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Extrusion Spheronization and the Recent Advancements in Pellets

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ABSTRACT

Pellets are multi-unit dosage forms, which are frequently used because they offer manufacturing and therapeutic benefits over single-unit solid dosage forms. Extrusion Spheronization is also known as maramuerization. It is a multi-step process that produces consistent-sized spherical particles known as spheres or pellets with diameters ranging from 0.5mm to 1.5mm. It is an ideal method because it has outstanding product scale-up, narrow particle size dispersion, flowability, high yield, and excellent process repeatability. The preparation of pellets involves four steps i.e. granulation, extrusion, spheronization, and drying. In the extrusion process, different types of extruders are used namely axial, radial, dome, rotary cylindrical, ram, etc. The different process parameters used in this technique are moisture content, temperature, speed, time, load, friction plate, mixer, etc. The characterization of pellets involves the particle size distribution, density, porosity, hardness, friability, etc. The surface area is identified by mean diameter, gas absorption, and air permeability. The recent approaches in the extrusion spheronization process are as follows, coating of the pellets/tablets and pellets as the delivery of the proteins and at last as the fast mouth dissolving pellets without the use of water.

INTRODUCTION

Advancements in drug delivery systems continue to be prevalent in pharmaceutical and food research. Macro, micro, and nanoparticulate systems, as well as uniparticulate and multiparticulate systems, are examples of novel techniques. Nanoparticulate systems, such as coaxial electrospraying or liposomes, are frequently employed to increase the bioavailability of solubility of poorly soluble substances. For high doses, Nanosystems can result in a high weight of the final formulation. Therefore, the improvement of macro and microsystems with high drug loads is of recent interest. Macro and microparticulate systems can also provide an enhanced bioavailability and/or site-specific administration into the human gut[1].

Because of possible benefits such as predictable gastric emptying, minimal risk of dose dumping, variable release patterns, and enhanced bioavailability with less inter-and intra-subject variability, multiparticulate dosage forms are gaining popularity over single unit dosage forms. One of the most common multi-particulate dose forms is pellets[2]. Pelletization is an agglomeration process in which fine powders or granules of bulk pharmaceuticals and excipients are converted into small, free-flowing, spherical, or semispherical units known as pellets. The pellets are a convenience for self-administration, compactness, and ease of manufacture. Pellets are typically in the range of 0.5 and 1.5 mm in size. Pellets as a drug delivery system provide not only therapeutic benefits, such as reduced gastro-intestinal irritation and a reduced risk of side effects from dose dumping, but also technological benefits, such as improved flow properties, a less friable dosage form, narrow particle size distribution, ease of coating, and uniform packing. Another advantage of using a pellet formulation is the repeatability of medication blood levels. Pellets are often placed in hard gelatin capsules, but they can also be compacted into tablets[3]. Pellets, which are multi-unit dosage forms, are frequently utilized because they have manufacturing and therapeutic benefits over single-unit solid dosage forms[4]. There are various techniques to manufacture pellets, extrusion spheronization, hot-melt extrusion, solution or suspension layering, powder layering, high shear pelletization, freeze pelletization, cryopelletization, crystallo-co-agglomeration, wet spherical agglomeration, spherical crystallization, and much other pelletization techniques[5]. Extrusion spheronization is one of the most commonly used techniques in the formulation of such multiparticulate beads and pellets providing sustained and controlled release or modified release drug delivery. The extrusion spheronization was introduced by Reynolds (1970) and by Conine & Hadley (1970) and these will be helpful to produce uniform size with high drug loading capacity[3].

Extrusion spheronization provides,

- Uniform size, smooth surface, and narrow size which is having good flow properties.
- For masking the bitter taste of API'S.
- Dose dumping can be minimized / avoided[6,7].

The following are some of the most current innovative pellet trends:

a. Help to the preparation of modified-release multiple dosage forms with different release patterns like immediate and sustained release patterns.

b. Available as mouth melt pellets.

c. Polymer-based pellets control the release pattern of the drug.

d. As fast dissolving tablets containing micro pellets.

e. As self-emulsifying pellets.

f. Gastro retentive floating pellets etc.

The patient acceptability of pellets has risen as a result of this tendency. This new trend aids in providing information about the drug's releasing pattern and bioavailability in the systemic circulation of the drug, as well as how it has increased patient acceptance of pH-sensitive drugs releasing the pattern, taste mask, self-emulsification of pellets, and polymer-based control release of the drugs, mouth melt pellets[8].

EXTRUSION SPHERONIZATION

The extrusion spheronization process creates a highly efficient and streamlined development of the pellets. This extrusion spheronization is mainly used to produce uniform size spheroids/pellets. The particle size distribution plays a major role which ensures the control of the variability and helps in improving the flow properties & also during this process there is less wastage, and the pellets are produced with low friability. Physical properties of the active pharmaceutical ingredient can be altered easily to produce high bulk density particles, low hygroscopicity, free dust, and also a smooth surface. This process can incorporate the higher levels of active components without producing excessively larger particles, two or more active agents /components with different ratios can be easily combined with the same units[9,10].

The extrusion-spheronization technology is widely utilized in the pharmaceutical industry due to its rapid manufacture of pellets of all sizes and shapes along with its low cost, simple design, and excellent performance[11].

Extrusion spheronization mainly involves four steps: -

- Granulation
- Extrusion
- Spheronization
- Drying of pellets

○ GRANULATION

The dry powders are mixed to obtain the uniform distribution later on wet granulation or wet mass is been prepared with good plasticity, by mixing the powder blend and granulating liquid. The commonly used granulators are planetary mixer or sigma blade mixer and Hobart mixer[12, 13].

○ EXTRUSION

The wet granulated mass undergoes the extrusion with the applied pressure to amass until the flow occurs through the orifice the obtained mass is known as an extrudate.

This process involves the shaping of wet mass into cylindrical rod shapes of uniform diameter. The extrudate particles at their weight break at an equal weight & also the extrudate should have enough plasticity[12,14].

When rolled during the spheronization process, the extrudate must have enough flexibility to deform but not so much that the extrudate particles cling to other particles. The granulation solvent acts as a binding agent for the granules as well as a lubricant for the extrusion process[15].

EXTRUDER

The extruder name itself implies that it is used to develop sufficient pressure to force the material to flow into uniform openings that produce the extrudate.

In simple words, we can say an extruder is a pump or it is a machine that can produce pressure[14,16].

The extruder is mainly classified into four categories:

- Screw type extruder
  - ➢ Axial or Endplate extruder
  - ➢ Dome extruder
  - ➢ Radial extruder
- Gravity feed extruder
  - ➢ Rotary cylindrical
  - ➢ Rotary gear
- Sieve and Basket feed extruder
- Piston feed extruder
  - ➢ Ram extruder

Screw type extruder

The screw extrusion has majorly 3 zones, all these zones are having the mechanical principle of feed zone, transport, comparison zone, and extrusion zone. The screw extruder has one or two (twin-screw) for feeding the wet mass to an axial or axial extrusion screen.

❖ Axial extruder

The axial extruder is having the die plate which is placed axially, this consists of a feeding zone, compression zone, and extrusion zone. During the extrusion, the jacketed barrels are used to control product temperature. The axial extruder screen has been placed at the end of the screw which is perpendicular to its axis. This extruder is used for making pellets ranging from 300 microns to a maximum of 1500 micron[16,17].

❖ Radial extruder

Radial extruder the screen is been placed perpendicularly on the axis of the screw where the extrudate is discharging around the screw. In this extruder the transport zone is short and the materials are been extruded radially around the horizontal axis of the screw which is mounted through the screens. The pellets range ranges from 400micron to 1500microns.

❖ **Dome extruder**

The Dome extruder is similar to the axis extruder, but in this type, the assembly is placed at the end of the screw by dome shape[18].

Gravity feed extruder

Gravity feed extruder consists of both rotary cylindrical and rotary gear extruder where there is a difference between the design of the two counter-rotating cylinders.

❖ **Rotary cylindrical extruder**

In the rotary cylindrical type, two cylindrical are present in which one counter-rotating cylinder is perforated and hallow, and another cylinder is solid and acts as a pressure roller.

❖ **Rotary gear cylinder extruder**

The rotary gear cylinder is having the counterbored holes with two hallow counter-rotating gear extruder[4,17].

Sieve and Basket feed extruder

Sieve extruders are like flour sifter & the sieve extruder is having a chamber that consists of a screen or screen and material to be extruded. The damp material passes through the perforated screen and sieve which forms short and long extrudates with the help of an oscillating and rotating arm press.

The basket-type extruder is similar to a sieve extruder in which a sieve or screen is a part of a vertical cylindrical wall, the extrudate is been forced around the vertical holes from the horizontal plane[14].

Piston extruder

This piston extruder is based on the principle of the piston, where the wet mass pushes through the two screens which are present at the end of the barrel[18].

Ram extruder

Ram extruder is the oldest technique of extruder, where a piston displaces & forces the material to pass through the die at the end. These extruders are mainly used in the

development phase, where these extruders are used for the formulation purpose as the rheological properties[4,7].

Spheronization

Spheronization is also known as mesmerizer, which consists of a static cylinder and a rotating friction plate. The spheronizer duration will be around 2-10min and the speed of the friction plate will be around 200-400 rpm, in this, the optimum spherical pellets are obtained. The damping of the extruded cylinder occurs in the spinning plate spheronizer known as friction plate, in which the smaller cylindrical equal length diameter is obtained by breakdown or extrude. Extrude cylindrically was broken due to interaction of the extrude with a smooth plate, stationary wall and other extrude particles[4,7].

The extrudate formulation determines how pellets are formed during the spheronization process. Cohesiveness, hardness, and plasticity must all be present in the extruded granulation. Breaking the cylindrical segments, or extrudate, agglomerating the fractured segments, and flattening the particles are the three stages of this operation. The extrudate interacts with the revolving plate, stationary wall, and other extrudate particles, resulting in the breaking of the cylindrical segments. When the smaller pieces formed during the breaking stage are scooped up by the bigger granules during the smoothing stage, agglomeration develops. During the smoothing stage, spherical particles are formed by rotating each granule around its axis in a variety of planes[15].

Drying of pellets

To achieve the desired moisture content drying stage is required. The pellets can be dried at room temperature and also by elevated temperature by using a fluidized bed drier or try drier. During the drying of wet mass, the solute gets migrated, which increases the dissolution rate, pellets with modified surface and this results in less/reduced adhesion[4,7].

PROCESS VARIABLES FOR THE EXTRUSION SPHERONIZATION

- **Starting material**

The starting material which is available in nature influences the hardness, particle size, and particle shape, this results in a difference in the release rate of the loaded drug. The materials used in the pellet's formulation, there is a difference in the quality of pellets of the different compositions. The pellets which are produced using MCC (microcrystalline cellulose) of

three different types, there is a difference in the shape and size even it is manufactured in same conditions of different manfactures[19].

- **Rheological characteristics**

The wet mass of the rheological condition determines the flowability of the extrusion machine. The presence of optimum rheological conditions leads to good flowability of the wet mass from the extrude. The variation in the rheological condition makes the extrusion non-uniform and improper, this leads to the formation of non-uniform pellets[9,20,21].

- **Moisture content**

Moisture content is one of the most critical parameters in the production of pellets from spheronization. The presence of moisture in the wet mass brings cohesiveness to the powder this wet mass can be extracted and the spheronizer produces a spherical shape[22]. For the preparation of the pellets, the moisture content should be 10-15%. If more amount of water is present, this leads to agglomeration of pellets spheronization process[21]. The fine extrudates are obtained by large variation if the moisture content is less in the dump mass. The percentage moisture content is obtained by using infra-red moisture content and heated by using an infra-red lamp[23].

- **EXTRUSION OPERATIONAL VARIABLES**

  - **Extruders**

Axial screw extruder produces the denser material compared to radial screw extruder, according to Reynolds and Rowe. At the end of the production process, the output is high and also it shows greater heat production during the process. The quality of the pellet depends on the screen thickness. The presence of a thinner screen produces rough & loosely bound extrudate, while the presence of a thicker screen produces smooth and well bound extrude. This occurs due to higher compaction of wet mass[19].

  - **Extrusion screen/ screen pressure**

The stress force is required for the wet mass to pass through small orifice[22]. The amount of water added to the granulation purpose is linearly related to screen pressure. The screen pressure is directly dependent on the amount of load, the amount of water that is used for the granulation, blend composition, and also a few operational parameters such as pore size and screw speed, by altering these above parameters leads to slight changes in the screen

pressure. The orifice screen's properties have an impact on pellet quality; when the orifice dimension grows, the pellet size grows as well[24]. But increase in the orifice depth there will be a decrease in the water content in the extrdate[25].

- **Extrusion screen hole diameter**

The quality of the pellet depends on the extrusion screen which is characterized by two parameters.

✓ The thickness of the screen

✓ The diameter of the perforations

The presence of dimension on the screen hole during the extrusion plays a major role in the formulation of the pellet, which affects the final product of the pellet and also the mean diameter of the pellet. The diameter of the screen hole perforations determines the pellet size, if we are using larger diameter perforations the larger diameter producing pellets are produced. With the increase in the extruder size opening, there will be an increase in the hardness of the tablet from these pellets. The presence of the above two parameters will affect the pellet formulation such as size, shape, hardness, and surface morphology. The main selection of the optimal screen size depends on the specific size requirements of pellets and also based on their application[24].

- **Extrusion extruder type**

The extruder type influences the extrudate quality and consequently pellet qualities. Extruders with screens require the least amount of force. Pellet characteristics will vary depending on the type of extruder used. The extruder selection is very critical because it is not interchangeable. All the extruders are not designed for pharmaceutical use and some are used for food-grade extruders in which it doesn't meet the GMP (Good Manufacturing Practices) requirements. In some cases, only water content is required when there is a change in extruder type[24].

- **Extrusion speed**

The output of the extrusion and final pellet quality depends on the extruder speed. An increase in the extrusion speed results in an increase in the compressed force of the extruder present in the wet mass. The increase in the speed causes surface impairment, roughness & shark skinning these lead to lower the quality of the pellets, because during the

spheronization process the extrude will break unevenly during the initial stages[26]. The surface impairment leads to the production of wider size distribution, lower the pellet quality and also the generation of fines occurs by the uneven breakage in the extrude[19].

- **Extrusion temperature**

The temperature control is important in extrusion spheronization during the formulation of the thermolabile drug and also to optimize moisture content. During the extrusion cycle, there is a rise in the temperature, which causes the granulating liquid to evaporate from the granules this leads to a difference in the quality of extrudate batches. To avoid the rise in temperature in the extrusion cycle the colling jackets are used around the barrel of the screw extruder to keep the temperature at the predetermined limits during the formulation process[19,27].

- **Spheronization operational variables**

- **Spheronizer load**

The pellets yield decreases at a specific range with an increase in the spheronization speed with less spheronization load. But there is an increase in the pellet yield that occurs with an increase in the spheronization time at the higher spheronization load. With the increase in the spheronizer load, there will be an increase in the mean diameter. Newton et al. reported that at low load it gives poor molecular interaction but using high load poor plate and molecular interaction, they studied that at low load i.e., they used 50 & 100g of load which produces pellets of best length and it is having a minimum thickness and the circular structural is least. But while using the higher load like 750 & 1000g these produce round granule in long run, these procedure takes more time[12,27].

- **Spheronizer speed**

Spheronizer speed plays a major role in the quality of the spheres. At very low speed no changes of the shape occur in the extrudate and at high-speed size reduction of the particles occurs. The spheronizer speed affects the hardness, size, shape\sphericity, flowrate, friability, porosity, and density of the pellets. The spheronizer speed should be around 1000 to 2000 rpm for better quality according to Wan et al[12]. The lower spheronizer speed leads to the low harsh environment in the extrudate but during the high spheronization speed there is an increase in the sphericity along with high residence time, and it enhances the densification of

the pellets according to Ronowicz et.al. The optimized spheronization speed is required to achieve spherical pellets with a narrow size distribution[27].

- **Spheronizer time**

The influence of spheronization duration during high spheronization speed is extremely small, but a lower spheronization speed in an appropriate environment will result in an increase in total pellet yield. However, at low spheronizer speeds, the extrudate allows wet particles to agglomerate fine particles, resulting in a reduction in fine particles in the spheronizer. According to Wan et al., spheronizer time will be around 5-15min range to obtain the good quality. These spheronizer times had a variety of effects during the formulation particle size distribution, higher sphericity, density, and also changes in the yield occurs these the changes occurred by altering the spheronization time. The residence time is the major factor to obtain the superior product, however, the yield in the targeted zone will get lowered by an increase in the spheronization time. According to Ronowicz et al., spheronization speed and residence are the two important factors in producing good quality pellets[26, 27].

- **Mixer**

Bryan et al. made a comparison between the screw mixer and planetary-based mixer process in extrusion spheronization were reported. The pellets which were formulated using the screw mixer showed better/higher yield, strength, and these forms narrow size distribution of small pellets has compared to the planetary mixer.

There are different types of granulators that are used for mixing the powders with the help of the granulating liquid. The planetary mixer, sigma, or high sear mixer are the most commonly used granulators[12,27].

- **Friction plate**

In the spheronization process, a friction plate plays an important role, it consists of a grooved surface, and the frictional force increases during the spheronization process. In the case of obtaining good quality pellets, the friction plate and the diameter of the friction plate plays an important parameter.

There are two types of geometry grooves

- Crosshatch grooves
- Radial grooves geometry[27]

Michie et al. has been investigated the effect of different designs plates of the spheronizer, there are mainly three effects which include radial, crosshatch & striated edge design. All of these will show the effect on the physical properties of the pellet formulation. The change in the plate design will affect the yield value and also the marginal effect of the pellet was observed[28].

Zhang et al. investigated the effect of plate surface protuberances on the pellet water content pellet size, shape, and yield of the pellets.

The experimental results showed pyramidal design gave satisfactory performance among all four criteria, that is pattern plates large studs, saw-toothed, pyramidal, and small studs[29].

CHARACTERIZATION OF EXTRUSION SPHERONIZATION

- **Particle size distribution**

The pellets sizing plays a significant role in the influence of kinetics release. The parameters which influence the size of the pellet are geometric mean diameter, mean ferret diameter, particle size distribution, and the width and length of the pellet size can be determined. Sieve analysis is the method that is widely used in measuring the particle size distribution by using the sieve shaker and also by using microscopy the particle size distribution can be determined directly. To check the diameter of the pellets scanning electron microscope (SEM) and optical microscopy are used[30].

- **Surface area**

The surface area controls the characteristics of pellets which includes the pellet's size, shape, porosity, and surface roughness.

There are three methods of measuring the surface area of pellets.

- Mean diameter
- Gas absorption
- Air permeability

❖ **Air permeability**

The air permeability techniques are commonly employed in the pharmaceutical industry for specialized surface measurements, particularly where batch-to-batch fluctuations must be controlled. Fisher sub-sieve sizer is a commercially available device. The surface area of a substance acts as the primary barrier to the passage of a fluid, such as air, through a plug of compacted material. The specific surface area of uncoated drug granules was estimated in this study using sieve analysis data[30].

❖ **Mean diameter**

The mean diameter doesn't useful / does not provide many contributions for arising morphological characteristics such as surface roughness, porosity, and also the pellet shape[25].

❖ **Gas absorption**

The gas absorption is commonly known as the BET method which was developed by Brunauer, Emmet, and Teller (1937). This method was carried out by placing the sample in the chamber and air was evacuated within it. In this method the volume of nitrogen is used which is absorbed by the substrate in the evacuated glass blub and it is measured at different pressures[19,25].

- **Porosity**

The capillary action of the dissolved medication is affected by the porosity of pellets, which determines the rate of drug release from the pellets. Scanning electron microscopy (SEM) and a mercury porosimeter can both be used to determine the porosity of the pellets. Optical microscopy and scanning electron microscopy, together with image processing, can be used to assess the porosity of pellets in a quantitative way[25].

- **Density**

Changes in the formulation and/or method can modify the density of pellets, which can have an impact on other processes or factors such as capsule filling, coating, and mixing. The bulk density of the pellets is measured using an automated tapping machine. True density is a term that describes the degree to which a substance is compacted or densified[25,30].

- **Hardness and friability**

During the handling, shipping, storage, and also other operational units result in producing dust, so these hardness and friability play a role in producing the pellets. The different variables in the variables as well as the different variations in the formulation process of pellets result in potentially significant variations in the hardness and friability of the pellets. The instrument which is used to check the hardness value is the Kaul pellet hardness tester. The instrument used to determine the friability is an Erkewa-type tablet friabilator and to generate the abrasion Turbula mixer is used for a fixed period which is combined with glass beads of a certain diameter. The other method to determine the friability is a fluidized bed with the Wurster insert, in which the steam of air is used[19,25].

- **Tensile strength**

The tensile strength of the pellet is determined by the tensile apparatus which is having 5 kg load cell, the pellets are strained until the failure occurs. The tensile strength is calculated and load is recorded by applying the value for failure load & by using the pellets radius[30].

RECENT ADVANCEMENTS IN PELLETS

TARGET SPECIFIC PELLETS

Pellets are of particular relevance for use as cores in the manufacture of coated oral delivery systems due to their spherical or pseudo-spherical shape, consistent size, and smooth surface. Pellet formulations for colon administration can be coated with enzymatically degradable, pH-sensitive, or time-controlled polymer coatings. While layers susceptible to microbial breakdown or pH-dependent dissolution allow for targeted release based on physiological characteristics of the environment in which the drug is to be delivered. Time-based coats have the inherent ability to delay release throughout the small intestinal transit of the dosage form, regardless of regional differences in pH, microbial population, and other variables. Colon delivery methods based on coated pellets have been developed to take advantage of physiological pH fluctuations in the small and large intestine, to be enzymatically degraded by the colonic microbiota, or to delay the onset of release dependent on the time it takes for dose forms to reach the colon[31].

FLOATING PELLETS

The possession of Gastro retentive floating pellets is to extend the residence duration of the medicine and release it in a regulated manner. Because the floating pellets have a low bulk density, they float for a longer time in the stomach environment, increasing the drug's bioavailability[32].

SELF EMULSIFYING PELLETS

The solid self-emulsifying pellets of nitrendipine(SE NTD), a weakly water-soluble medication, were found and analyzed by Zhiyuan Wang. The recent findings suggest that SE NTD pellets with a 30% liquid self-emulsifying drug delivery system (SEDDS) may be efficiently produced utilizing the extrusion/spheronization method. The SE pellets that were produced were uniform in size, spherical in shape, and hard enough. The self-emulsifying properties of pellets were found to be intact. After self-emulsification in water, the droplet size distribution of the SE pellets was nearly equal to that of the liquid SEDDS, and in vitro dissolving performance was comparable for the liquid SEDDS and SE pellets, both of which were significantly larger than conventional tablets. When compared to liquid SEDDS, the oral bioavailability of NTD from SE pellets was much greater than that of conventional tablets, with no apparent difference. As a consequence, the extrusion spheronization technique may be utilized to generate solid SE pellets from liquid SEDDS, which can aid the oral absorption of poorly soluble medicines such as NTD[33].

COATING OF PELLETS

The development of better coating processes has been a major focus of recent advancements in pellet technology. Because the characteristics of the polymer coating, including the thickness of the polymeric film, can affect the release pattern of a pharmaceutical product, new approaches are being developed that give greater flexibility and stability. One of these processes is Wurster fluidization, a bottom-spraying technology known for its accurate film coating capabilities. The spray nozzle is centered on the coating zone and is positioned at the bottom of the product container. The impact and acceleration forces that occur during this process cause agglomerates to develop, which are subsequently smoothed out into homogenous and dense pellets before being dried. Despite the benefits of merging the several phases of pelletization into a single processing unit, which reduces processing time and

material handling, this approach is still not commonly used in the industry due to considerations such as cost and equipment availability[10].

PELLETS AS PROTEINS

Protein-based therapeutics such as vaccines, antigens, and hormones have become more popular, but limitations in biology limit the development and production of protein pharmaceuticals. Various tactics of drug delivery have been explored, including, different sizes, compositions, and shapes. The rapidly expanding pharmaceutical business is constantly looking for new active compounds to produce, which necessitates the development of an appropriate dosage form capable of properly delivering those molecules in the body. The use of pellets as a means for drug delivery offers biopharmaceutical advantages and overcomes the limitations of therapeutic proteins. Most commonly and effectively, extrusion spheronization can be used to produce multiparticle delivery systems for the oral administration of therapeutic enzymes and other proteins of interest with high-retained activity. Industrial use of therapeutic proteins and enzymes has increased, and these macromolecules are replacing low molecular weight chemicals due to their potency and specificity. As pharmaceutical industries develop new oral formulations and delivery technologies, they will continue to focus on these molecules in the future[34].

MELT IN MOUTH PELLETS

Extrusion-spheronization is a common method for producing dense granules with regulated and high sphericity in pharmaceutical and other industries. It is a multistep procedure incorporating several variables that have an impact on the final qualities of the pellets produced. The creation of "Melt in mouth pellets," or Meltlets®, is a revolutionary expansion of pellets as a delivery technique. Meltlets® are delightfully scented, rapid dissolving medication or nutraceutical pellets packaged in single-serve sachets. The contents of the sachet should be poured immediately into the mouth, where they will break down into a soft mass that may be taken without water. These mouth-dissolving pellets can include a wide range of medications and nutraceuticals, resulting in improved patient compliance and a competitive advantage in therapeutic categories where similar products are available. Ketkeedeshmukh et al. worked on the antioxidant activity of Meltlets of Soy Isoflavones showing that there is no change/alteration in the process parameter of the extrusion spheronization[35].

DEM MODEL IN PELLETS

Various interfering factors, including plastic deformation, breaking, attrition, and coalescence, influence the rounding of wet cylindrical extrudates in the spheronizer after the extrusion step. The particle rounding process in the spheronizer is not adequately described due to the complexity of these mechanisms, which are dependent on particle dynamics. To describe how the particle shape changes due to collisions, the Discrete Element Method (DEM) on the microscale is combined with a Particle Shape Evolution (PSE) model on the macro scale in this study. A new contact model was built for the DEM simulation to represent the cyclic, dominating viscoplastic deformation behavior. A precise contact model in the DEM is required in order to acquire correct deformation data for use in the PSE model. As a result, a single-particle elastic-plastic contact model was used[36].

SUGAR PELLETS

DSP (dexlansoprazole) is a proton pump inhibitor that degrades at an acidic stomach pH and is used to treat gastro-oesophageal reflux disease (GERD). Enteric coating slows the release of the drug in the stomach & makes it more effective. The inert core material was a sugar pellet that was exposed to drug loading, barrier coating, immediate delayed-release, and prolonged delayed-release coating. For drug retardation, L-HPC-31(low substituted hydroxypropyl cellulose) 5%was used[37]. The study was made on a multiparticulate drug delivery system loaded with galantamine hydrobromide in the drug was applied to the sugar pellets using a medium HPMC(hydroxypropyl methylcellulose suspension)a study was to refine the layering process to influence the critical process parameters in the formation of agglomerates. These five factors showed a critical impact on the degree of agglomeration of pellets i.e., product temperature, spray rate, spray pressure, airflow, HPMC concentration using factorial design. It was found that there is the highest agglomeration when the first factor was at a high level and the second factor was at a high level[38].

CONCLUSION: -

The aim of this study is to outline the numerous elements of the extrusion spheronization process that affect pellet quality. Process parameters, equipment parameters, and formulation parameters in the extrusion–spheronization method should all be thoroughly explored because they have the greatest impact on the final pellet properties. The hardness, porosity, surface morphology, and sphericity of the pellets are influenced by process parameters such

as drying rate, extrusion–spheronization speed, and time. Equipment parameters, on the other hand, have an impact on pellet yields, size distribution, and strength characteristics. Surface morphology, density, structural, and mechanical properties of pellets are all affected by formulation parameters such as moisture content and friction plate, etc. Pelletization has taken a unique place in the pharmaceutical business, particularly in the creation of multiparticulate oral controlled release dosage forms, because of its simple design, great efficiency in creating spherical pellets, and quick processing.

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