A Comprehensive Review on Morden Techniques Of Granulation

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ABSTRACT

One of the most crucial unit processes in the manufacturing of oral pharmaceutical dosage forms is granulation. The granulation process will improve the flow and compression characteristics.
lessen segregation, enhance consistency of the substance, and get rid of too many fine particles. The result will be improving yield reduce table defects, increase productivity, and reduced down time. All across the world, the processes of dry granulation, wet granulation, and direct compression are used to process pharmaceutical products. Choosing a technique necessitates a comprehensive analysis of each element in the recipe, their combination, and how they interact with one another. The method that is selected depends on the specific properties of the ingredients and their ability to flow, compress, eject, and disintegrate. After that, the appropriate granulation procedure can be used.
The objective of present article waste focus on the novel granulation technology

KEYWORDS: *Dry granulation, wet granulation, spray drying, freeze granulation, Morden techniques*

INTRODUCTION

The term Granulated is derived from the Granulate, a Latin word denoting a grained mixture. In the pharmaceutical industry in the granulation process, the term granules denote finely powdered particles that aggregate to create a larger, intricate structure. These formations usually range from 0.2 to 0.4 mm.[1-4]Generally particles, which range in size from 0.2 to 0.5 mm, are ideal for compression or mixing prior to compaction. Pharmaceutical granulation efficiently disperses agglomerates, improving the quality of drugs. Agglomeration techniques are used by industries not just to reduce dust but also to enhance handling but also to optimize the material's overall functionalityWetting and nucleation, coalescence or growth, consolidation, and attrition or breakage are the essential elements of granulation.
Granulation is the process of assembling particles by using binding agents or compression to form bonds between th e particles. For instance, granulated sugar is easier to compress into tablets compared to powdered sugar due to its better flow and compression characteristics. It is crucial to have sufficient fines to fill the void spaces between granules, promoting better compaction, along with optimal moisture hardness to prevent breakage and dust formation during processing.[1-4] Granulation serves the purpose of preventing segregation. The granules encompass a rounded shape to improve flow properties and

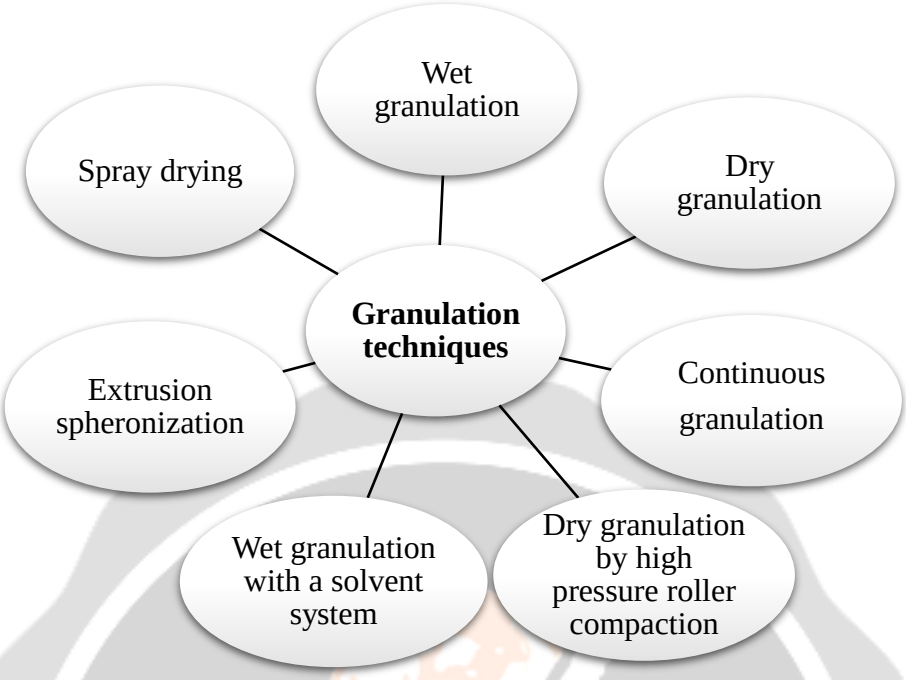

Fig.1: Types of Granulation Techniques

enhance compaction. The key components of granulation are influenced by factors such as spray rate or fluid distribution, as well as the properties of the feed powder and existing granules. The choice of a granulation process hinges on factors like drug physicochemical properties, excipients, desired flow, and release properties. The pharmaceutical industry witness's continual evolution in granulation techniques, including roller compaction, spray drying, supercritical fluid, low/high shear blending, fluid bed granulation, extrusion or spherization. The ongoing advancements and innovations further shape the landscape of granulation processes. Granulation serves various crucial processes. There are three types of granulations in the pharmaceutical industry: Dry granulation, Wet granulation and Melt granulation. [1-4] Granulation involves the assembly of particles by creating bonds between them through compression or the use of binding agents The qualities of the feed powder and existing granules, as well as variables like spray rate and fluid distribution, all have an impact on the essential elements of granulation. The physiochemical features of the medication, the excipients, the desired flow, and the release property all influence the property as granulate procedure.

Granulation processes, such as roller compaction, spray drying, supercritical fluid, low/high shear blending, fluid bed granulation, extrusion, or spherization, are constantly evolving in the pharmaceutical sector. The landscape of granulation processes is further shaped by continuous breakthroughs and advance cements. Granulation is useful for several important processes.

Granulation is a well-known size-enlargement technique that is frequently employed in the powder processing sector to enhance the stability, stability, and aesthetics of material handling qualities. Granulation can take place either dry or with the assistance of a liquid (wet granulation). High Shear Granulators (HSG), Fluidized Bed Granulators (FBG), and Twin-Screw Granulators (TSG) are frequently used for wet granulation. whereas Roller Compactors (RC) are primarily used for Dry Granulation. [1-4]

Studies on how much energy each of these activities uses, particularly in relation to one another, are still in their infancy, despite a growing body of research on the mechanics underlying each process. When it comes to the HSG, most of the research that has already been done uses the process's power demand to forecast how the granulation mix would behave, as opposed to using it as a foundation for energy efficiency ratings. As an example, assessed an HSG process's power consumption to determine the mix's over wetting point. In the interim, Similar research has been done on the TSG, with studies looking into how torque may be used as a process control tool to monitor granule size or

how power consumption can be correlated with granule shape. The literature in the FBG places a little more emphasis on energy efficiency and discusses ways to improve technology's energy efficiency, such as by temporally separating the steps of spraying and drying. The dearth of research on the RC was particularly severe, as there was no available literature assessing the process's energy usage. There isn't any literature that examines the energy usage of the entire granulation technology pathway while taking power consumption into consideration. [1-4]

Moreover, although extensive multi-granulator studies are available, they only take into account a few characteristics, like granule properties. There was not a single study comparing the energy efficiency of the granulation systems to one another. Gaining understanding of the energy economy of various granulation pathways and the important process parameters influencing them is crucial for making well-informed judgments on the best granulation pathway. The objective of this research is to conduct a thorough investigation into the energy consumption of the primary granulation technologies now in use in industry, taking into account the complete production pathway. he process energy efficiency component that considers both the process's granular output and energy expenditure will be evaluated based on their specific energy (kWh per kilogram of in-specification granules produced).

Aside from yield, other parameters like specified time (hours per kilogram of in-specification granules produced) were taken into consideration for assessing process affordability and sustainability. Important granule properties like friability, flowability, and dissolving time were also assessed to provide a quality factor that would set the technologies apart. Then, analytical and graphical tools have been suggested to assist producers in making decisions based on the combination of process appropriateness (determined by granule qualities) and process sustainability (determined by the material, time, and energy aspects).

AIM & OBJECTIVE:

AIM: A Comprehensive Review on Morden Techniques Of Granulation

OBJECTIVE:

- To improve the compaction characteristics of the mix
- To control density
- To produce a uniform mixture
- To improve the flow property of mix
- To eliminate poor content uniformity
- To produce dust free formulation
- To capture and fuse small quantities of active material
- It offers better content uniformity
- It also helps to minimize segregation risk

REVIEW OF LITERATURE:

Authors Name	**Year**	**Description**
Anu Rita Alves Marta Filipe Simoes Sergio Simoes Joao Gomes	2024	WET GRANULATION The pharmaceutical business still makes extensive use of the wet granulation method. Dicompression technology hasn't completely replaced it, in part because to habits and development expense considerations, and in part because it's still a useful technique in some situations. Even for high drug contents, it offers improved control over bulk density and, eventually, compatibility (brittle fracture), as well as improved control over drug content homogeneity at low drug concentrations.
A. Michrafy A. Zavaliangos 'J.C. Cunningha	2023	DRY GRANULATION: The pharmaceutical industry uses a powder agglomeration technique called "dry granulation" to increase the particle size (granules) of powders in order to improve their flowability.

B. Van Melkebeke, C. Vervaet, J.P. Remon	2022	CONTINUOUS_GRANULATION: The pharmaceutical sector is becoming more and more interested in continuous processes because to the growing need for solid dosage forms. These processes allow for increased production capacity, cost reduction, labor and space savings, and the avoidance of scale-up issues. Because they are the easiest to make and for patients to swallow, tablets are the most often used solid dose form. Tablets are made via wet granulation, which enhances the powder mix's compressibility,decreases dust and particle segregation, and improves flow characteristics.
Krzysztof Cal 'Krzysztof Sollohub	2021	SPRAY DRYING: The concept of spray drying has been around for a very long time. It involves spraying feed into a gaseous drying medium in order to change it from a fluid condition into a dried particulate form.

TECHNEQUES OF GRANULATION

WET GRANULATION

Using agitation and a liquid binder, small primary particles are bonded together in the wet granulation process, which increases particle size.[5-8] The goal is to enhance the characteristics of extremely fine cohesive powders that are used in goods like detergents, fertilizers, ceramics, and medication.

In the pharmaceutical sector, granulation is frequently utilized during the tablet-making process. Granulated fine powders enhance flow during tableting and lessen the chance of dusting. Granule formation also contributes to improved content consistency and decreased segregation in the finished product.

Pharmaceutical manufacturing uses a variety of wet granulation technologies, such as a twin-screw extruder, fluidized bed, rotating drum, and high-shear mixer.[5-8]

Pharmaceutical manufacturing uses a variety of wet granulation technologies, such as a twin-screw extruder, fluidized bed, rotating drum, and high-shear mixer. Particle size augmentation in wet granulation is accomplished by agitating the powder bed and adding a liquid binder to create agglomerates. Due to the fact that most granulation techniques use a fixed powder bed, they arebed

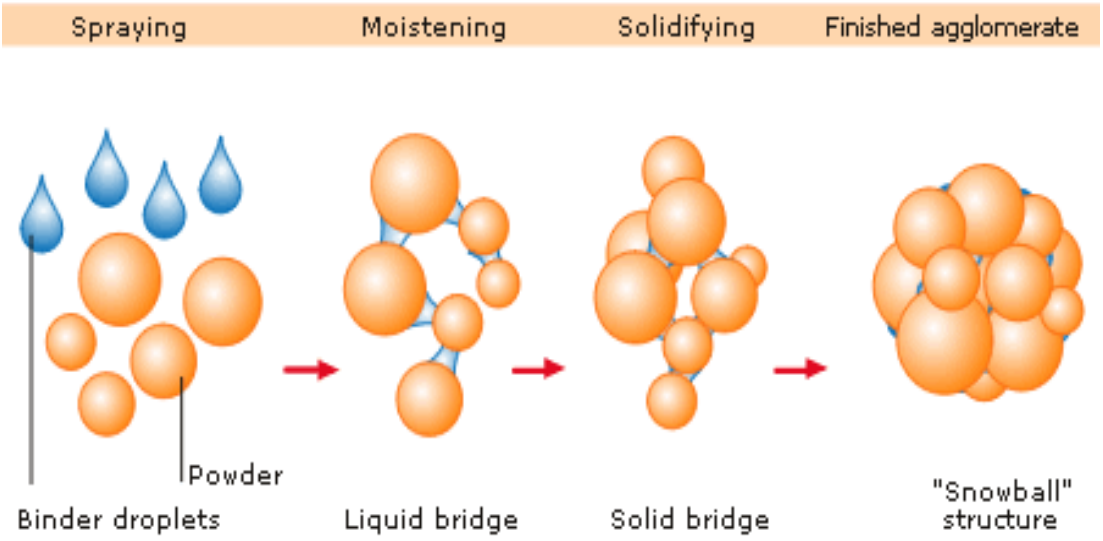

Fig 2: process of wet granulation

DRY GRANULATION

Other names for dry granulation include "slugging," "double compression," and "recompression method. It can be applied in situations when the components in the tablets are moisture-sensitive or cannot tolerate high temperatures during the drying process. [9-11]If the tablet ingredients have adequate intrinsic binding or cohesive qualities, dry granulation is the recommended technique in these conditions. Weighing, mixing, dry blending, dry screening, lubricating, and compressing are crucial processes in this process. Remington[9-11]

ADVANTAGES:

The primary benefits of dry granulation include Better disintegration for materials sensitive to heat or moisture because powder particles are not bound together by a binder.

DISADVANTAGES:

To form slug, a heavy-duty, specialized tablet press is needed.

It does not allow for the same homogeneous distribution of color as is possible with wet granulation, in which the dye is mixed into the binder liquid.

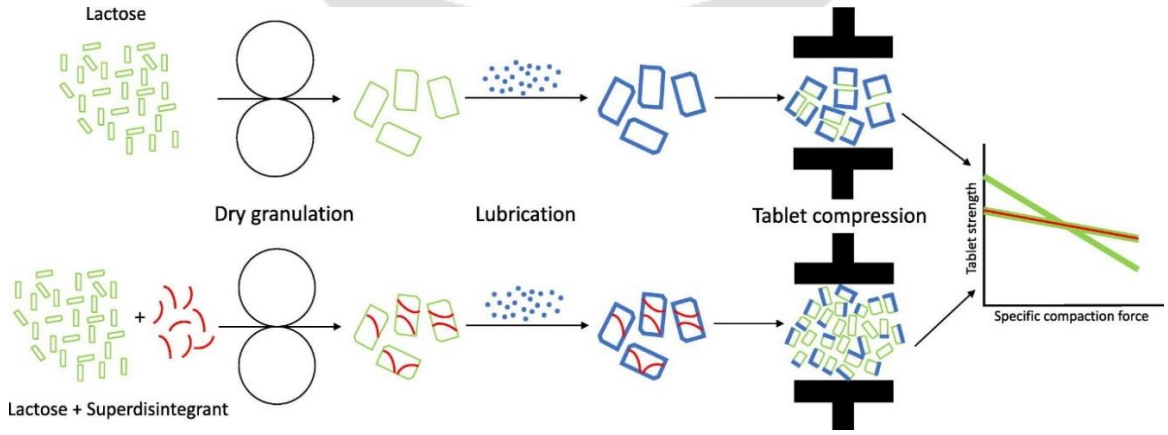

Fig 3: process of dry granulation

CONTINUOUS GRANULATION

In contrast to the food and bulk chemical industries, which have a long history of using continuous processing, the pharmaceutical sector has always manufactured its products using batch processing. The pharmaceutical industry has historically benefited from higher profit margins on its products, and over the years, little has been done to shift the primary manufacturing concept from batch to continuous processing.[12-14] In contrast, other industries have been driven by low profit margins to transition to continuous processing as a means of integrating time- and cost-efficient strategies into the production lines. Furthermore, it was widely held (mis)belief that (a) continuous manufacturing techniques could only be used for large-scale productions, far exceeding the capacities needed by the pharmaceutical , frequently even daily, in a pharmaceutical manufacturing facility; (c) continuous processes could not continuously meet the strict standards for product quality established by the pharmaceutical industry; and the regulatory authorities' of continuous.[12-14]

Continuous production lines have scarcely been introduced even for the production of tablets, the most popular dosage form. However, conventional equipment can be used to perform numerous processes in a tablet production line, such as tableting and packing, in a continuous mode. The granulation stage, where particle agglomeration is occurring, is a bottleneck that is preventing the adoption of a fully continuous tableting process, which would begin with the dispensing of the individual powder components and end with the packing of the tablets in blister packs or bottles is frequently necessary to enhance the powder mix's homogeneity, compressibility, or flow characteristics.[12-14] However, a number of factors have encouraged pharmaceutical companies to look at the possibilities of continuous processing as a way to lower the cost and time-to-market of their products in recent years: (a) using production in batches The only ways to meet the increasing demand for tablets are to install multiple batch processors in tandem if one is at capacity or to use larger batch processors, both of which require a significant financial expenditure.[12-14] (b) A wide variety of granulators are needed to scale up a batch granulation process from the lab to the production scale.

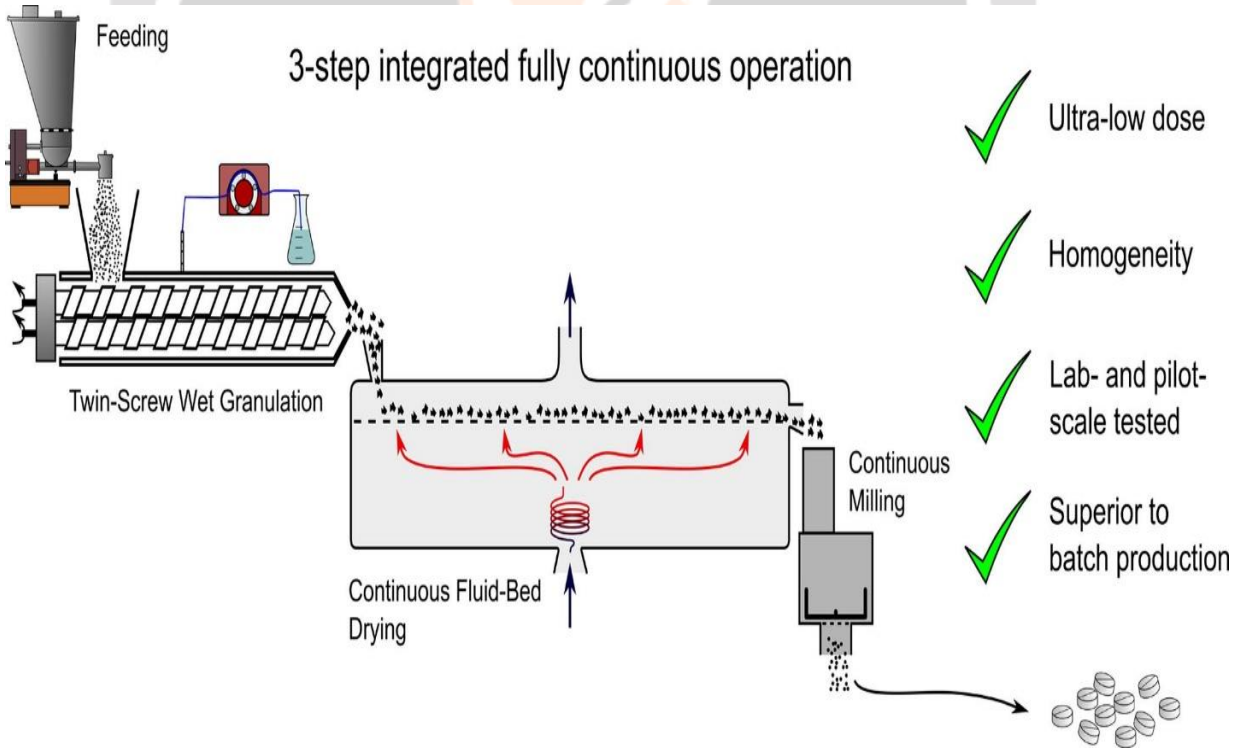

Fig 4: process of continuous granulation

DRY GRANULATION BY HIGH PRESSURE ROLLER COMPACTION

In the chemical, pharmaceutical, and life science industries, roller compaction is a well-established method of continuous dry granulation. The most typical goal in pharmaceutical applications is to make a powder or powder mix more flowable so that a tablet press may be filled quickly and uniformly. Producing tablets with a consistent weight and adequate strength while preserving a uniform distribution of the active pharmaceutical ingredients (API) is a difficulty. For a variety of items, roller compaction can accomplish this without the use of extra components like binders, moisture, or lubricants. Moreover, the use of roller compaction for dry granulation reduces storage volume, boosts bulk density, enhances handling, and modifies the dissolution properties[15-17]

There are two steps involved in roller compaction dry granulation. Agglomeration is the initial stage, which proceeds from powdered raw materials to flake. The flake, often called the ribbon, is a band that emerges from the roller compactor looking like a tablet. The Feed Screw with Vacuum Unit is used to transport the poorly flowing raw material powder from the Feed Hopper to the Rollers, where it is compressed into a flake. The second phase, From Flake to Granulate, reduces size. Here, a flake crusher, pre- and fine granulator are used to mill the flake and reduce it to a well-flowing granulate The following crucial factors determine the flake quality:

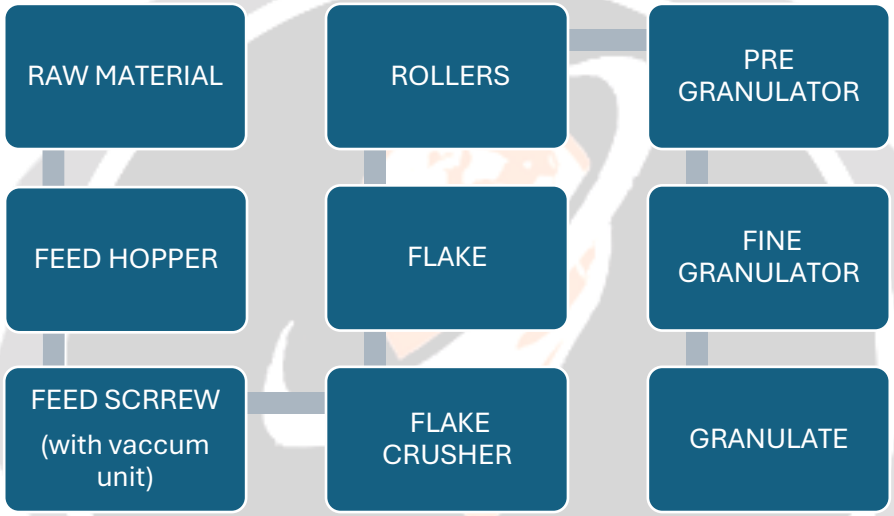

Fig 5: Flow Diagram of a Roller Compactor

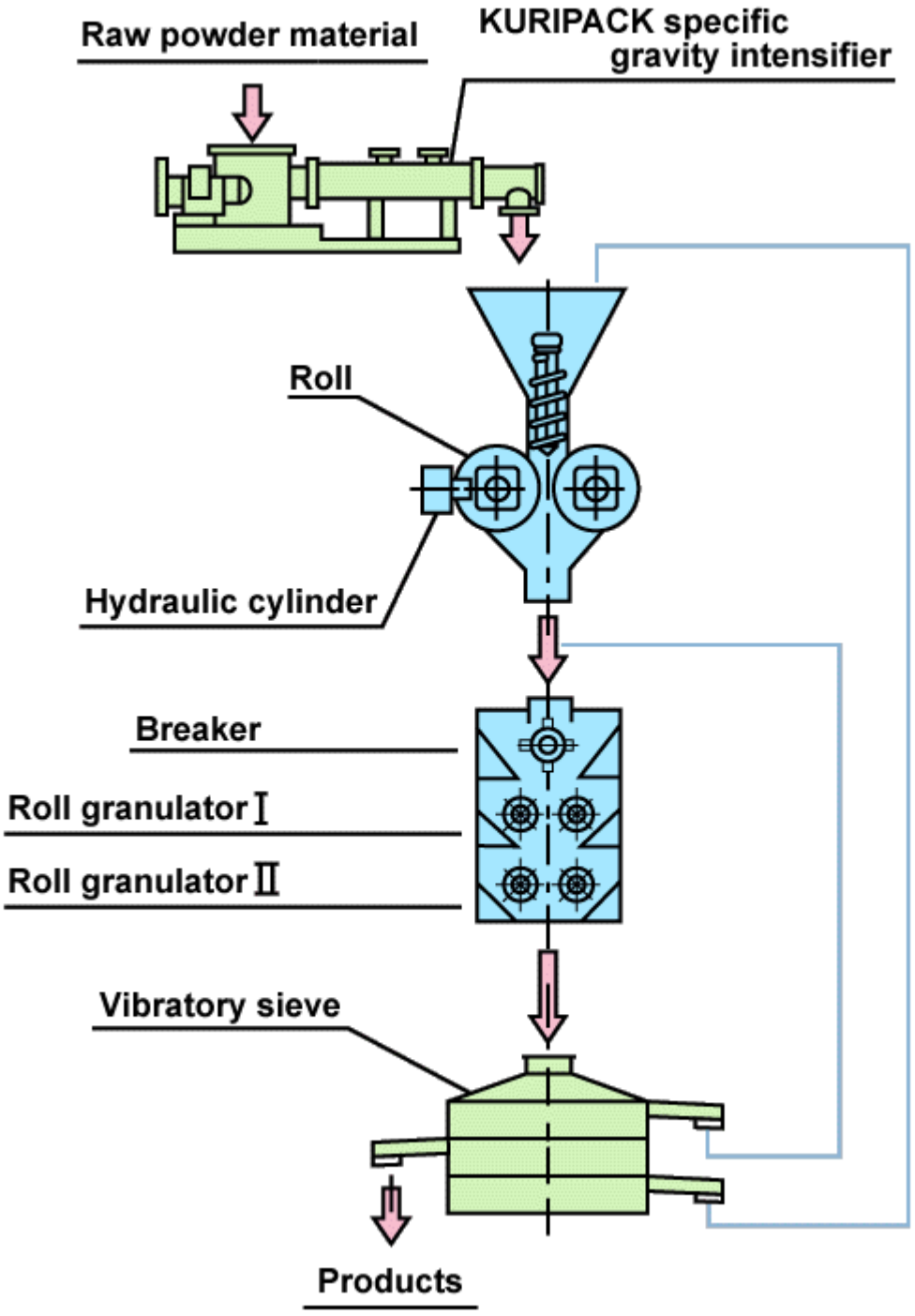

Fig 6: Detailed view on a Roller Compactor

EXTRUSION SPHERIZATION

The extrusion–spherization technique is the most popular method of producing pellets .This process was first reported by Reynolds and by Conine and Hadley and involves four steps:

(i) preparation of the wet mass (granulation).

(ii) breaking up the extrudate and rounding of the particles into spheres (spherization);
(iii) drying of the pellets

According to Galland wetting operation brings the material to a state in which porosity to water content. Spherization is merely a shaping procedure that preserves the hydro-textural state of the material, whereas extrusion densifies the material to the point of saturation.[18–20] Through the process of induced shrinkage, the drying procedure densifies the medium and completes the textural qualities of the product. Compared to other techniques, extrusion-spheronization offers a number of benefits, including the ability to integrate active ingredient concentrations that are greater.
without creating unduly large particles; the ease with which two or more active agents can be combined in any ratio within a single unit; the ability to modify the physical properties of the active ingredients and excipients; Having the capacity to create particles with a smoother surface, dust-free, narrow particle size distribution, high sphericity, low hygroscopicity, and high bulk density.[18-20]

EXTRUSION

The physical properties of the materials to be extruded, the extrusion process, and the way the particles are treated after extrusion can all affect the extrudate length. There are four primary types of extruders used for extrusion: screw, sieve and basket, roll, and ram extruders[18-20]

SPHERIZATION

Spherization is the process by which the extruded, cylindrically shaped particles break into uniform lengths and eventually take on spherical shapes; plastic deformation is responsible for this shaping. The process of breaking extrudates into nearly uniform lengths yields spheres with a nearly uniform diameter and determines the three dimensions of the agglomeration[18-20] shape.

Depending on the shape of the particles, different stages of the spherization process can be identified, such as cylinders over rounded-edge cylinders, dumbbells, and elliptical particles, leading to the eventual formation of perfect spheres. In this mechanism, the cylinder twists after rounded-edge cylinders form, ultimately resulting in the cylinder breaking into two distinct parts.

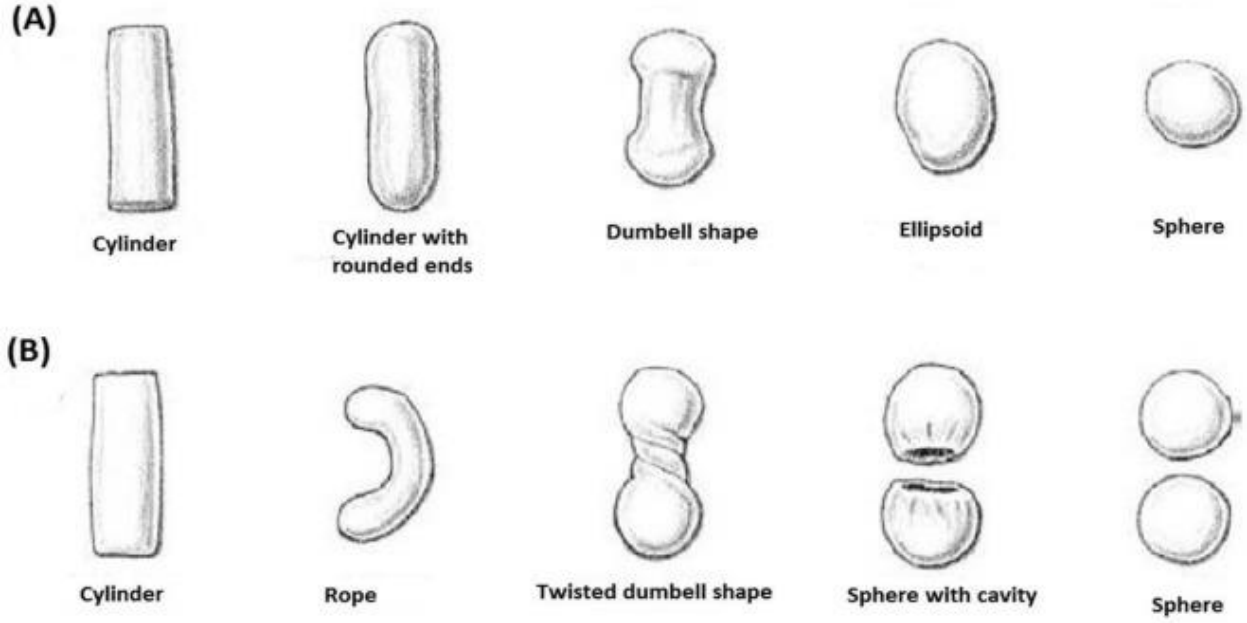

Fig 7: Pellet-forming mechanism according to (A) Rowe and (B) Baert.

(Placeholder1)

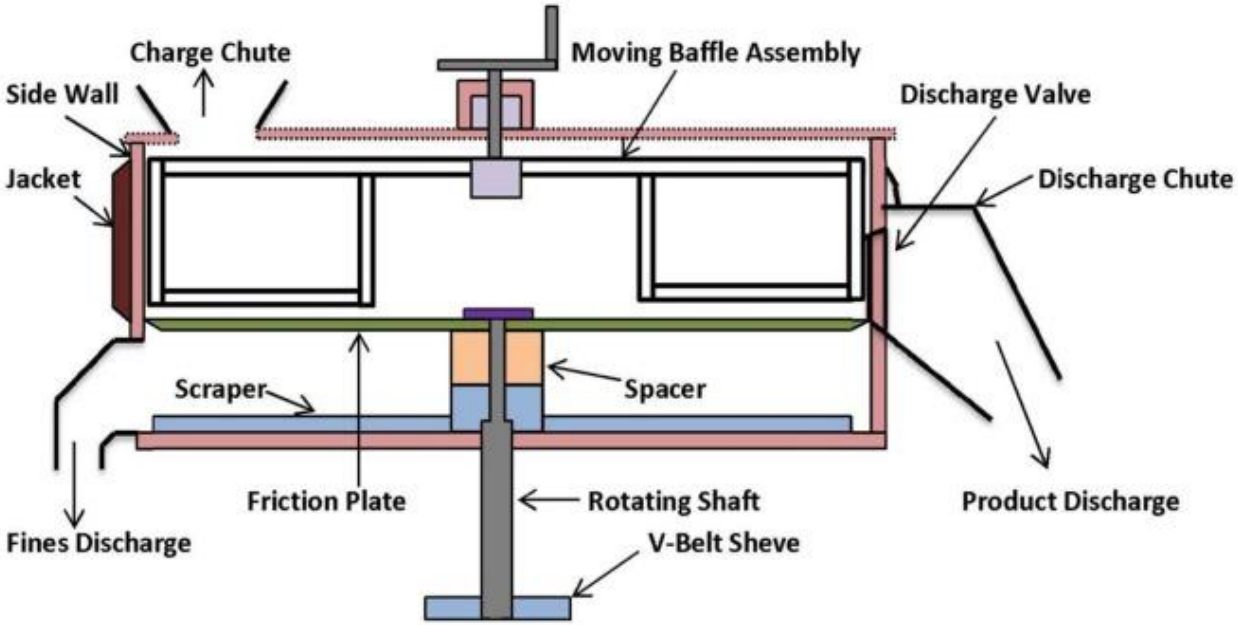

Fig 8: Schematic of spheronizer.

SPARY DRYING

For a very long time, people have discussed the concept of spray drying, which involves turning feed from a fluid state into a dried particle form by spraying the feed into a gaseous drying medium.[21–23] The earliest reference to the use of this drying technique dates back to 1860, and the first spray drying patent was filed in 1872. At the time, the spray dryers were antiquated machinery with issues with process efficiency and constant

SPRAY DRYING PHASES AND SPRAY DRYER CONSTRUCTION

The first one is the atomization of the liquid stream by an appropriate device[21-23] Next, fine droplets of the feed are subjected to the interaction with a drying gas at adequate (usually higher than feed) temperature

During the drying phase, the solvent contained within the dispersion droplets is vaporized, which results in the formation of solid product particle.

ESSENTIAL GUIDELINES FOR HEAVY DRYING PROCRDURE

Spray drying is one of the trickiest drying methods that an operator may find particularly challenging. [24-25] The drying air's input temperature is directly influenced by the spray dryer operator.

The atomizing air's pressure (and volume); for the pneumatic nozzle, this refers to other suitable atomization-related additional process variables, including the drying air's exit temperature.

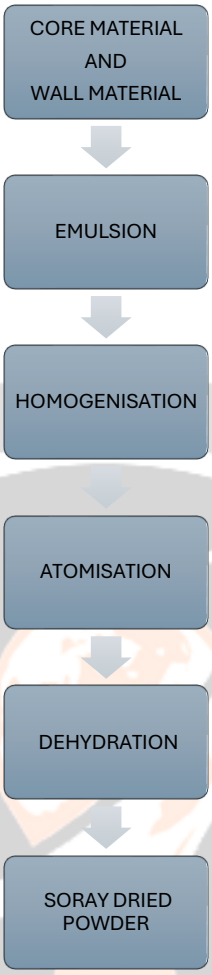

Fig 9: steps involved in spray drying

CHARACTERSTICS OF GRANULS

extracellular polymeric substances (EPS)[26-27]],
settling velocity,
permeability,
size distribution,
hydrophobicity,
physical strength,
microbiological activity

CHARACTERSTICS OF GRANULAR MATERIALS

The topology of a granular assembly is determined by the collection (set) of particles that make up a granular material[26-27] These particles are connected to one another through physical interactions as well as potentially through virtual connections between adjacent but non-touching particles.

ADVANTAGE OF GRANULATION

Masking of Tabulation Deficiencies It can be difficult to create a tablet with the ideal shape, particularly if the material isn't ideal. However, this is possible with the help of wet granulation because this procedure hides the flaws in the ingredients used to make the medication.

However, dry granulation will yield to the properties of the substance.[28-30] As a result, moist granulation typically yields more spherical tablets. Moreover, their flow qualities are frequently better.

Better Compressibility Dry granulation presents a challenge in that it typically necessitates the application of high compression pressure. Manufacturers of pharmaceutical items won't have better compressibility is provided by this process, negating the requirement for high compression pressure.

Aids Tablet Coating In certain pharmaceutical processes, tablet coating is required because of things like the active ingredient's odor.
At that moment, dry granulating will not be effective. Instead, because the tablet is still pliable for post-processing activities, moist granulation simplifies this process. Wet granulators are more expensive, but this is one of the reasons why many pharmaceutical businesses choose to use them.

Reduce The Risk Of Air Entrapment[28-30] Air entrapment is a major obstacle to tablet compressibility. Once air is trapped between the drug's powder particles, it becomes difficult to compress, and a tablet loses its professional appeal. As a result, pharmaceutical companies work hard to prevent this from happening. Wet granulation, on the other hand, gives higher powder compressibility than dry granulation because it fortunately offers an efficient answer in this regard.

Limits The Level OF Dust Drug contamination throughout the production process is the last thing that makers of pharmaceutical products want to happen. The purpose of drugs is to treat patients, not to cause illness. Preventing dust during this operation is one method of avoiding contamination. By lowering the likelihood of dust exposure, wet granulation safeguards the workers engaged in the procedure.

DISADVANTAGE OF GRANULATION [28-30]

The method's main drawback is that it produces a larger percentage of fines or particles.
Not all materials are acceptable for the technique.
The roller compaction method requires a piece of specialized heavy-duty equipment
The process tends to produce friable tablets.

Conclusion

We examine both dry and wet granulation techniques in our comprehensive review, which dives into the intricate realm of conventional and advanced granulation techniques in pharmaceutical dosage forms. We look at three primary methods of dry granulation: roller compaction, slugging, and pneumatic dry granulation. We go over each method's operation, advantages, disadvantages, and useful applications. We investigate eleven methods for wet granulation, from Twin screw wet granulation to High shear granulation. Every method is thoroughly described, emphasizing its functions, benefits, drawbacks, and particular uses. Pharmaceutical professionals can benefit from the knowledge in this article, which covers everything from the inventive Twin screw wet granulation to the efficient High shear granulation. This review highlights the various granulation techniques and provides a thorough reference for researchers and practitioners.

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