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MULTI-UNIT PELLET SYSTEMS (MUPS): A GAME-CHANGER IN ORAL DRUG DELIVERY

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ABSTRACT

Pelletization is an advanced agglomeration technique widely used in pharmaceutical formulation to improve drug delivery, enhance bioavailability, and achieve controlled or sustained release. This process involves converting fine powders or granules into small, spherical, free-flowing units, commonly referred to as pellets. The pharmaceutical industry has adopted pelletization due to its ability to minimize dose dumping, reduce gastric irritation, and improve patient compliance. Various techniques, such as extrusion-spheronization, layering, balling, and fluidized bed coating, are employed to produce pellets with uniform drug distribution and controlled release properties. The formulation of pellets requires careful selection of excipients, including binders, fillers, disintegrants, and surfactants, to ensure stability and optimize drug release profiles. Factors such as moisture content, particle size, drying technique, and polymer selection play crucial roles in determining pellet characteristics. The use of polymers like hydroxypropyl methylcellulose (HPMC), microcrystalline cellulose (MCC), and β-cyclodextrins enhances pellet integrity and functionality. Recent advancements in pelletization technology, such as liquisolid pellets and micropellet-containing formulations, have further improved drug solubility and bioavailability. Innovative techniques like hot-melt extrusion, cryopelletization, and freeze pelletization allow for the development of novel drug delivery systems with enhanced therapeutic efficacy. Additionally, fluidized bed coating techniques, including top-spray, bottom-spray (Wurster), and tangential spray coating, provide precise control over drug release kinetics. This review explores the principles, methods, and recent developments in pelletization, highlighting its significance in modern pharmaceutical formulations. As research continues to advance, pellet-based drug delivery systems hold great promise for improving patient outcomes and expanding the range of therapeutic applications in oral dosage forms.

KEYWORDS: *Pelletization, Bioavailability, Micropellet, Cryopelletization.*

INTRODUCTION

Historically, a range of industries have used the term "pellet" to refer to a variety of agglomerates made from a wide range of basic materials. Since the turn of the 20th century, many sectors have been using pelletisation techniques; nevertheless, it wasn't until the early 1950s that the pharmaceutical business began to show a significant interest in this technology because of the growing demand for sustained release preparations.[1]

In 1949, Smith Kline & French (SKF) pharmaceutical experts started creating little medicine pellets that could be put into capsules after realising the potential of candy seeds in creating sustained-release treatments.[2] More and more rapid, effective, and affordable pelletisation methods were created as a result of intensive study.[1]

In place of traditional tablets and capsules, pellets are now a common pharmaceutical solid unit dose form. Multiple unit particulate systems (MUPS) are dosage forms made with pellets that range in size from 250 µm to 2000 µm. Common names for these free-flowing granules or spheres include beads, seeds, spherical agglomerates, vermicelli, spheres, globules, and more. They have a consistent and narrow size distribution.[3] They are often made via pelletisation, which is the agglomeration of a powder mixture of excipient particles and an API into spherical granules. Pellets are usually compressed into tablets or inserted into firm gelatin capsules after processing. They can then be coated to effectively deliver a medication to a particular site of action in the gastrointestinal tract, or they can be manufactured as an immediate release dosage form or as a sustained drug release over an extended period of time. Because of its free-flowing qualities Pellets offer a significant degree of versatility in formulation creation. As a result, they pack easily and without any issues. Pellets with a low surface area to volume ratio and a spherical shape are ideal for homogenous film coating. Compared to tablets, pellets reduce the dosage dumping

effect, resulting in a smoother plasma concentration profile and slower drug absorption, both of which lessen the negative effects of medications.[4]

High local drug concentrations and their possibly irritating effects on the stomach mucosa are less likely when a drug is uniformly dispersed into small dose units.[5] Another benefit of using a pellet format is that the medication blood levels can be repeated.[6] To provide a controlled release effect, the pellet formulations that are sold commercially are mostly covered with a polymer film. Fine medication and excipient powders aggregate into tiny, spherical units during the pelletisation process. Applications can be found in the food sector, detergent additives, polymer, agrochemicals, pharmaceuticals, and sweeteners.[1]

ADVANTAGES[7]

1. It is possible to divide the required dose strength without modifying the formulation or procedure.
2. The product looks better.
3. Because of their tiny size and form, pellets flow more easily than powders.
4. Pellets that are enclosed are easy to handle.
5. It is possible to combine incompatible components into a single dose form.
6. Pellets can be film coated to prevent oxidation or moisture from degrading the active components.
7. Because capsules are more elegant than tablets, patients are more likely to take pellets when they are put in them.
8. There is a high drug loading capacity without the production of big pellets.
9. Pellets are less likely to have dose damping effects and have fewer adverse effects.
10. Because the pellets are smaller than tablets, there is less gastrointestinal discomfort.
11. It lessens variations in intestinal transit time and stomach emptying rate across and within patients.
12. Coating the pellets allows for the formulation of targeted, controlled, or sustained drug administration.
13. Beneficial for children and the elderly, such as when they have dysphagia or swallowing difficulties.
14. The wide surface area of quick release pellets allows for better distribution.
15. A significant degree of flexibility can be achieved in the development and design of oral dosage forms, such as tablets, capsules, and suspensions.

DISADVANTAGES

1. Typically, pellets are enclosed in capsules, which raises the cost, particularly when several subunits are involved.
2. When pellets are compressed into tablets, their film coating may be destroyed.
3. The size of the pellets varies depending on the formulation, often falling between 0.05 and 2 mm.
4. The proportion of excipients used is high.
5. Ineffectiveness and repeatability in manufacturing.
6. A significant number of process variables.
7. Different stages of formulation.
8. Advanced technology is essential.
9. Manufacturing requires a skilled worker.
10. It is more costly and more complex to make several unit dose forms.

THEORY OF PELLET GROWTH AND FORMATION[7]

Numerous theories have been proposed to explain the mechanism of pellet production and growth. Techniques like revolving drums, pans, or discs are used in the most methodically researched and categorised pelletisation process, which is further broken down into three stages: nucleation, transition, and ball growth. On the other hand, the following actions were expected based on the experiments on the mechanism of pellet growth and formation:

1. Nucleation
2. Coalescence
3. Layering
4. Abrasion transfer

The primary processes that can result in a rise in particle size and growth include nucleation, coalescence, layering, abrasion transfer, and size reduction. For the nucleation procedure, a suitable solvent system is used to wet powder (API + appropriate polymer).Coalescence is a big particle created when well-formed nuclear moieties collide. Layering is the process of adding materials one after the other on top of nuclei that have already formed. The technique of moving materials from one particle to another without favouring one direction over another is known as abrasion transfer. The attrition mechanism may cause well-formed particles to shrink in size.

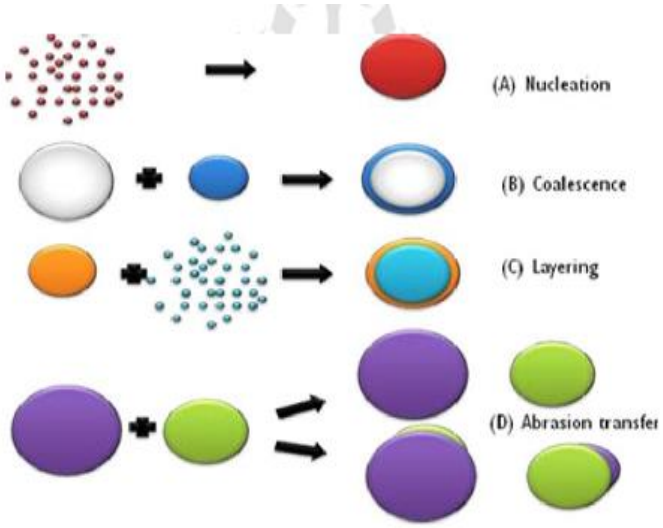

FIG. 1: Mechanism of Pellet Formation.

Formulation variables enlisted below[9]

1. Fillers: To improve bulk qualities, fillers are added to pellet formulation. Fillers can either dissolve in water or not. Thus, the choice of pellets is determined by the formulation's intended qualities. the application of fillers according to the drug's properties, production technique, and dosage. Fillers might be as much as 90% or as little as 1% of the formulation. The amount and physical characteristics may have an impact on the rate and degree of drug release from pellets in the intended formulation. The stability of pellets is also impacted by the physicochemical characteristics of fillers.
2. Binders: Due to their adhesive properties, binders are used to combine and bind the powder for pellet manufacturing. It is a crucial part of the formulation and production of pellets.
3. Lubricants: To lessen friction between manufacturing equipment, lubricants are employed in pellet formulation.
4. Separating agent: To encourage the separation of pellets into individual units, separating agents absorb on the surface during the pelletisation process. During manufacturing, pellets increase surface charge, which could cause them to attract one another.
5. Disintegrant: Disintegrants can be added to formulation at any appropriate stage of the process, although they work best when added to granulation or during the lubrication step before compression. These are compounds that disintegrate the compacted mass of a solid dosage form when fluid is present.
6. pH adjuster: For a variety of purposes, pH adjusters are employed to regulate the drug molecules' microenvironment in pellets. Generally to preserve the acid labile substances from acidic environment via enteric film coating.
7. Surfactants: Generally used in pellet formulation for the same reason they are used in other different dosage forms, surfactants improve solubility, wettability, and dissolution rates. The formation of liquid bridges holds particles together during initial and subsequent growth, so lowering surface tension may weaken these bridges and cause the pellets to form.
8. Spheronization enhancers: These formulation aids are used to produce spherical pellets, which provide the pellets binding properties which give them strength and integrity.
9. Glidants: These are used to develop a flow characteristics during layering of pellets. For simultaneous binder application, glidant must be added at a carefully regulated rate during binder addition.

Drug selection criteria

- Poorly water soluble drugs have more than 40% identified through combinatorial screening programs. Poor solubility is drug of choice for formulation development.
- Drugs with plasma half-life 22.1 hrs. and water insolubility is good candidate for instant release pellets. The medicines with long biological half-life, reduced clearance and lower elimination are excellent candidates for instant release pellets.
- The drug and the excipients should work well together. By using the extrusion/spheronization process, poorly soluble BCS class II medications (piroxicam and hydrochlorothiazide) can be combined with modified starch (high amylose, crystalline, and resistant starch).
- Aceclofenac and other non-steroidal anti-inflammatory medications (NSAIDs) irritate the gastrointestinal tract. Aceclofenac is a BCS class-II medication with high permeability and poor water solubility. Therefore, it is a viable option for immediate release pellets with restricted bioavailability. In addition to forming complexation with HP-β-Cyclodextrins (HP-β-CD), aceclofenac-

loaded agarose beads, and chitosan-aceclofenac co-crystals, it should be compatible with the solid dispersion process that uses mixed surfactants. Reducing the particle size of poorly soluble medications is crucial for increasing their solubility and, consequently, their bioavailability. Drugs should not be harmful to the gastrointestinal tract.

- A small number of researchers use a drug that works well with the solid dispersion approach to increase the solubility of H2-receptor antagonists. Famotidine, an H2-receptor antagonist, has a low and inconsistent bioavailability. To address this issue, two hydrophilic carriers are developed that work well with the solid dispersion method. The preferred medication for immediate release pellets is one with improved wetability and dispersibility. Drugs similar to famotidine have a 40%–50% bioavailability and first pass metabolism. Therefore, increasing the drug's surface area improves its solubility and dissolving rate for drugs with high polarity and poor water solubility.
- In the stomach's acidic environment, proton pump inhibitor medications are easily inactivated, very unstable, and only weakly soluble in water. For immediate release pellets, medications that break down quickly at low pH levels are preferred.
- The best candidates for pelletisation are also medications that are bitter and sensitive to temperature.

Selection criteria for polymers

1. Spheronization aids for water-insoluble polymers have a longer water absorption and retention capacity, which is an ideal property for extrusion. Similar to a reservoir, lubrication and surface plasticization are necessary for extrusion and spheronization, respectively, to provide the best rheological conditions. They have a cohesive surface area that is substantial enough for water interaction and formulation. In quick release pellets, polymers can improve medication release.
2. The nature of fillers is both water soluble and insoluble. The required dosage, the drug's physical characteristics, and the production method all influence the choice of fillers.
3. Binders such as sucrose, starch, HPMC, HPC, gelatin, and PVP are employed to give seal-coated pellets a uniform coating and prevent medication from clinging to them. In order to prevent sticking during film coating, talc is utilised as a glidant to lower static charges.
4. Drug taste masking by inclusion complex, or "host-guest" relationships, in which the host is an agent that complexes and the guest is an active chemical, is another basis for polymer selection. In the oral cavity, the complexing agent may reduce solubility. A popular complexing agent that works via van der Waals forces and is non-toxic is β-cyclodextrin.
5. The active nature of excipients and polymers affects the production, efficacy, safety, and quality of therapeutic substances in dosage forms. They have the best qualities: they improve drug stability, control the solubility and bioavailability of active components, and help the active substance keep its polymorphic form.
6. To optimise the high quality surface, desirable release, and size distribution in the range, a 2-5% concentration of HPMC is added to the total weight of itraconazole instant release pellets.
7. Modified starch with suitable binder gives narrow particle size distribution, spherical shape with high process yield. Modified starch works well for the extrusion-spheronization method ofpelletising poorly soluble medications.
8. The most common excipient for pellets made by extrusion spheronization is microcrystalline cellulose (MCC), which gives good plasticity to wet mass and good binding properties. However, MCC has a major problem with disintegration for immediate release pellets; MCC-based pellets do not disintegrate poorly water-soluble drugs in immediate release form, which prolongs the drug release.
9. Despite MCC's excellent qualities, it is not used as an excipient for pellet production because it adsorbs drug onto the surface; many drugs are chemically incompatible with MCC, so alternative excipients such as powder cellulose, starches, chitosan, pectinic acid, β-cyclodextrins, sodium alginate, polyethylene oxide, and carrageenan are used.
10. Sucrose is the main component for core pelletisation by layering process.
11. The final drug characteristics of pellets are impacted by binder, which is also crucial in the wet granulation and drug stacking processes. While any kind of binder can be used to prepare pellets, gelatin and carboxymethyl cellulose worked best.

Pelletization

Pelletisation is a unique method for preparing pellets. This method is known as an agglomeration process, which creates small, free-flowing, spherical or semi-spherical pellets from fine powder or granules of bulk medication or excipient. This method is required to provide uniformly sized pellets with a high medication loading capacity while avoiding dust and segregation.[10]

PELLETIZATION TECHNIQUES

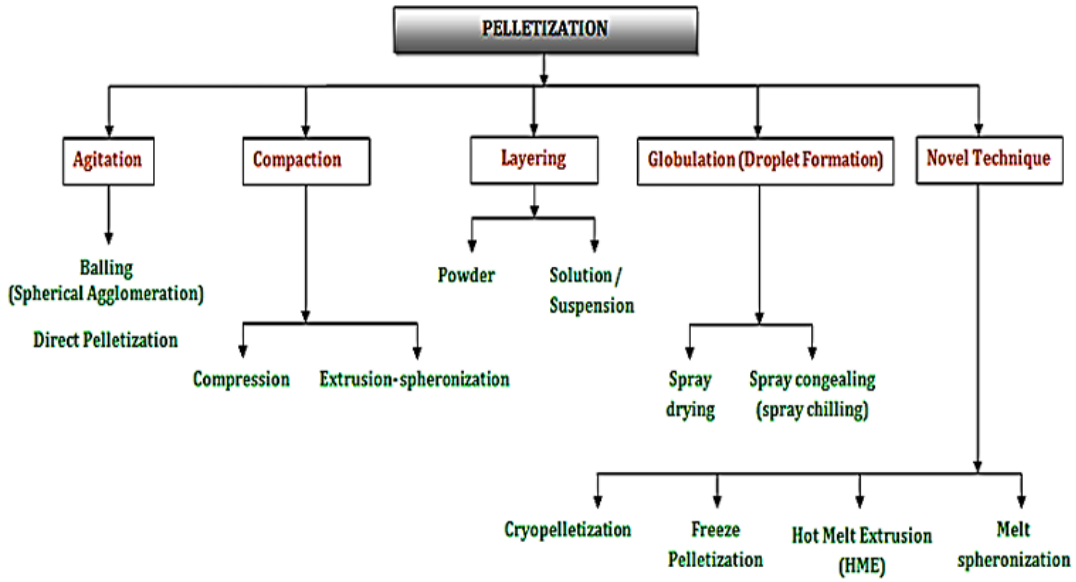

FIG. 2: Classification chart of Pelletization Techniques.

A. AGITATION: By adding the necessary liquid and rolling or tumbling continuously, agitation transforms finely split particles into spheroidal particles. During the agitation process or at the start of the process, the liquid can be introduced. Pellets can be made via the balling process in mixers, discs, drums, or pans. It is the most traditional and ineffective method of producing pellets.

1) Balling

Either applying a high temperature or adding the necessary amount of liquid to powder can do this. There are two types of spherical agglomeration: melt-induced agglomerations and liquid-induced agglomerations. devices such as rotating fluid-bed granulators, inclined dish pelletisers, tumbling blenders, and traditional horizontal drum pelletisers. The fertiliser and iron ore industries make extensive use of this approach. Formulation factors such particle size, liquid saturation level, liquid phase viscosity, and powder solubility affect the rate and degree of agglomeration formation.

B. COMPACTION: When pressure is present, drug particles or granules aggregate to form pellets with a distinct size and shape.

1) Compression: One kind of compaction method for pellet preparation is compression. Mixtures or blends of active substances and excipients are compressed under pressure to create pellets with certain sizes and forms. The formulation and process parameters governing the quality of the pellets produced are comparable to those employed in the production of tablets.

2) Spheronization-Extrusion: Manufactures pellets with a high active ingredient loading capacity without generating a lot of bigger particles and particles with a consistent size distribution and acceptable flow characteristics. The extrusion-spheronization process.

a) Dry Mixing: Using a tumbler mixer, planetary mixer, high speed mixer, and twin shell blender, ingredients are dry mixed to create a uniform powder dispersion.

b) Wet massing: It is done to produce a sufficient plastic mass for extrusion, by applying normal equipment and technique as applied in wet granulation for compaction.

c) Extrusion: It turns moist matter into rod-shaped particles with a consistent diameter. After being pushed through dies, the moist substance is formed into tiny, uniformly sized cylindrical particles. This process of forming wet mass into long rods is known as "extrudate."

Extruder types

1. Screw feed extruder
2. Gravity feed extruder
3. Piston feed extruder (Ram).

d) The spheronization process Also referred to as a "merumerizer," it is made comprised of a static cylinder and a revolving friction plate that breaks the extrudate into smaller cylinders that are the same length as their diameter. Frictional forces cause these plastic cylinders to round. Typically, two geometric motifs are employed. It features a radial pattern with grooves radiating outward from the disc's centre, as well as a crosshatched pattern with grooves running at right angles to one another.

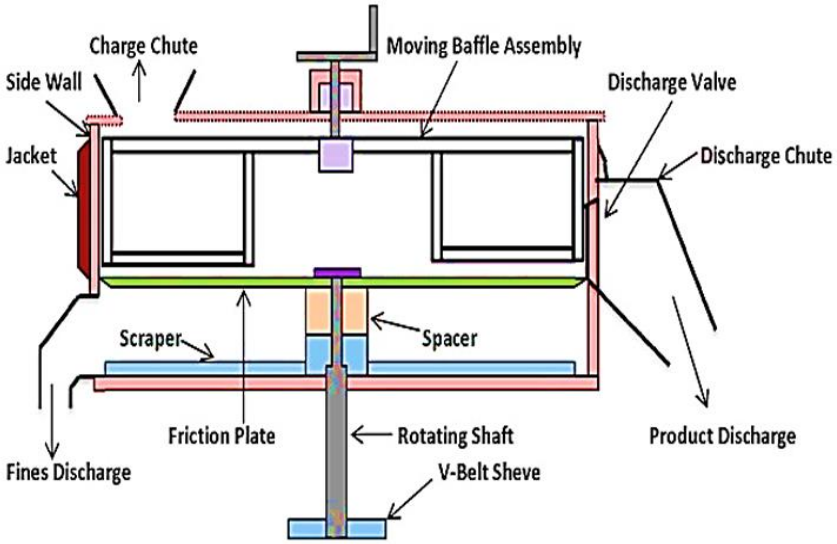

FIG. 3: Schematic diagram Extrusion Spheronizer.

e) Drying: To attain the appropriate moisture content, a drying stage is necessary. More porous pellets are produced when the drying rate is increased since the drying process reduces pellet densification.

f) Examining: The intended size distribution must be attained, and sieves are employed for this.
C. LAYERING: Drug molecules are deposited in successive layers from dry powder or granules, suspension, or a solution of drug particles in order to form a pellet by layering.

1) Layering of powder
Liquid saturation is low in powder stacking, and total dissolution does not happen regardless of how soluble the medicine is in the binding liquid. Usually, the nuclei are sprayed with a binder solution first, and then powder is added. Using capillary forces created in the liquid phase, the majority of nuclei tumble in the revolving disc pan, pick up powder particles, and create layers of tiny particles that stick to the nuclei and each other. Until the required particle sizes are reached, more powder is layered on the nuclei as more bonding and liquid are sprayed. The binder and other dissolved materials crystallise out as the material dries, and solid bridges partially replace the liquid bridges. Fines may absorb moisture and enter a nucleate phase after being sprayed with binder.

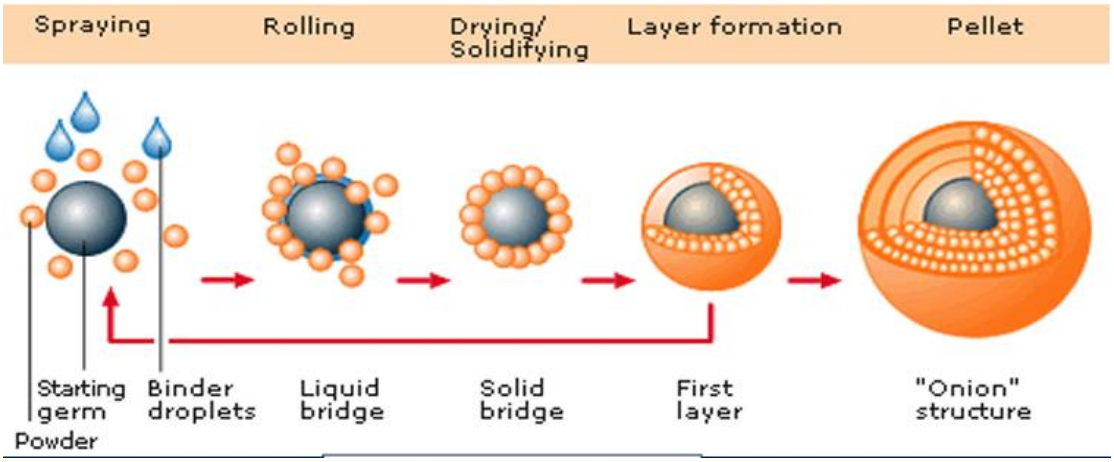

FIG. 4: Mechanism of Pellet Formation by the Layering Technique.

2) Layering of Solutions and Suspensions
The idea behind the layering process of suspension and solution: On beginning seeds, which could be inert materials, crystals, or granules of the same drug, successive layers of drug ingredient solutions or suspensions are deposited. This process is known as solution and suspension layering. Theoretically, solution or suspension layering is directly impacted by the same elements that govern coating processes. All of the formulation's ingredients dissolve or suspend in the application medium during solution or suspension layering, which establishes the liquid's viscosity and solids content. If the drying conditions and fluid dynamics are right, the droplets of the solution or

suspension that are sprayed over the product bed will strike the beginning seeds or cores and disperse uniformly across the surface. The drying step that follows enables the dissolved components to crystallise and create solid bridges between the pharmacological substance's core and first layer as well as between its subsequent layers. The procedure keeps going until the targeted drug layers and, consequently, pellet potency are reached. The gradual addition of the dissolved or suspended medication results in a relatively modest rate of particle development. Even though the particle population stays constant during this process, the pellets' sizes grow over time, increasing the system's overall mass.

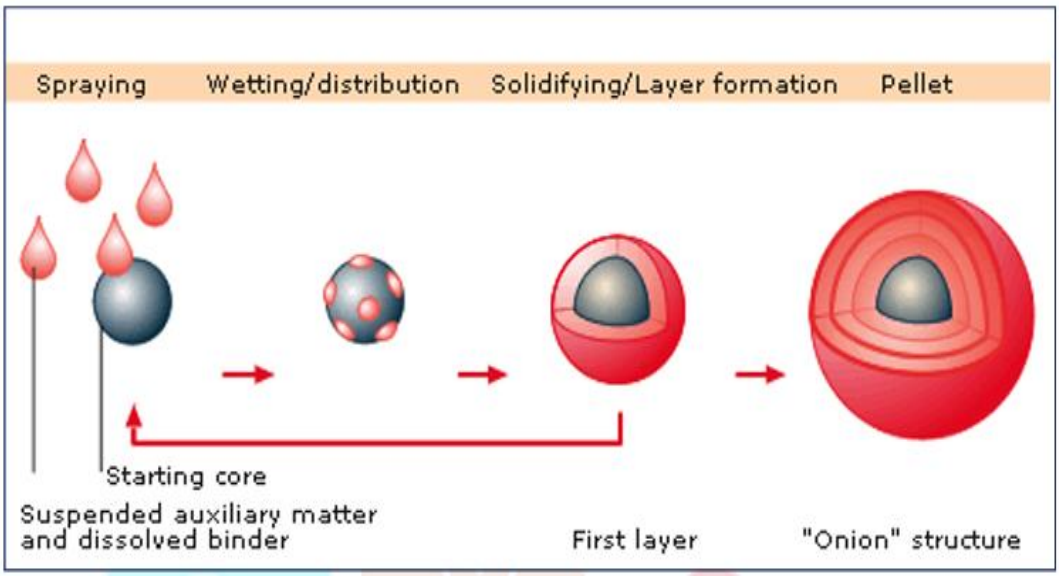

FIG. 5: Solution/Suspension Layering Mechanism.

D. HOT-MELT EXTRUSION TECHNOLOGY (HME)

It involves forcing raw materials through a die at a high temperature using a revolving screw to create a uniformly shaped result. A more uniform dispersion is achieved by the de-aggregation of suspended particles in the molten polymer due to the mixing and agitation caused by rotating screws.

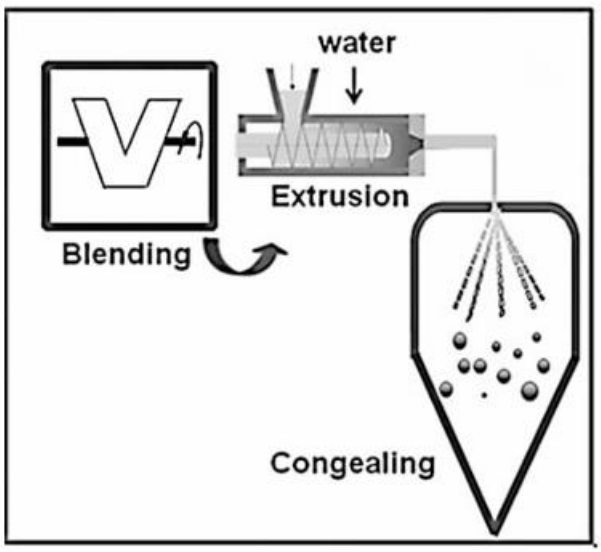

FIG. 6: Process flow of extrusion followed by congealing.

E) GLOBULATION: Also referred to as droplet production, this procedure includes two steps: spray drying and spray congealing. It creates pellet particles by atomising hot melts, suspensions, or solutions. Spray drying and spray congealing are examples of globulation, or droplet production.

1) Spray drying: This method creates extremely dry and spherical particles by spraying drug molecules in suspension or solution form—with or without excipients—into a hot air stream. This procedure is typically used to boost the bioavailability and dissolving rate of poorly soluble medications.

2) Spray congealing: This method creates congealed spherical pellets under ideal storage conditions by allowing the drug to melt, diffuse, or dissolve in worm melts of gums, waxes, fatty acids, etc. The drug is then sprayed into an air chamber with a temperature lower than the melting point of formulation ingredients.

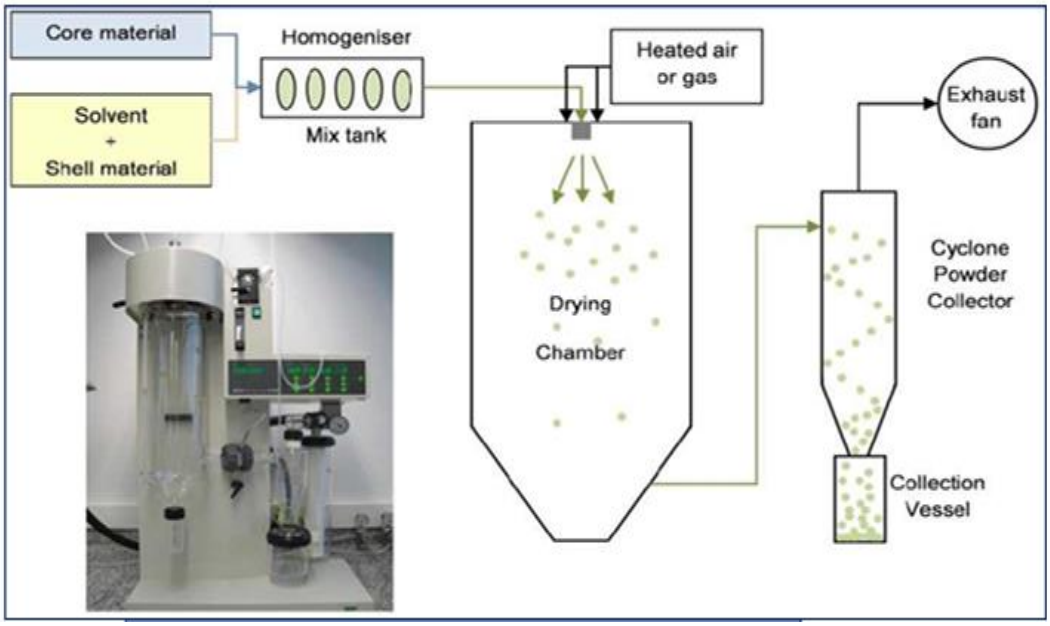

FIG 7: Spray Drying Process.

F) CRYOPELLETIZATION: In this process, droplets of a liquid formulation, such as a solution, suspension, or emulsion, are allowed to come into contact with liquid nitrogen at -160˚C. The liquid nitrogen is then employed as a solidifying medium to create pellets. Depending on the temperature and solid content of the solution or suspension being processed, the method allows the material to freeze because of the quick heat transfer between the droplets and the liquid nitrogen. This allows for the production of a specific quantity. To get rid of water or organic solvents, the pellets are dried in traditional freeze dryers.

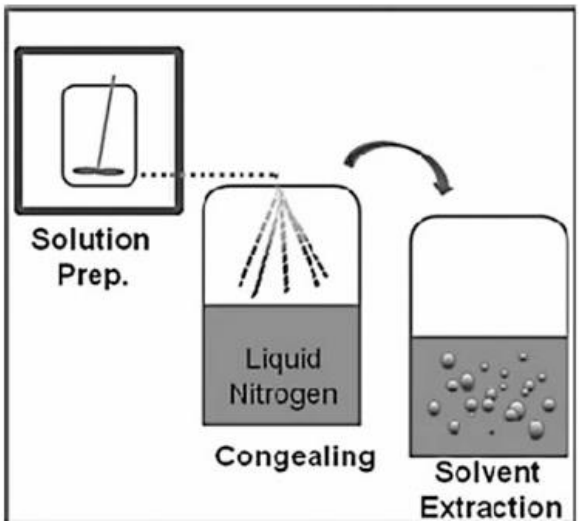

FIG. 8: Cryopelletization Process.

G) FREEZE PELLETIZATION

The process of freeze pelletisation involves introducing a molten-solid matrix or carrier in the form of droplets into an inert liquid column where the molten solid is immiscible. Depending on their density in relation to the liquid in the column, the molten solid droplets either go upward or downward in the liquid column before solidifying into spherical pellets. Droplets are introduced from the top of the column and the pellets solidify at the bottom if the density of the molten-solid carrier or matrix is lower than that of the liquid in the column. In contrast, droplets are supplied from the bottom and the pellets solidify at the top if the density of the molten solid carrier or matrix is greater than that of the liquid in the column.

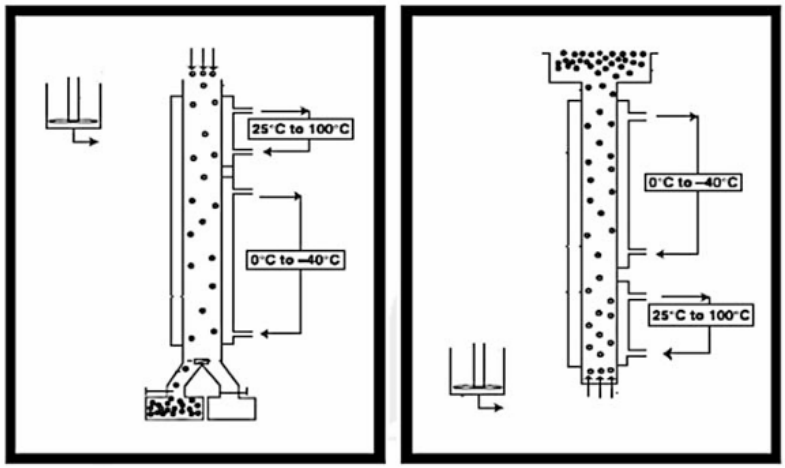

FIG. 9: Freeze Pelletization.

l) Fluid Bed Coating: There are three types of fluid bed coating used to prepare pellets:

A) Top Spray Coating: Particles are fluidised in the flow of heated air injected into the product container through the base plate when top spray coating is applied in the fluid bed (batch and continuous). Through a nozzle above, the coating liquid is sprayed over the fluid bed against the air flow (counter-current). As the particles continue to ascend in the air flow, they dry. Because the droplets are small and the spray medium has a low viscosity, the coating liquid distributes evenly. For protective or colour coatings with high product throughput rates, coating on a continuous fluid bed is appropriate. This process involves continuously feeding the product into one side of the machine, then moving it forward trough the sieve bottom via air flow. Continuous extraction is performed on the dry coated particles.

B) Wurster Coating (Bottom Spray Coating): This method is employed when a regulated release of active substances is necessary. By using less coating material, the Wurster coating method thoroughly seals the surface. When the spray nozzle is installed in the base plate, a spray pattern is produced simultaneously with the air feed. The particles to be coated are supplied through the spray cone while being accelerated in the wurster tube using a base plate with various perforations and a wurster cylinder. The particles dry as they ascend and return to the base plate outside the wurster tube. They are directed from the exterior back into the tube, where the spray accelerates them once more, creating a very consistent layer even on particles of varying sizes.

C) Continuous Fluid Bed Bottom Spray Coating: This method works well for protective or coloured coatings with high product throughput rates. The product is constantly fed into one side of the machine and is moved forward via the sieve bottom by air flow. The system is separated into pre-heating, spray, and drying zones based on the application. In the latter, coating liquid is sprayed from below as a bottom spray. Continuous extraction is used to remove the coated and dried particles.

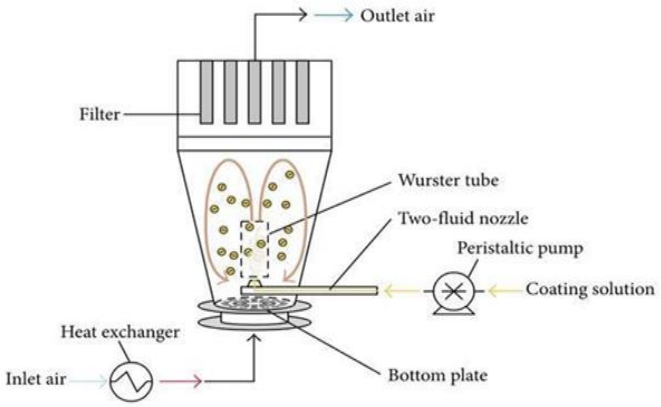

FIG. 10: Wurster Process used in fluidized bed coating.

D) Tangential Spray Coating: This method involves using a rotating base plate with air supplied into the powder bed at its edge to set the product into a spiral motion. Spraying into the powder bed simultaneously, the spray nozzle is positioned tangential to the rotor disc. This technique works best for applying thick film layers and coatings with a high solid component.[4]

VARIOUS FACTORS INFLUENCING PELLETIZATION

1. **Temperature and Drying Method:-** Proper drying can result in ideal pellets. The pellets produced at optimal drying will have the right size, shape, and flow, but the drying process should be consistent and repeatable for every batch. Features like weight variations and improper filling can change the size, shape, and flow of pellets, changing the fin dosage form and potentially impairing the effectiveness of the delivery system.
2. The extruder's screen: The extruder's orifice will affect the pelletisation process; a larger orifice's S dimension will increase the extrusion force due to the presence of water. ii. The distribution and shape of pellets may be impacted by this increase in extrusion force at the extrudate surface.
3. Spheronizer Speed Rate: The spheronizer's speed rate and pellet size. A high spheronizer speed produces a smoother surface and high crushing strength.
4. Starting Material: The Pelletisation Process Is Significantly Affected by the Variables of Starting Materials, Including Their Contents, Variety, Type of Filler, and Particle Size.
5. Drug: Pelletisation, a versatile technique, can be used to prepare a variety of materials with a variety of release mechanisms, such as modified or immediate. Several process variables and formulation strategies must be used in order to accomplish this. Pellets are used to mask the taste of medications that are not palatable, like quinine sulphate. Since the currently available formulation of Budesonide exhibits low efficacy due to premature drug release, Raval et al. prepared an enteric coated pellet of the drug.
6. Granulating fluid composition: Wet granulation is used to prepare the pellets, hence the concentration and composition of the granulating fluid are crucial factors in the Pelletisation Spheronization process[3]
7. Moisture Content: Water content is a greatly significant process variable since it plays a significant role in determining the quality of spheres. When using spheronization techniques, a decrease in moisture content below the lower limit would result in the production of many fines.
8. Rheology: The rheological makeup of the wet mass will affect the extruder's flowability as well as the spheronization process. Therefore, differences in the theory of wet mass could lead to uneven and incorrect extrusion.[13]

RECENT ADVANCEMENT IN PELLETIZATION[13]:- a)Liquisolid Pellets:- Liquisolid Pellets are being developed by De Espindola et al. as a technological advancement to increase the solubility of drugs that are poorly soluble. In order to increase the solubility and, thus, the bioavailability of the antiretroviral medication ritonavir, they developed liquid-solid pellets by extension spheronization. This formulation combined liquidsolid technology with the additive benefits of a multiparticulate system.

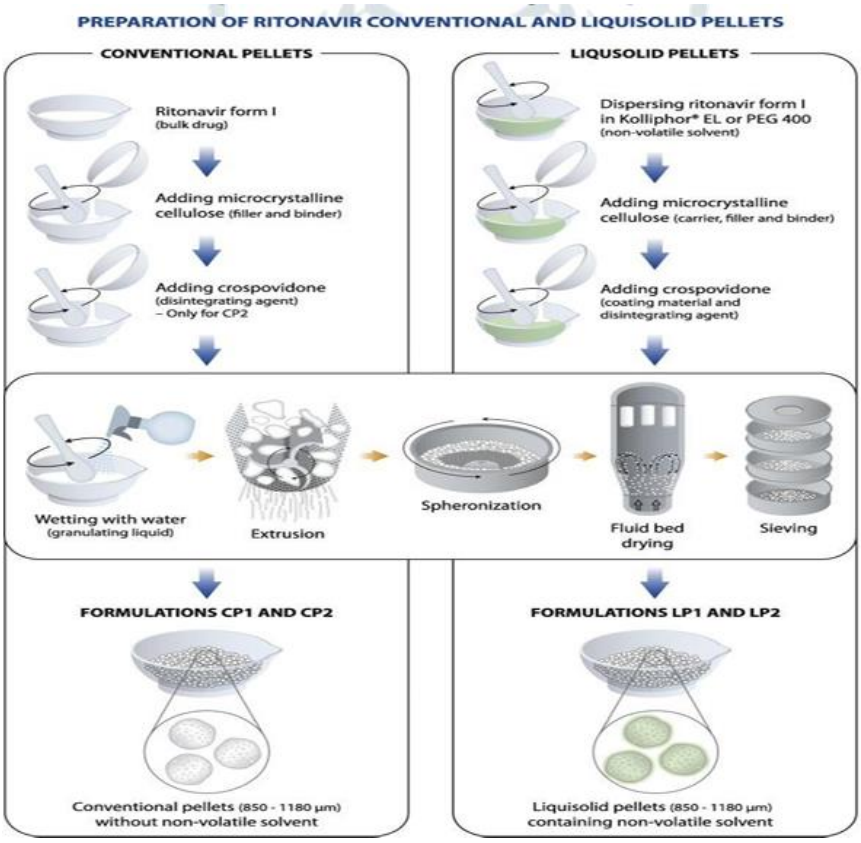

FIG. 10: Preparation of Ritonavir Conventional and Liquisolid Pellets.

Pellets with micropellets inside: In this medication dosage, pellets are made where an inner zone contains micropellets (with an average diameter of 50 to 500 microns are dispersed across an excipient matrix. A water-insoluble polymeric coating, with or without an active ingredient, may make up the outer zone. In order to formulate a multiple unit pellet system into a tablet, Hamman et al. used Sedem EDS as a formulation tool.

Iron ore and pelletization technology

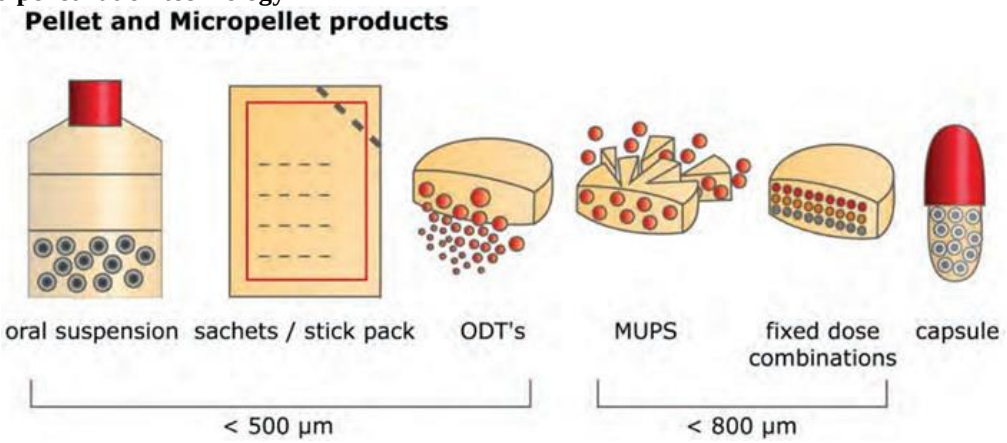

FIG. 11: Pellet and micropellet-based pharmaceutical dosage forms.

Improve resource efficacy Our world is composed of iron ore, which is the primary source of iron and steel. Iron ore is present in everything, even the computers we use and the chairs we sit on. It is nearly impossible to imagine a world without iron ore because it is so prevalent in our daily lives. Iron and steel are used in all contemporary energy generation and transmission methods. Fines of Iron Ore Are Agglomerated Iron ore pellets are then formed by inducing them in a furnace. These are usually fed into a DRI plant or blast furnace as part of the steel-making process. The world's greatest system for designers.

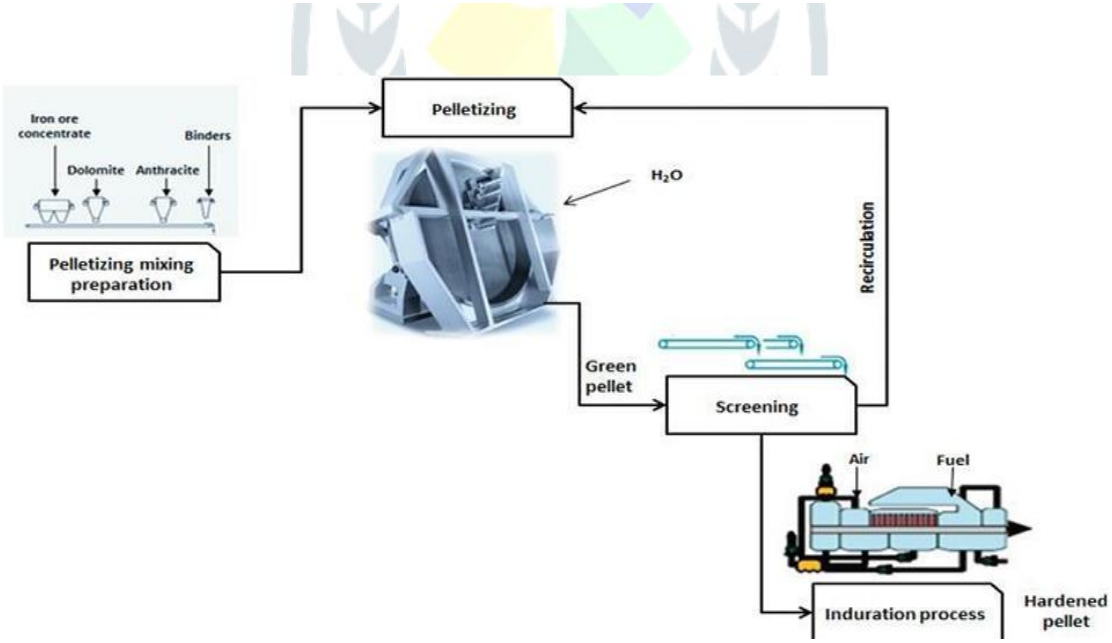

FIG. 12: Pelletizing process flow diagram, specifically used in the iron ore pellet manufacturing industry.

CONCLUSION

Pelletization has emerged as a vital technique in pharmaceutical drug delivery, offering advantages such as controlled drug release, enhanced bioavailability, reduced side effects, and improved patient complience. The various pelletization techniques, including extrusion- spheronization, layering and spray drying, allow for the development of highly stable, uniform and effective dosage forms.

Despite its advantages, challenges such as high production costs, complex manufacturing processes, and the need for specialized equipement and expertise remain barriers to widespread adoption. However, recent advancements, including liquisolid pellets and micropellet- containing pellets, continue to enhance the

efficiency and applicability of pelletized drug formulations.

Overall, pelletization continues to be a promising approach in modern pharmaceutical formulations, providing innovative solutions for a drug delivery challenges while ensuring better therapeutic outcomes.

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