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## **AN OVERVIEW ON MULTI UNIT PELLET DRUG DELIVERY SYSTEM**

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### **ABSTRACT**

At present time pharmaceutical research and development showing its interest on drug delivery which enhances therapeutic action while minimizing side effect. Use of multi-particulate is the gift of that research which achieves delayed or controlled release with low risk of dose dumping, flexibility of blending to attain different release pattern as well as reproducible and short gastric residence time. Pelletization is a novel approach for the formation of spherical beads or pellets from fine powder or blend in order to develop site specific drug delivery system. Different techniques of pelletization such as suspension/solution layering, extrusion and spheronisation, cryopelletization etc. can be used for the formation of multi particulate drug delivery system. In order to provide extended or delayed release formulation, thus extending the frontier of future pharmaceutical development.

### **Keywords:**

Multi particulate drug  
delivery system,  
Pelletization Technologies

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## INTRODUCTION

MUPS is an abbreviation for Multiple-Unit Pellet System. However, from pharmaceutical industry and research perspective, the term in general refers to MUPS compacted into tablets. Thus, the resulting tablets prepared by compaction of modified release coated pellets are called as MUPS. Traditionally, the word “Pellet” has been used to describe a variety of systematically produced, geometrically defined agglomerates obtained from diverse starting materials utilizing different processing conditions. 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 pellets. Pellets range in size, typically, between 0.5 – 1.5 mm, though other sizes could be prepared. 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 the development scientist with a 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 intra-patient variability. 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 spheronization and solution or suspension layering, and powder layering. Other processes with limited application in the development of pharmaceutical palletized products include globulation, balling, and compression.

### **HISTORICAL DEVELOPMENT**

A major breakthrough occurred in 1949 when a pharmaceutical scientist SmithKline and French (SKF) realized the potential application of candy seeds in sustained release preparation and embarked on the development of tiny drug pellets that could be loaded in capsule. In 1964, a new pelletization technique that provided sustained release pellets ranging in size between 0.25 – 2.0 mm was patented by SKF at the same time marumerizer or spheronizer was commercially introduced. The new machine was developed in Japan and could produce large quantity of spherical pellets in short time. The marumerizer and variation of it were subsequently patent in USA. Direct pharmaceutical application of the process for the development of pellets was first published in literature in the early 1970 and the process has been the subject of intensive research ever since. Although pellets have been used in the pharmaceutical industries for more than 4 decades, it has only been since the late 1970s, with the advent of controlled release technology, that the advantages of pellets over single – unit dosage forms have been realized.

### **ADVANTAGES OF PELLETS**

Pellets offer more sophisticated drug-delivery systems as they provide greater advantages over other single unit drug- delivery systems.

a) **Process Advantages:** As subunits various kinds of particles with defined less-porous surface, spherical shape, low surface area to volume ratio are suitable for flexible and uniform drug - polymer coating.

b) **Formulation Advantages:** Pellets offer greater flexibility in the design and development of active ingredient into oral dosage forms like tablets, capsules and suspensions with significant therapeutic advantages over single units . The functional coating usually being applied in a fluid bed coating process provides each subunit with the characteristic drug release properties. Controlled-release, gastro-resistant, sustained-release or site-specific drug delivery finds a greater advantage of drugs formulated as coated pellets that can be filled into capsules or compressed into tablets. They can be divided into desired dose strengths without formulation or process changes, and can also be blended to deliver even incompatible

bioactive agents simultaneously or particles with different release profiles at the same site or at different sites within the gastrointestinal tract. The safety and efficacy of the formulation is higher than that of other dosage forms 6.

c) **Therapeutic Advantages:** When administered orally, pellets pass the pylorus even in the closed state and disperse freely throughout the gastro-intestinal tract and maximize the drug absorption; minimize local irritation of the gastro-intestinal mucosa by certain irritant drugs because of the available drug quantity in a single pellet is considerably small; provides less risk of dose dumping; improves safety and efficacy of a drug; reduce peak plasma fluctuations and minimize potential side effects with improved drug bioavailability offers reduced variation in gastric emptying rate and transit time which is less dependent on the state of nutrition; reduce inter and intra patient variability more suitable for fabrication of formulations with acid-sensitive drugs like Erythromycin. As the advantages of pellets over single units became clear, the pharmaceutical industry as a whole started to devote resources to conduct research in pelletization technology, whenever possible, acquire advanced equipment suitable for the manufacture of pellets.

#### **DISADVANTAGES**

In accordance with single units, the volume per dose is high because of its high bulk density. Since specific surface area per dose is higher, more amount of coating should be given. Preparation of pellets is a complicated and time consuming process. In spite of these facts, predominance of advantages with regard to patient compliance, safety and efficacy; pelletization technology is gaining demand in pharmaceutical product manufacturing.

#### **IDEAL CHARACTERISTICS OF PELLETS:**

*Core or uncoated pellets* are of uniform spherical shape and smooth surface with improved flow characteristics; high physical strength and integrity; good hardness and low friability for ease and superior properties of coating. They have a narrow particle size between 500  $\mu\text{m}$  to 1000  $\mu\text{m}$ , a prerequisite for efficient coating, prevents segregation during capsule-filling and compression. The high bulk density of pellets plays an important role in achieving content and weight uniformity; reproducible packing of beds and columns. Whereas functional or non-functional *coated pellets* in addition to the above properties; contain as much as possible of the active ingredient to keep the size of the final dosage form within reasonable limits, uniform coating thickness and desired drug release characteristics. Perfect pellets and layers of coating are depicted in Figure 1.

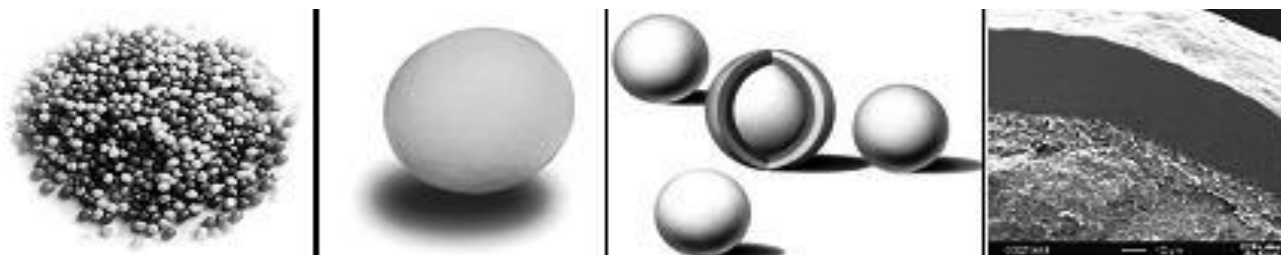


Figure 1- Perfect pellets and layers of coating are depicted

## DESIRABLE PROPERTIES OF PELLETS:

### 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

## METHODS OF PELLETTIZATION

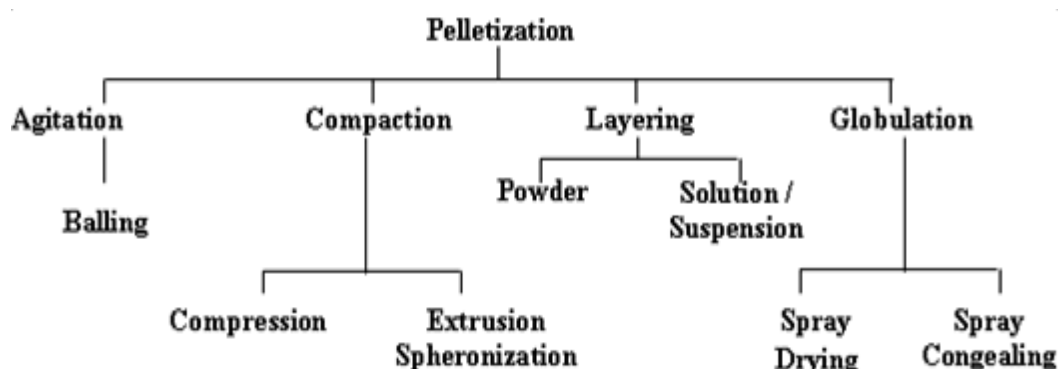


Figure 2: Different Pelletization Techniques

### 1. Powder Layering technique

Layering processes are probably the most well controlled and straight forward pelletization techniques. The layering process comprises the deposition of successive layers of drug entities from solution, suspension or dry powder on nuclei which may be crystals or granules

of the same material or inert starter seeds. They are classified into two categories: solution/suspension layering and powder layering.

In solution/suspension layering drug particles and other components are dissolved or suspended in the application medium. The droplets impinge on the started seed or cores and spread evenly as the solution or suspension is sprayed on the cores. Followed by drying phase allows dissolved material to crystallize and form solid bridges between the cores and initial layer of the drug substance and among the successive layers of drug substance or polymer. Continue this process until the desired layers of drug or polymer formed.

In powder layering the binding liquid helps to form successive layers of dry powder of drug and other components on starting cores. In this technique the drug particles are bound to the starter seeds and subsequently to the forming pellets with the help of liquid bridges originated from the sprayed binding liquid. These liquid bridges are eventually replaced by solid bridges derived either from a binder in the liquid medium or from any material. Successive layering of the drug and binder solution continues until the desired pellet size is reached. The most commonly used equipments for layering are the standard or conventional coating pans and fluidized bed granulators (bottom spray, top spray and tangential spray).

Conventional pan coaters have been used from the very beginning of the history of drug layering pelletisation. From the economic point of view, however, use of conventional pan coaters is not very reasonable due to the higher labour costs and time consumption, and lower yield. An important disadvantage of pan coaters is the shortage of process control. More recently modified forms of pan coaters have been developed, which resolves many of the drawbacks related to the old system .

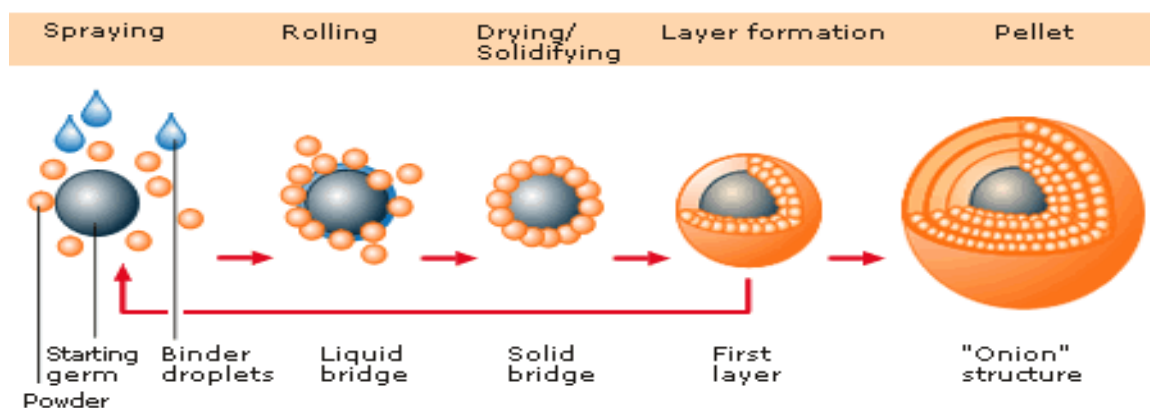


Fig. 3: Principle of Powder layering

### Suspension / Solution layering technique

This technique involves the deposition of successive layer of solution and /or suspension of drug substances and binders on starter seeds which may be inert material or crystal of granules of the same drug. In this technique drug particles and others component are dissolved or suspended in the application medium. The droplets impinge on the starter seeds or cores and spread evenly as the solution or suspension is sprayed on the cores. Followed by drying phase allows dissolved material to crystallize and form solid bridges between the cores and initial layer of the drug substances and among the successive layer of drug substances or polymer. Continue this process until the desired layer of drug or polymer formed. Consequently conventional coating press, fluidized bed centrifugal granulator or wurster coater has been used successfully to manufacture pellets.

The most common configuration for bottom spray coating is known as the Wurster system. In this study solution/ layering of neutral pellets has been conducted applying novel fluidized bed technology from .This technology claims to improve the product movement in defined direction in all the equipment by the Disk jet gas distribution plate. Furthermore, a 3 component spray nozzle is used in order to improve the film formation on the pellets due to constant and reproducible drop size distribution. Accessibility of clogged nozzles without stopping and interrupting the process makes the equipment advantageous in respect to Wurster system. Hüettlin's three component nozzle is an air nozzle with an additional channel through which a second gas or component can be introduced to create a special microclimate around the nozzle which prevents excessive spray drying or clogging of the nozzle. Such microclimates near nozzle apertures are very useful when a film former with a relatively high minimum film-forming temperature (MFT) issued. The MFT of aqueous shellac suspensions, lies between 35 and 55°C, depending on the plasticizer selected.

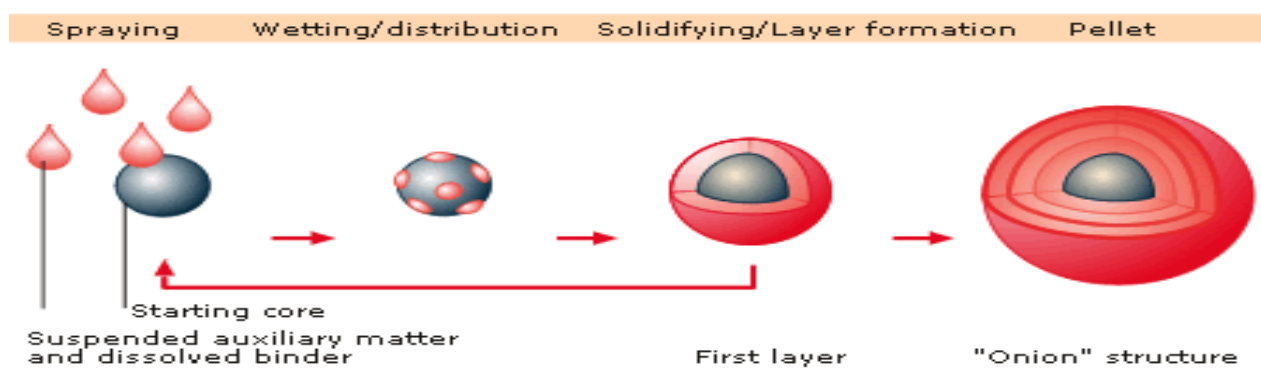


Fig. 4: Principle of solution / suspension layering

## **Extrusion and Spheronization**

Extrusion spheronization was developed in the early 1960s as a pelletization technique. The extrusion-spheronization process is commonly used in the pharmaceutical industry to make uniformly sized spheroids. It is especially useful for making dense granules with high drug loading for controlled-release oral solid dosage forms with a minimum amount of excipients. Extrusion spheronization is a multi-step compaction process comprising of following steps.

### **I. Dry mixing**

Dry mixing of all ingredients is done to get homogeneous powder dispersion or mixer using different types of mixers like twin shell blender, high shear mixer, tumbler mixer and planetary mixer.

### **II. Wet Massing**

This process of powder dispersion is done to produce a sufficient plastic mass for Extrusion. It is similar to the wet granulation method but the granulation and point is determined by the behaviour of the wetted mass during the extrusion operation. The most commonly used granulator is Planetary mixer or sigma blade mixer or high shear mixer and Horbat mixer.

### **III. Extrusion**

This is a method of applying pressure to a mass until it flows through an opening and determine two dimension of an agglomeration of particles .This operation is the major contributing factor in the final particle size of the pellets. In this process the wetted mass is passed through the extruder to form rod shaped particles of uniform diameter. The extrudate must have enough plasticity to deform but not so much that the extrudate particles adheres to other particles when rolled during spheronization process. The granulation solvent serves as the binding agent to form the granules and as the lubricating during the extrusion operation.

### **IV. Spheronization**

This process is used to round up these rod shaped particles in to spherical particle in to spherical particle with narrow size distribution. The instrument used is called Spheronizer where the extrudate is rotated at higher speed by friction plate that breaks the rod shaped particles in to smaller particles and rounded them to form spheres.

### **V. Drying**

In order to get desired moisture content in pellets a drying stage is required the pellets are dried at room temperature or at a elevated temperature in a tray dryer or in a fluidized bed dryer, according to DI.Wilsons et. Al, 2006 freeze drying method retains the shape and size and the granules whereas the oven drying produce rough granules.



## **VI. Screening**

It is necessary to achieve the desired size distribution and for this purpose sieves are used. Based on the type of feed mechanism and to transfer the mass towards the die, Variety of extruders is used in the above mentioned technique. These extruders are classified in to following classes

### **i. Screw fed extruders**

The screw rotates along the horizontal axis and hence transports the material horizontally; They may be of two types:

- a) **Axial screw extruders**- These have a die plate that is positioned axially, consist of a feeding zone, a compression zone, and an extrusion zone.
- b) **Radial screw extruders**-The transport zone is short, and the material is extruded radially through screens mounted around the horizontal axis of the screws.

### **ii. Gravity-fed extruders:**

These are of two types, which differ primarily in the design of the two counter-rotating cylinders.

**The Rotary Cylinder** - One of the

- a) two counter-rotating cylinders is hollow and perforated, whereas the other cylinder is solid and acts as a pressure roller.
- b) Rotary-Gear Extruder: There are two hollow counter-rotating gear cylinders with counter bored holes

### **iii. Ram Extruders:**

This is probably the oldest type of extruders; a piston displaces and forces the material through a die at the end. These extruders are preferentially used in the development phase, because they can also measure the rheological properties of formulations.

### **iv. Marumerizer:**

It consists of a two parts:

- a) Static cylinder or stator
- b) Rotating friction plate.

A typical friction plate has a crosshatch pattern, where the grooves intersect at a 900 angle. The rotational speed of the friction plate is variable and ranges from 100 to 2000 rpm; depending on the diameter of the unit. Spheronizer friction plate with a cross hatch pattern.

#### 4. Spherical Agglomeration

Spherical agglomeration, or balling, is a pelletization process in which powders, on addition of an appropriate quantity of liquid or when subjected to high temperatures, are converted to spherical particles by a continuous rolling or tumbling action. Spherical agglomeration can be divided into two categories— Liquid-induced and Melt-induced agglomerations.

**Liquid-induced agglomeration:** During liquid-induced agglomeration, liquid is added to the powder before or during the agitation step. As powders come in contact with a liquid phase, they form agglomerates or nuclei, which initially are bound together by liquid bridges. These are subsequently replaced by solid bridges, which are derived from the hardening binder or any other dissolved material within the liquid phase. The nuclei formed collide with other adjacent nuclei and coalesce to form larger nuclei or pellets. At this point, coalescence is replaced by layering, whereby small particles adhere on much larger particles and increase the size of the latter until pelletization is completed.

**Melt-induced agglomeration:** Melt-induced agglomeration processes are similar to liquid-induced processes except that the binding material is a melt. Therefore, the pellets are formed with the help of congealed material without having to go through the formation of solvent-based liquid bridges. If the surface moisture is not optimum, some particles may undergo nucleation and coalescence at different rates and form different sizes of nuclei admixed with the larger pellets. As a result, spherical agglomeration tends to produce pellets with a wide particle size distribution.

**5. Spray Drying And Spray Congealing** Spray Drying and Spray Congealing, also known as globulation process, involve atomization of hot melts, solutions, or suspensions to generate spherical particles or pellets. The droplet size in both processes is kept small to maximize the rate of evaporation or congealing, and consequently the particle size of the pellets produced is usually very small.

**Spray Drying:** The drug entities in solution or suspension are sprayed, with or without excipients, into a hot air stream to generate dry and highly spherical particles. As the atomized droplets come in contact with hot air, evaporation of the application medium is initiated. This drying process continues through a series of stages whereby the viscosity of the droplets constantly increases until finally almost the entire application medium is driven off and solid particles are formed. Generally, spray-dried pellets tend to be porous.

**Spray Congealing:** This process consists of suspending the particles in a molten coating material and pumping the resultant slurry into a spray dryer in which cold air is circulated. The slurry droplets congeal on contact with the air. The coating agents normally employed is low melting materials such as waxes. The congealing process require higher ratio of coating agents to active material than does the spray drying, because only the molten coating agent constitutes the liquid phase.

**6. Melt Spheronization :** Melt Spheronization is a process whereby a drug substance and excipients are converted into a molten or semi molten state and subsequently shaped using appropriate equipment to provide solid spheres or pellets. The drug substance is first blended with the appropriate pharmaceutical excipients, such as polymers and waxes, and extruded at a predetermined temperature. The extrusion temperature must be high enough to melt at least one or more of the formulation components. The extrudate is cut into uniform cylindrical segments with a cutter. The segments are spheronized in a jacketed Spheronizer to generate uniformly sized pellets.

**7. Cryopelletization:** Cryopelletization is a process whereby droplets of a liquid formulation are converted into solid spherical particles or pellets by using liquid nitrogen as the fixing medium. The technology, which was initially developed for lyophilization of viscous bacterial suspensions, can be used to produce drug-loaded pellets in liquid nitrogen at -160°C. The procedure permits instantaneous and uniform freezing of the processed material owing to the rapid heat transfer that occurs between the droplets and liquid nitrogen. The amount of liquid nitrogen required for manufacturing a given quantity depends on the solids content and temperature of the solution or suspension being processed. The equipment consists of a container equipped with: Perforated Plates A Reservoir Conveyor belt with Transport baffles Storage Container The perforated plates generate droplets that fall and freeze instantaneously as they come in contact with the liquid nitrogen below. The frozen pellets are transported out of nitrogen bath into a storage container at -60°C before drying.

#### **CHARACTERIZATION OF PELLETS**

Pellets are evaluated for certain quality measures, which reflect the suitability and endurance of material during various operations like filling, transportation and handling.

The most common physical characteristics evaluated are:

1. **Pellet size and size distribution**, determined by sieve analysis which is simple and economical; microscopy methods like Scanning electron microscopy (SEM) and laser

diffraction. This characteristic feature of pellets affects coating and rate of drug release. Another method to determine the size of pellets is estimation of fret diameter obtained from four different angles. In all cases, the size data was best fitted by a normal distribution.

2. **Shape** influences flow of pellets during coating, filling into capsules and dies. The most common method of analysis is by ring gap analyzer; scanning electron microscopy (SEM) for qualitative and quantitative analysis. Visual inspection of pellets by microscope and stereomicroscope also determine shape of pellets.

Another method to determine spherical shape (sphericity) is by taking optimum size pellets, stained with dye solution in a petri dish and dried on a hot air oven. Each pellet is recorded for two dimensional image i.e., length and width using camera lucida fixed to an optical microscope and circularity factor(s) was calculated using the equation  $S = P^2/(12.56 * A)$ ; where A is the area (cm<sup>2</sup>) and P is the perimeter(cm) of circular tracing. Circularity, another parameter to determine shape is calculated as  $4\pi A/P^2$ , where A is projection area and P is projection perimeter.

3. **Surface area** has an effect on drug release and results in batch to batch variability. To ensure the production of consistent shape pellets, surface area is analyzed by particle size distribution, gas adsorption (BET method- Brunauer, Emmett & Teller) and air permeability method. *Surface roughness* is analyzed by fractal geometry of particle obtained by microscopy with image analysis and SEM. This property influences flow and packing of pellets.
4. **Porosity** influences rate of drug release from the pellets by affecting the capillary action of the dissolved drug; analysed qualitatively by scanning electron microscopy and quantitatively by mercury porosimetry. The sample is introduced into the chamber, degassed, and then completely covered with mercury. Pressure is applied and the volume of mercury that penetrates into the pores is recorded. Pore radius is given by Washburn equation:

$$R = 2 \gamma \cos \theta / P;$$

Where  $\gamma = 480 \text{ ergs/cm}^2$ ,  $\theta = 140^\circ$ , r = pore radius, p = mercury-intrusion pressure.

5. **Bulk Density and tap density** affects potency of finished product, produces segregation during mixing and leads batch to batch variation. The bulk density was calculated by the ratio of weight to the occupied volume and is measured by automated tapper or a pycnometer.
6. **True density** indicates extent of densification or compactness. Air- comparison pycnometer, helium pycnometer or solvent displacement method are different methods of analysis.

7. **Friability and hardness** helps to withstand subsequent coating and high attrition during coating. Roche friabilator, Erweka friabilator, Pharma Test friabilator are different equipment used. The % friability of pellets should be less than 0.08% . Relative hardness of the pellets is determined by using Kaul pellet hardness tester.
8. **Tensile strength** is determined by using tensile apparatus with a 5 kg load cell. The radius of pellets is recorded and these pellets were strained continuously until failure occurs. Further load is recorded. The tensile strength is calculated by applying the value for the failure load (F) and the radius of the pellets (R) by the formula  $\sigma f(s) = 0.4F / \pi R^2$ .
9. **Flowability** is determined by angle of repose. If  $\Theta < 30^\circ$ -excellent Flowability and  $\Theta > 40^\circ$ -poor flow ability.
10. **In-vitro Dissolution Testing** most commonly is by USP I (basket) and USP II (paddle) apparatus to study the release pattern of the coated pellets.

### PHARMACEUTICAL APPLICATIONS

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

### MARKETED TECHNOLOGIES

Presently marketed multiparticulate drug delivery systems are listed in Table 1. In 1998, Elan Drug Technologies got FDA approval for their chronotherapeutic technology, CODAS® as multiparticulate pH dependent system, for delivery of Verapamil HCl (Verelan® PM) in form of extended release capsule This was followed by the FDA approval of DIFFUCAPS®, a

multiparticulate technology by Reliant Pharmaceuticals LLC, for chronotherapeutic delivery of a combination of two drugs, Verapamil HCl and Propranolol HCl, as an extended release tablet (Innopran®). But the biggest breakthrough in multiparticulate technology was achieved when MiddleBrook™ Pharmaceuticals, Inc. (earlier known as Advancis Pharmaceutical) got the green signal from FDA in 2008 for its proprietary, once-a-day pulsatile delivery technology called PULSYS™, which enables the delivery of antibiotic amoxicillin in regular concomitant pulses. MiddleBrook™ is developing a broad portfolio of drugs based on the novel biological finding that bacteria exposed to antibiotics in front-loaded, sequential bursts, or pulses, are killed more efficiently and effectively than those exposed to standard antibiotic treatment regimens. When an immediate release antibiotic is administered, bacteria respond to it by going into a dormant stage, while the administration of a pulsatile system in such a case is more effective because the regular release of increased pulses of antibiotic does not let the defense system of the bacteria to go into a dormant stage. By examining the resistance patterns of microorganisms and applying its improved technologies, MiddleBrook™ has redefined microbial infection treatment significantly improving drug efficacy, shortening length of therapy, and reducing the emergence of antibiotic resistance.

**Table 1: Marketed technologies of Multiparticulates drug delivery**

Technology	Proprietary name	Drug	Indication	Design parameters	Advantages
<b>CODAS®</b>	Verelan® PM XL release capsule	Verapamil HCl	Hypertension	Nonenteric releasecontrolling polymer(combination of water soluble and insoluble polymers) applied to drug loaded beads	Lag-time–4–5 h. Early morning peak plasma concentrations following bed time dosing. Rate of release is independent of pH, posture and food and gastrointestinal motility
<b>DIFFUCAPS®</b>	Innopran® XL tablet	Verapamil HCl, Propranolol HCl	Hypertension	Drug was layered on sugar bead, followed by a controlled release and delayed release coatings	Lag time–4–5 h Cmax-12–14 h after dosing trough levels after 24–27 h of dosing. The rate of release is independent of pH, posture and food and gastrointestinal motility
<b>PULSYS™</b>	Moxatag™ tablet	Amoxicillin	Infection	Consisting of three components: one Immediate release and two delayed release(by soluble and insoluble coatings)	More efficient killing of bacteria exposed to antibiotics in front-loaded, sequential bursts Reduces duration of therapy

## CONCLUSION

Formulation design and development is the most promising and impending face of innovative pharmaceutical technologies in the current epoch for exploring newer formulations with high-quality. Recent and advanced pelletizing technologies like melt agglomeration, hot melt extrusion, freeze pelletization, cryopelletization, minitables, CPS™, MicroPx™ and ProCell™ represent potential and efficient pathways not only in achieving better therapeutic and financial benefits but also product throughputs such as a small pellet size of < 500 µm, uniformity of particle size distribution, smooth particle surface, high density and high drug loading. In conclusion, these novel technologies due to their unique benefits, in particular are achieving a prominent role in new chemical entity and generic development.

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