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A Review of Recent Techniques for Granulation

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Abstract

Granulation is the process of designing particles by combining primary power particles into massive multiparticle structures known as granules. Its primary purposes are to boost the flow of power, prevent segregation, improve the compaction characteristics of mix uniformity, and improve the flow and compressibility of powders. It also produces a combination that is uniform. Wet granulation and dry granulation are the two primary categories of granulation methods. The granulation process is contingent upon the description of the ingredient entity and its ability to surge appropriately, compact, and collapse. Choosing the appropriate granulation method necessitates a methodical examination of each ingredient in the combination and how they interact. Granule particle size is determined by the amount and feeding rate of the granulating liquid. New methods have been added to the granulation process to improve it: foam binder granulation, fluidized bed granulation, melt granulation, activated dry granulation, heat adhesion granulation, steam granulation, spray drying granulation, and freeze granulation. The major purpose of this page is to provide an overview of each advancement, including its limitations and relevance.

Introduction

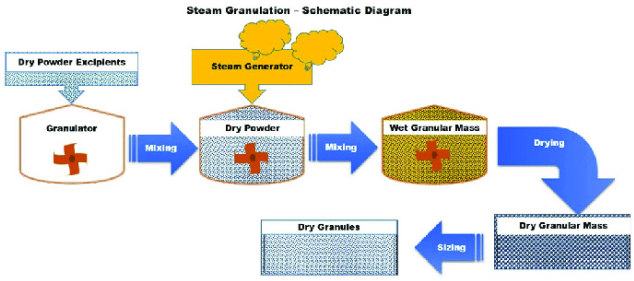
Granulation is a particle design process where small particles are gathered together for the formation of physically strong agglomerates. The primary powder particles are made to adhere to form larger, multi particle entity called granules. Pharmaceuticals granules typically have a size range between 0.2-4.0 mm, depending on the subsequent use of the granules [1]. Although granules used in the pharmaceutical industry have particle size in the range of 0.2-4.0 mm, they are primarily produced as an intermediary with a size range of 0.2-0.5 mm to be either packed as a dosage form or be mixed with other excipients before tablet compaction or capsule filling [2]. Pharmaceutical granulation is the rapid breakdown of agglomerates, are important to maximize the available surface area and aid in solution of the active drug. In ancient times the granulation process used within the pharmaceutical industry but in modern time, granulation technology has been widely used by a wide range of industries, such as Pharmaceutical. "granulated" material is derived from the Latin word "gran latum," meaning grained [3, 4]. Granulation is process of particle designing [2]. Granulation is required to prevent segregation, to improve flow properties, to improve (compaction [1].

Granulation is a single mostly significant component operation into manufacturing of oral dosage forms in pharmaceutical industry. Granulation procedure get better compression and flow quality get better comfortable consistency quantity of well element. The result is production be process all over the use a direct-compression, dry-granulation and wet granulation techniques.

Reasons to Granulate

- Improve the flow
- Densify the materials
- Improve compression characteristics
- Control the rate of drug release
- Facilitate metering or volume dispensing
- Decrease dust generation and reduce employee exposure to drug product
- Improve the appearance of the tablet
- Volumetric dispensing.[6]

STAGES OF GRANULATION



1) Pendular stage: This is initial stage just after addition of binding agent.

2) Funicular stage: This is a second stage where adequate binding solution incorporated between the particles.

3) Capillary stage: In this stage binding solution entrapped by capillary action. This is a perfectstage where good granules were obtained.

4) Droplet stage: over wetting particles may form. This stage is not desirable.[4-7]

Classification of Granulation Technologies

Based upon the type of processing, that had been involved, GT can be classified asfollows:

1. Conventional methods[8]
   - Dry granulation
   - Wet granulation
   - High shear granulation
   - Low shear granulation2.Novel methods[9]
     - Moisture activated dry granulation
     - Thermal adhesion granulation
     - Pneumatic dry granulation
     - Melt granulation
     - Fluidised bed granulation
     - Spray drying granulation
     - Freeze granulation
     - Foam binder granulation
     - Steam granulation

FREQUENTLY USED GRANULATION METHODS

- WET GRANULATION
- DRY GRNAULATION

WET GRANULATION

We granulation involves the massing of a mix of dry primary powder particles using a granulation fluid. The granulating fluid contains a solvent that must be volatile, so that it can be isopropanol either alone or in combination. [3]

Advantages

- The cohesiveness and compressibility of powders are improved.
- Good distribution and uniform content.
- A Wide variety of powders can prepared in a single batch.
- Controlled release dosages from can be accomplished by the selection of a
- Suitable binder and solvent.[1-10]

Disadvantages

- Expensive: time & energy consuming process
- specialized equipment required.
- stability issues for moisture sensitive and thermolabile API with aqueous granulation.
- It requires a number of pieces of expensive equipment also time consuming.
- There is a possibility of material loss during processing due to transfer of materials from one unit to another and have possibility of cross contamination. [1-10]

DRY GRANULATION

Dry Granulation Dry granulation is a simple and low cost method and becoming more popular because of its simplicity and cost efficiency. Methods available to improve dissolution include salt formation, and addition of solvent or surface active agents [20]. In dry granulation method the primary powder particles are aggregated at high pressure. There are two main processes – either a large tablet (known as slug) is produced in a heavy duty tableting press or the powder is squeezed between two rollers to produce a sheet of material (roller compaction) [9]

ADVANTAGES

- Eliminates exposure to moisture and drying
- Eliminates binding solution process. [13]

DISADVANTAGES

- Dusty procedure
- Not suitable for all compounds
- slow process

NEW GRANULATION TECHNOLOGIES

- Steam granulation
- Melt granulation
- Moisture activated dry granulation
- Thermal adhesive granulation
- Freeze granulation
- Fluidized bed granulation.
- Spray drying granulation
- Foam binding granulation.[1-4]

STEAM GRANULATION

In steam granulation technique steam is used as a binder instead of water [12]. A steam granulation technique involves the injection of a jet of steam into a bed of fluidized particles to be granulated. The jet of steam is substantially enveloped by a jet of air to inhibit the premature condensation of the steam onto the fluidized particles and/or the condensation of the steam onto the neighbouring walls of an apparatus employed to fluidize the particles, thereby this process inhibits excessive wetting and lumping of the particles during their granulation

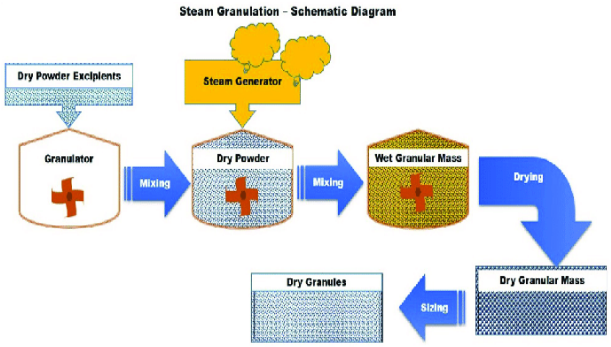


Figure: 1

Advantages

- Uniformity distributed in powder particles.
- Higher diffusion rate
- Results more in spherical granule formation
- No health hazards
- Maintain sterility. [8]

Disadvantages

- Requires special equipment for steam generation and the transportation
- Requires high energy inputs
- Thermos labile materials are poor candidates
- More safety measure required
- Not suitable for all the binders. [1-4]

Melt Granulation

Granulation technique is a process by which pharmaceutical powders are efficiently agglomerated by a meltable binder. The advantage of this technique compared to a conventional granulation is that no water or organic solvents is needed. Because there is no drying step, the process is less time consuming and uses less energy than wet granulation [21]. Melt granulation is an appropriate alternative to other wet granulation techniques which are used for water sensitive materials. Melt granulation process is currently applied in the pharmaceutical for the manufacture of variety of dosage forms and formulation such as immediate release and sustained release pellets, granules and tablets [22,23].

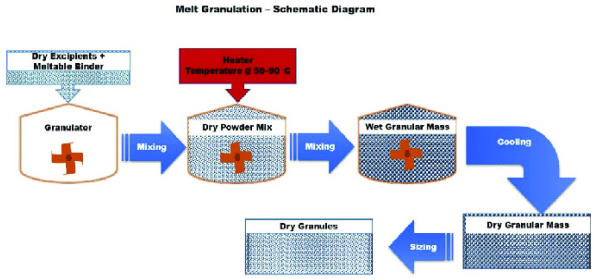


Figure: 2

Advantages

- Time and cost effective
- Controlling and modifying the release of drugs
- Water sensitive drugs are good candidates. [20]

Disadvantages

- Heat sensitive materials are poor candidates
- Lower melting point. [16]

MOISTURE ACTIVATED DRY GRANULATION

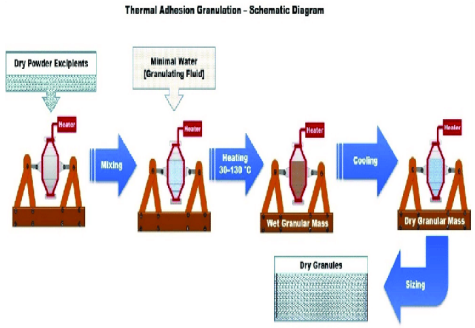


Figure: 3

In the moist granulation technique (MGT), a minimum amount of liquid is used to activate a binder in a planetary mixer [15]. Then, any excess moisture is absorbed by the addition of a moisture-absorbing substance. Based only on the particle size, moist granulation appears comparable to conventional wet granulation for this formula. However, this technique could not be used for the preparation of granules that require high drug load and for moisture sensitive drugs and hygroscopic drugs due to stability and processing problems associated with these types of drugs [11-18]

Advantages

- Applicable t0 more than 90%of the granulation need for pharmaceutical, food andnutritional industry
- Time efficient
- Suitable for continuous processing
- Less energy involves during processing

Disadvantages

- Unsuitable for thermos-liable, moisture sensitive, high moisture adsorbing substances.
- Difficult to develop formulations with high drug loading. [8]

Applications

- Sustainable for eutectic and hydro-phobic substances. [8]

FOAM BINDER GRANULATION

This method involves the addition of liquid /aqueous binder as foam instead of pouringliquid on to the powder particles. No spraying nozzle is used, less water required and cost effective. A simple foam generation apparatus is used to incorporate air in to a conventional water soluble polymetric excipients binder such as METHOCEL [6]

Advantages

- No spray nozzle is used
- Improve process robustness

Disadvantages

- Increase in temperature may cause chemical degradation of thermolabile material.
- Over wetting of granules can lead to large size lumps formation. [8]

Fluidized Bed Granulation

Fluidized bed granulation process involves spraying of binder solution on to the fluidised powder bed to get

finer free flowing and homogeneous granules employing single equipment known as FPB it contains air handling unit product container and air distributor spray nozzle disengagement area and process filters exhaust blower or fan, control system, solution delivery system. [21]

Advantages

- It involves short processing time.
- Requires less amount of liquid binders required with respect to fluidized bed granulation technology
- High cohesive material can be handled. [14]

Disadvantages

- Mechanical degradation could take place in case of fragile particles.
- Results in the uneven distribution binder solution throughout moving powder bed during high shear granulation.
- Unsuitable for thermolabile material
- Over wetting leads to formation of lumps and large sized granules. [17]

SPRAY DRYING GRNANULATION

This method is continuous process where a dry granular product is obtained by feeding a binding solution or a suspension of active agent with or without excipients to dry system where the feed is atomized and dried with a heated gas stream followed by subsequent separation of granular product from gas stream. Alternately particle agglomeration was brought about by spraying the binder solution on to bed of powder particlesin fluidized state archived with the passage of air follower by drying using hot air [19-25]

Advantages

- It is a fast and continuous process
- Cost lost
- Reduce apparatus exposure to dust [16]

Disadvantages

- Substances which are sensitive to heat are poor candidates
- Improper spray inadequate sized particles [12]

Applications

- In preparation of dry syrups and dusting particles

Conclusion

Improvements in granulation technology have made it possible to formulate dosage forms with improved stability and content homogeneity. The pharmaceutical businesses still need to conduct a great deal of research and study to support content uniformity and stability in dry syrups, different other formulations, and tablets and capsules.

Author contributions

All authors are contributed equally.

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Declaration of Competing Interest

The authors have no conflicts of interest to declare.

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