine and is transported onwards via the sieve bottom by means of the air flow. Depending on the application, the system is sub-divided into pre-heating zones, spray zones and drying zones whereby spraying can take place from below in the form of a bottom spray. The dry, coated particles are continuously extracted.

C.) Tangential spray coating (Rotor pellet coating):

Tangential spray is ideal for coatings with high solid content. The product is set into a spiral motion by means of a rotating base plate, which has air fed into the powder bed at its edge. The spray nozzle is arranged tangentially to the rotor disc and also sprays concurrently into the powder bed. Very thick film layers can be applied by means of the rotor method.

EQUIPMENT DESCRIPTION:

A GPCG (Glatt-Powder-Coater-Granulator) from Glatt are used for processes those are uniform, reproducible and gentle on the product using fluid bed techniques.

It offers advantages such as:

- **All in one:** From demanding powder coating to simple drying. Whether granulation/ agglomeration, particle coating or pelletizing. Whether spraying from above (Top Spray), from below (Bottom Spray) or from the side (Tangential Spray): simply anything is possible with a GPCG. In this way, you are just as flexible as your machine.
- **Unique technology:** All GPCGs provide an optimum ratio of air volume flow to quantity of product used. The conical pressure relief zone and the resulting reduced flow speed allow even very fine products to be processed. At the center of granulation is the legendary Glatt single pipe nozzle. This combines outstanding spray behavior with optimum media delivery and easy cleaning.
- **Simple handling:** Both horizontal and vertical product flow can be realized with all sizes. Contained feed

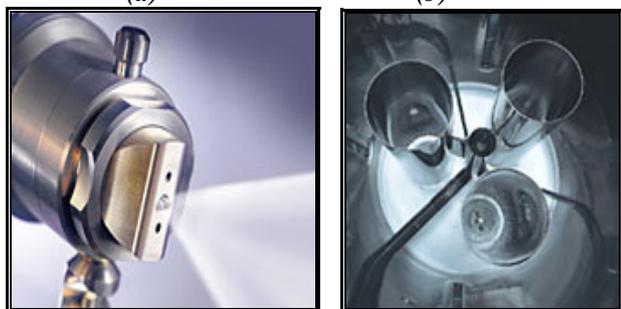
systems using gravity or suction can be provided. The container is emptied by rotating it in the moving carriage (up to certain batch sizes). Dust-free tipping and feeding into the container on one lifting column. Emptying can likewise be carried out from the side by means of suction or by gravity or - as the fastest and most effective method of all - vertically with the unique Glatt rotating bottom.

- **Innovative ABC-technology:** The unique ABC-technology (Anti-Bearding-Cap) allows spraying without bearding. The perfect supplement to the ABC-technology: The unique nano-coating to the nozzle prevents the deposit of coating material on the nozzle cap.
 - No process downtime due to cleaning of the nozzle
 - No blocked liquid inserts
 - No interference of spray pattern



(a)

(b)



(c)

(d)



(e)

Figure No-11: (a) & (b) GLATT GPCG equipment, (c) ABC technology nozzle, (d) Glatt HS Wurster® column technology, (e) Glatt rotating bottom

PHARMACEUTICAL APPLICATIONS²⁶:

The process of FBP is used to produce a wide variety of engineered, controlled release drugs. These solid dosage forms are mostly in the form of tablets or capsules containing high levels of an Active Pharmaceutical Ingredient (API). Product characteristics include:

- Dense pellets
- Smooth coatable pellets
- Narrow particle size distributions, and
- High yield and flow ability.

Important pharmaceutical applications include:

- Controlled release pellets for encapsulations
- Sustained release pellets / Delayed release enteric coated pellets
- Multi-particulate systems
- Multi-unit erosion matrix pellets
- Pellets for special tableting applications
- Immediate release pellets for sachets

CONCLUSION:

Multi-Unit particulate drug delivery systems are mainly oral dosage forms consisting of a multiplicity of small discrete units, each exhibiting some desired characteristics. In these systems, the dosage of the drug substances is divided on a plurality of subunit, typically consisting of thousands of spherical particles with diameter of 0.05-2.00mm. The palletized product can freely disperse in the gastrointestinal tract as a subunit, thus maximizing drug absorption and reducing peak plasma fluctuation. Consequently, potential side effects can be minimized without impairing drug bioavailability. Local irritation derived from high local concentration of a drug from a single unit dose, can be avoided. They reduce variation in gastric emptying rate and overall transit times. It reduced the risk of dose dumping i.e. failure of system leading to immediate release of the drug. The palletized products can improve the safety and efficacy of the active agent.. It is helpful in achieving unique release pattern and Simultaneous administration of two or more incompatible drugs. It also offers combination of pellets of different release rates of same drug in single dosage form with reproducibility and robustness. Multi unit particulates system (MUPS) improves patient comfort and compliance.

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