AN OVERVIEW OF PELLETIZATION TECHNIQUES USED IN MULTIPARTICULATE DRUG DELIVERY SYSTEM

Samreen Mansoori*,1, Asish Dev2 and Saritadevi Gupta3

1,2 M.Pharm Student, Department of Pharmaceutics, Oriental College of Pharmacy, Sanpada, Navi Mumbai-400705, Maharashtra, India.

2 Assistant Professor, Department of Pharmaceutics, Oriental College of Pharmacy, Sanpada, Navi Mumbai-400705, Maharashtra, India.

ABSTRACT
Pharmaceutical research are increasingly focusing on new delivery systems which enhances desired therapeutic objective and therefore minimising side effects. The multiparticulate drug delivery systems are suitable for oral formulation to achieve controlled or delayed release. It has advantages like low dose dumping, flexibility of blending to attain different release pattern and for short gastric residence time. Therefore multiparticulate drug delivery system (MPDDS) provides opportunities in designing controlled and delayed release oral formulation. Pellets are defined as spherical/ semi-spherical, free flowing solid units with a narrow size distribution, typically in diameter between 0.5-2.0 mm. Pelletization technique is used to produce pellets. Pelletization techniques include Extrusion sponerization, layering, Cryopelletization, freeze pelleting, spray congealing, spray drying and compression. Extrusion sponerization is widely used technique due to high efficiency and fast and simple processing.

KEYWORDS: Multiparticulate system, Pellets, Pelletization, Extrusion-sponerization, Cryopelletization, Spray Congealing.

INTRODUCTION TO MPDDS
There is an advancement of the technologies in the pharmaceutical field, drug delivery systems has developed an increasing interest over the last few decades. Pharmaceutical research and development has started focusing on delivery systems which enhance desirable
therapeutic objectives while minimizing side effects.\textsuperscript{[1,2,3]} Multiparticulate drug delivery systems are oral dosage forms consisting of multiplicity of small discrete units, in which active substance is present as a number of independent subunits.\textsuperscript{[4]} It is based on subunits such as granules, beads, microspheres, pellets, spheroids and minitable. In MPDDS, drug substances are divided into number of subunits, typically consist of thousands of spherical particles having diameter of about 0.05-2.00 mm. To administer or to recommend total dose these subunits are compressed into a tablet or filled into a sachet or encapsulated.\textsuperscript{[5]} Multiparticulate dosage form has all the advantages of a single unit formulations and is devoid of the danger of alteration in drug release profile and formulation behaviour due to unit to unit variation, change in gastro luminal pH and enzyme population.\textsuperscript{[6]} Multiparticulate are less dependent on gastric empty time, resulting in less inter and intra-subject variability in gastrointestinal transit time. They are better distributed and less likely to cause local irritation.\textsuperscript{[7]} Recently much emphasis is being laid on the development of Multiparticulate dosage forms in preference to single unit systems because of their potential benefits such as increased bioavailability, reduced risk of systemic toxicity, reduced risk of local irritation and predictable gastric emptying.\textsuperscript{[8]}

Reasons for formulating a drug as a Multiparticulate system are 1) to facilitate disintegration in the stomach, or 2) to provide a convenient, fast disintegrating tablet that dissolves in water before swallowing which can aid compliance in older patients and children. It shows better reproducible pharmacokinetic behavior than conventional (monolithic) formulations. After disintegration which occurs within a few minutes often even within seconds, the individual subunit particles pass rapidly through the GI tract. If these subunits have diameters of less than 2mm, they are able to leave the stomach continuously, even if the pylorus is closed. These results in lower intra and inter individual variability in plasma levels and bioavailability. Drug safety may also be increased by using Multiparticulate dosage forms, particularly for modified release systems. For example, if the film coat of a single-unit (monolithic) enteric coated tablet is damaged, the complete dose will be released into the stomach where it may cause pain or ulceration or reduced efficacy, depending on the reason for choosing the protection of the enteric coating. Equally, if there is damage to the film coating of a monolithic tablet with a sustained release formulation, this can lead to “dose dumping” and result in dramatic side effects. By contrast, in multiparticulate formulation, the release characteristics are incorporated into every single subunit and any damage will only
affects the release behavior of the subunit involved, which represents a small part of the total dose, reducing the likelihood of safety problems.\cite{9}

**TYPES OF MULTIPARICULATE SYSTEM**

- **Matrix Coated Pellets**
  In matrix systems, drug solution or dispersion is granulated with excipients to form pellets or sprayed onto pellets in order to achieve extended drug release. The drug homogeneously distributed within the polymer is dissolved, dispersed or dissolved and dispersed.

  **Advantages:** Easy manufacture, low cost, lower risk of dose dumping, improvement of aqueous drug solubility.

  **Disadvantages:** fast initial release and incomplete release in a defined time.\cite{10}

- **Reservoir Coated Systems**
  Such systems consist of a drug layered core surrounded by a polymer. The mechanism of controlling the drug release from reservoir type systems is often complex and depends on coating type, thickness, drug type and core type.

  **Advantage:** High drug load capacity and obtaining variable release profile by type of polymeric membrane.\cite{10}

---

**MECHANISM OF DRUG RELEASE FROM MULTI-PARTICULATES\cite{11,12,13}**

<table>
<thead>
<tr>
<th>Diffusion</th>
<th>Erosion</th>
<th>Osmosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>On contact with aqueous fluids in the gastrointestinal tract (GIT), water diffuses into the interior of the particle. Drug dissolution occurs and the drug solutions diffuse across the release coat to the exterior.</td>
<td>Some coatings can be designed to erode gradually with time, thereby releasing the drug contained within the particle.</td>
<td>In allowing water to enter under the right circumstances, an osmotic pressure can be built up within the interior of the particle. The drug is forced out of the particle into the exterior through the coating.</td>
</tr>
</tbody>
</table>
INTRODUCTION TO PELLETS

Pellets are spherical, free-flowing granules with a narrow size distribution, typically varying between 500 and 1500 μm in size.\(^{[14]}\) They are formed as a result of a pelletization process which is an agglomeration process that converts fine powders or granules of bulk drugs and excipients into small, free-flowing, spherical or semi-spherical units.\(^{[15,16]}\) After being processed, pellets are usually filled into hard gelatin capsules or compressed into tablets. They can be formulated as immediate release dosage form or in sustain drug release over a long duration time or can be coated also to deliver a drug to a specific site of action in the gastrointestinal tract. They can be divided into desired dose strengths without formulation or process changes and also be blended to deliver incompatible bioactive agents simultaneously or particles with different release profiles at the same site or at different sites within gastrointestinal tract.

Pellets provide high degree of flexibility due to free-flowing characteristic. So can be packed easily without any difficulties. The spherical shape and a low surface area to volume ratio of pellets made uniform film coating. Pellets eliminate the dose dumping effect, which gives smoother plasma concentration profile and gradual absorption of drug than tablet, which further decrease the adverse effect of drugs.

NEED OF PELLETS / RATIONALE BEHIND DESIGNING THE MPDDS

There are many reasons for designing and delivering drug as a Multiparticulate system e.g.

i. To facilitate disintegration in the stomach. Shows better reproducible pharmacokinetic behaviour then conventional (monolithic) formulations.

ii. After disintegration, the individual subunit particles pass rapidly through the g.i.t. If these subunits have diameter of less than 2 mm, they are able to leave the stomach continuously, even if the pylorus is closed. These results in lower intra and inter individual variability in plasma levels and bioavailability.

iii. Drug safety may also increased by using Multiparticulate dosage forms.\(^{[17,18]}\)

Advantages\(^{[19,20,21]}\)

- They can be divided in to desired dosage strength without process or formulation changes.
- Improve appearance of product.
- Pellets are of small size and have good flowability compare to powder form.
• Ease of handling, such as filling into capsules
• Incorporation of incompatible ingredients in a single dosage form
• Different release profiles at different sites in the Gastrointestinal tract
• Protection against degradation of active ingredients by oxidation or moisture by providing film coating
• High degree of patient acceptance when filled in capsules due to their elegance as compared to tablets
• Ideal shape for application of film coatings due to low surface to volume ratio
• High drug loading capacity without producing large particles
• Pellets are less susceptible to dose dumping effect and decrease the side effect
• Due to their small size reduction in gastrointestinal irritation compare to tablet
• Pellets reduce variation in gastric emptying rate and intestinal transit time thus reduce inter and intra patient variability
• Less sensitive to food ingestion compared to single unit dosage forms because the small pellets can pass the pylorus even in closed state. This leads to reduced variability in drug plasma absorption profiles between subjects and within the same patient, as a result of even distribution in GI tract.
• They can be formulated as sustained, controlled, or site-specific delivery of the drug from coated pellets.
• Density increase can be achieved as bulk density of powder is increased by spheronization process. This can improve the process and packaging
• Useful in case of difficulty in swallowing and dysphagia like in case of children and aged people.

Disadvantages\[12, 19, 20, 21, 22]\n• Pellets filling involve capsule filling which can increase the costs
• Tableting of pellets destroy film coating on the pellets.
• The size of the pellets may vary formulation to formulation but usually is in range of 0.05 mm and 2 mm.
• Low drug loading.
• Proportionally higher need for excipients.
• Lack of manufacturing reproducibility and efficacy.
• Large number of process variables.
• Multiple formulation steps.
• Need of advanced technology.
• Trained/skilled personal needed for manufacturing.

Desirable Properties of Pellets\textsuperscript{[23]}  

1. For Uncoated pellets  
• Uniform spherical size  
• Narrow particle size distribution  
• Good flow property  
• Low friability  
• Even surface  
• Low dust formation  
• Reproducible packing  
• Ease of coating  

2. For Coated pellets  
• Maintain all above properties  
• Desirable drug release characteristics.

PELLETIZATION  
Pelletization can be defined as an agglomeration (size-enlargement) process that converts fine powders or particles 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.\textsuperscript{[24,25]}

ADVANTAGES OF PELLETIZATION\textsuperscript{[26,27,28]}  
• Pelletization produces spheroids with high loading capacity of active ingredient without producing extensively large particles.  
• Pellets exhibit better roundness than the commercial nonpareil seeds and have excellent flow and packing properties by the pelletization technique.  
• Particles less than 2-3 mm rapidly pass the pylorus regardless of the filling level of the stomach or the size and density of chyme. Also, GI irritations are limited spread as the particles spread in the intestine these sizes are achieved by pelletization.
NEED / PURPOSE OF PELLETIZATION\textsuperscript{[26,28]}

- To improve flow, dispersion, solubility, stability and compaction.
- To have less variation in transit time through the GIT than single-unit dosage forms like tablets prepared by granulation and compression.
- To produce pellets of uniform size with high drug loading capacity.
- To prevent segregation and dust.
- Pellets can be compressed into tablets called “pelltabs” and can also be filled into capsules.

FACTORS AFFECTING PELLETIZATION\textsuperscript{[29,30]}

\begin{itemize}
  \item Moisture content:- High moisture contents lead to agglomeration of pellets during the process of spheronization due to excess of water in the surface of pellets and low moisture content lead to generation of fines with large variation in size distribution.
  \item Rheological characteristics:-The Rheological condition of the wet mass determines the flow ability in extruder and further spheronization operation. So, wet mass variation in rheology make improper and non uniform extrusion.
  \item Solubility of excipients and Drug in granulating fluid:-A soluble drug get dissolve in a granulating liquid. Thus increasing the volume of liquid phase lead to over wetting of system of agglomeration of pellet sand increase in wetting liquid increases plasticity but induces sticky mass.
  \item Composition of Granulating Fluid: Besides water, alcohol, water / alcohol mixture, Ethyl Ether, Dilute Acetic Acid, Isopropyl alcohol is also used as a granulating liquid. A minimum of 5\% of granulation liquid have to be water in order to produce pellets of good quality.
  \item Physical Properties of Starting Material:-the parameters such as content, composition, different grades of starting materials, type of filler and its particle size have the effect on the pelletization process. The swelling property of material used in pelletization technique decides the release rate of the drug in pellets.
  \item Speed of the Spheronizer:-The speed of the Spheronizer affects the size, hardness, sphericity and density of pellets, high speed gives high sphericity, lower friability, smooth surface and higher crushing strength.
  \item Drying technique and drying temperature: Variation in pellets size, shape and flow will lead to difference in physicochemical properties of final dosage form like weight variation, improper filling etc, which will further affect the therapeutic efficiency of the
delivery system. Wider particle size distribution may lead to variation in the dose of drug delivery.

✓ Extrusion Screen: The quality of the extrudate/pellets is greatly influenced by the characteristics of the orifice of the screen. An increase in orifice dimension resulted in increased mean pellet size.

TECHNIQUES AND EQUIPMENTS OF PELLETIZATION

1. Drug Layering
It includes 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.

In solution/suspension layering, drug particles are dissolved or suspended in the binding liquid. The droplets is sprayed immediately on the starter seeds and spread evenly on the surface, provided the drying conditions and fluid dynamics are favourable. This is followed by a drying phase that renders dissolved materials to precipitate and form solid bridges that would hold the formulation components together as successive layers on the starter seeds. The process is continued until the desired quantity of drug substance is layered and the target potency of the pellets are achieved. In this, the particle population remains same, but size and total mass of system increases with time.
In powder drug layering, a binder solution is first sprayed onto previously prepared inert seeds, followed by the addition of powder. In this, the successive layers of powder and excipients are added on starting seeds by the help of binding liquid. The small particles and nuclei adhere to each other by means of capillary forces developed in liquid medium. The process continues till the desired pellet size is obtained. The major problem is formation of fines due to interparticulate and wall to particle friction at the end of process which can be avoided by spraying the application medium at the end of process. If the powder addition rate is high, dust generation may occur and if the liquid addition rate is high, over wetting of the pellets may take place and neither the quality nor the yield of the product can be maximized.

**Figure 3:** solution/suspension layering

**Figure 4:** powder layering
The most commonly used equipments for layering are coating pans (standard or conventional) and Fluidized bed granulators-bottom spray (wurster coating and continuous fluid bed), top spray and Tangential spray (rotor pellet coating).\textsuperscript{[33,36]}

![Different Spray Patterns in Fluidized Bed Processor: (A) Bottom Spray, (B) Top spray, (C) Tangential spray\textsuperscript{[20]}](image)

2. Extrusion-Spheronization\textsuperscript{[14,28,31]}

It produces pellets with high loading capacity of active ingredient without producing extensively larger particles and particles of uniform size distribution with good flow properties. Steps involved in Extrusion-spheronization-

1. Dry Mixing-Dry mixing of ingredients is done to achieve homogenous powder dispersion using Twin shell blender, planetary mixer, High speed mixer and Tumbler mixer.
2. Wet massing-It is done to produce a sufficient plastic mass for extrusion, by employing normal equipment and process as employed in wet granulation for compaction.
3. Extrusion-It produces rod shaped particles of uniform diameter from wet mass. The wet mass is forced through dies and shaped into small cylindrical particles with uniform diameter. Such shaping of wet mass into long rods, commonly termed ‘extrudate’.

Types of extruder: Screw feed extruder
Gravity feed extruder
Piston feed extruder (Ram)
4. Spheronization-It is also known as ‘Merumerizer’ consists of a static cylinder and a rotating friction plate where the extrudate is broken up into smaller cylinders with a
length equal to their diameter and these plastic cylinders are rounded due to frictional forces. The instrument used is called Spheronizer where the extrudate is rotated at higher speed by friction plate that breaks the rod shaped particles into smaller particles and rounded them to form spheres. The spheronization operation has been divided into 3 stages:

- Breaking of extrudate
- Agglomeration of broken segments
- Smoothing of particles.

The smoothing stage creates spherical pellets by generating rotational motion of each granule about its axis in constantly changing planes. The friction plate is responsible for providing the energy necessary to produce pellets and for controlling the extent of pellet growth.

![Figure 6: Process of Extrusion-Spheronization](image)

5. Drying-A drying stage is required in order to achieve the desired moisture content. An increase in drying rate gives more porous pellets due to decrease pellet densification during drying process.

6. Screening: It is necessary to achieve the desired size distribution, and for this purpose sieves are used.

**Advantages**

1. Optimum Flow and Handling Characteristics:- The flow characteristics of spheres make them suitable for transportation by most systems found in the pharmaceutical industry, including vacuum transfer.

2. More Reproducible Packing Into Small Containers: - a) The packing of small sphere into small containers, such as hard gelatin capsules, or larger packages is much more convenient.
than other dry forms such as powders or granules. b) Eliminate quality problems with variable dosage due to packaging problems with powder.

3. Minimum Surface Area/Volume Ratio: Spheres provide the lowest surface area to volume ratio and thus pharmaceutical compounds can be coated with a minimum of coating material important for effective release of some drugs.

4. Optimum Shape for Coating and for Controlled Release: a) Coating can provide controlled, targeted release at different locations within the body. b) Spheres are a dense material that can easily be coated with a minimum of coating material. Since, smooth spheres are ideal for coating. Hence, minimum coating material and coating time is required.

5. Easy mixing of non-compatible products: Spherical particles are easily mixed.

6. Elimination of Dust: a) The elimination of dust removes the hazards and problems associated with material in this form. b) Contamination is reduced. c) The amount of fines and dust will be reduced during transport and handling.

7. Improved Hardness and Friability: a) Dependent upon adhesive forces and surface characteristics. b) Spheronization increases the hardness and reduces friability of granules.

8. Improved Packing of Beds and Columns: a) In some chemical processes porous beds or packed columns are used as chemicals reactors and catalysts. b) Spherical surfaces allow the reproduction of beds with always the same volume of void space. c) Modelling and calculations are easier when the products flow around symmetrical bodies.

**Disadvantages**\(^{[37]}\)

This process is more labour and time intensive than other commonly used granulation techniques.

### 3. Cryopelletization

Pellets here can be produced by allowing droplets of liquid formulation such as solution, suspension or emulsion to come in contact with liquid nitrogen at -160°C in which liquid nitrogen used as solidifying medium. The procedure permits freezing of the material being processed due to rapid heat transfer that occurs between the droplets and the liquid nitrogen. The pellets are dried in conventional freeze dryers to remove water or organic solvents.\(^{[14,28,31]}\) The equipment consists of a container equipped with perforated plate below which a reservoir of liquid nitrogen in which a conveyer belt with transport baffles is immersed. The variable speed of conveyer belt provides the required residence time required for freezing the pellets. Surface tension of the liquid formulation also influences droplet
formation and size. Addition of a surfactant reduces the surface tension and produces smaller particle.[19,33] When it is desirable to have pellets with diameter less than 2 mm. the liquid nitrogen should be stirred continuously to prevent agglomeration. Generally, 3-5 kg of liquid nitrogen is required for preparation of 1Kg pellets.[39]

4. Compression[14,28,31]
It is one type of compaction technique for preparing pellets. Pellets of definite sizes and shapes are prepared by compacting mixtures or blends of active ingredients and excipients under pressure. The formulation and process variables controlling the quality of pellets prepared are similar to those used in tablets manufacturing.

5. Balling[14,28,31]
It is pelletization process in which pellets are formed by a continuous rolling and thumbing motion in pans, discs, drums or mixtures. The process consists of conversion of finely divided particles in to spherical particles upon the addition of appropriate amounts of liquid.

6. Hot-Melt Extrusion technology (HME)
It is process of pumping raw materials with a rotating screw under elevated temperature through a die into a product of uniform shape. Rotating screw impose mixing and agitation result in the de-aggregation of suspended particles in the molten polymer resulting in the more uniform dispersion.[14,28,31] Hot melt-extrusion is initially used in the plastic industry, slowly gaining popularity in the pharmaceutical industry for the production of pellets.[40] HME has been used to improve the bioavailability of drug substances especially those having low water solubility by formation of molecular dispersions.

![Schematic Representation of a hot melt extrusion system](image-url)

**Figure 7:** Schematic Representation of a hot melt extrusion system[41]
Advantages
Neither solvent nor water is used in this process which prevents degradation of many drugs. Fewer processing steps needed thus time consuming drying steps are eliminated. Uniform dispersion of fine particle occurs. It is simple and efficient. Good stability at varying pH and moisture levels, do not require additional film coating since the drug release is diffusion controlled. Safe application in humans due to their non-swellable and water insoluble nature. It helps to mask the bitter taste of the active ingredient. Poorly compatible materials can be incorporated into tablets produced by cutting an extruded rod.

Disadvantages
Lower-melting-point binder risks situations where melting or softening of the binder. Higher-melting-point binders require high melting temperatures. Type and amount of plasticizer may affect the dissolution and stability of the product. Cleaning is difficult and the material requirements for extruder often conflict with good manufacturing practices (GMP) issues.

7. Freeze pelletization
In this technique, a molten-solid carrier/matrix is introduced as droplets into an inert column of liquid in which the molten solid is immiscible. The molten solid moves in the liquid column as droplets and solidifies into spherical pellets. The molten solid droplets can move upward or downward in the liquid column depending on the droplet’s density with respect to the liquid in the column. If the density of the molten-solid carrier/matrix is less than that of the liquid in the column, then droplets are introduced from top of the column and pellets solidify in the bottom portion of the column. Conversely, if the density of molten-solid carrier/matrix is less than that of the liquid in the column, then the droplets are introduced from the bottom of the column and pellets solidify at the top portion of column.

Figure 8: Schematic Representation of Freeze pelletizer I and II[22]
In case of freeze pelletizer I the molten solid carrier are introduced from the upper portion of the column because density of the solid carriers is more than the density of the liquid used in the column and the carriers solidify in the bottom portion, while in case of freeze pelletizer II the molten solid carrier is introduced from the bottom of the column because density of the solid carrier is low as compared to the liquid used in the column and the carrier solidify at the top. Suitable carrier for freeze pelletization are those, which are solid at room temperature and have melting point below 100°C in order to minimize degradation of the active constituent. For freeze pelletizer I, hydrophilic carrier such as polyvinyl alcohol, polyethylene glycol and low melting point sugars (dextrose, maltose) are used. Suitable liquids for column are low density oil such as mineral oil, vegetable oil and silicone oil. For freeze pelletizer II, hydrophobic carriers of low density such as glyceryl palmitostearate, glyceryl behenate and glyceryl monostearate are used as solid carriers. Suitable liquids for column are high density hydrophilic liquids such as liquid polyethylene glycol, ethyl alcohol, glycerine and water.\textsuperscript{[33,40,36,22]}

8. Spray-drying and Spray-congealing

1. Spray-Drying

During spray drying, a drug solution or suspension is sprayed, with or without excipients, into a hot-air stream generating dry and highly spherical particles. Though this technique is suitable for development of controlled release pellets, it is generally employed to improve the dissolution rates and hence improve the bioavailability of poorly soluble drugs. The spray dried powder particles are homogenous, approximately spherical and nearly uniform in size. The design and operation of spray drier can influence a great number of the characteristics of the final product, such as particle size and size distribution, bulk density, porosity, moisture content, flowability and friability.\textsuperscript{[14,28,31]}

This technique offers advantages like: 1) increase in solubility & dissolution of poorly soluble drug. Hence, increases bioavailability. 2) Produces homogeneous, approximately spherical, nearly uniform pellets.\textsuperscript{[19,34]}
2. Spray-congealing (Spray-chilling)

It is a technique similar to spray-drying. Spray congealing is a process in which a drug is allowed to melt, disperse or dissolve in hot melts of gums, waxes, fatty acids or other melting solids. The dispersion is then sprayed into stream of air and other gases with a temperature below the melting point of formulation components. Under appropriate processing conditions, spherical congealed pellets are obtained.\textsuperscript{14,28,31}

Evaluation parameters:\textsuperscript{31}

1. Bulk density and tapped density\textsuperscript{40,45,46}
2. Carr’s compressibility index\textsuperscript{13,46}
3. Hausner ratio\textsuperscript{13}
4. Angle of Repose\textsuperscript{13,46}
5. Moisture content\textsuperscript{13}
6. Content uniformity\textsuperscript{13}
7. Drug content\textsuperscript{47}
8. Surface morphology\textsuperscript{40}
9. Sphericity & shape analysis\textsuperscript{48}
10. Pellet surface roughness\textsuperscript{40}
11. Wettability\textsuperscript{49}
12. Floating behaviour\textsuperscript{13,18}
13. Disintegration time\[^{40}\]
14. Dissolution test\[^{13}\]
15. Particle size distribution\[^{40}\]

16. Surface Area\[^{29}\]
17. Porosity\[^{40,48}\]
18. Hardness and Friability\[^{36,44,48}\]

**Table 1:**- Showing Different Polymers Used In the Pelletization Process.\[^{40}\]

<table>
<thead>
<tr>
<th>Polymer Used In Pelletization</th>
<th>Formulation</th>
<th>Applications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbopol 974P, NF, Resin.</td>
<td>Beads containing Weakly basic drugs.</td>
<td>Slower release of the salts of weakly basic drugs.</td>
</tr>
<tr>
<td>Crosscarmellose sodium or sodium starch glycolate.</td>
<td>Super-disintegrants in avicel pellets.</td>
<td>Increase dissolution rate, increase the pellet micropore volume.</td>
</tr>
<tr>
<td>Eudragit RS PO and RL PO.</td>
<td>Polymer (with combination) based pellets.</td>
<td>Better characterization like elastic modulus of the pellets, surface characteristics, sphericity.</td>
</tr>
<tr>
<td>Eudragit RL 30D, RS 30D, NE 30D.</td>
<td>A multiple-unit floating drug delivery system.</td>
<td>Prolong the gastric residence time and to increase the overall bioavailability of the dosage form.</td>
</tr>
<tr>
<td>Methocel-E5 (HPMC) or AMB, Eudragit L 30D-55.</td>
<td>Enteric coated pellets.</td>
<td>Improved film formation and polymer coalescence.</td>
</tr>
<tr>
<td>Microcrystalline cellulose, Ac-Di-Sol.</td>
<td>Floating pellets with bacterial antagonist.</td>
<td>Improving floating property.</td>
</tr>
<tr>
<td>Microcrystalline cellulose and hydroxypropyl methyl cellulose.</td>
<td>Pellets with water insoluble drugs in self-emulsified form.</td>
<td>Controlling the drug release from the oral dosage forms.</td>
</tr>
</tbody>
</table>

**APPLICATIONS OF PELLETS**

1. Controlled release pellets for encapsulations.
3. Floating Multiparticulate oral sustained release drug delivery system.
5. Multi-unit erosion matrix pellets.
6. Pellets for special tableting applications.
7. Immediate release pellets for sachets.
9. Taste masking: The pelletization technique solves difficult taste masking problem while maintaining a high degree of bioavailability due to their high surface area, especially for oral products. Many products, such as antibiotics (clarithromycin, roxithromycin and cephelexin)
and anti-inflammatory drugs with a bitter taste, can now be formulated in products with high patient compliance.

10. Chemically Incompatible Product: In the compressed tablet dosage form separate tablets would have to be administered, but the pellets can be administered in a single capsule.

11. Varying dosage without reformulation: Pellets have excellent flow properties, due to this, they can be conveniently used for filling capsules and the manufacturer can vary the dosage by varying the capsule size without reformulating the product.[25,36,44,50,51,52]

CONCLUSION
Pelletization technique has gained much interest in pharmaceutical industry due to its simple design, more efficiency and faster processing. Nom dose dumping is seen unlike single unit dosage form. It does not depend on gastric emptying time. Extrusion is widely used technique in pelletization because of its high efficiency, greater yield, high product quality and it is easy to manufacture.

REFERENCES


