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AN OVERVIEW OF WET GRANULATION TECHNIQUE FOR BULK DRUG TABLET FORULATION

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ABSTRACT

The wet granulation method is simple, precise, accurate, and selective for the estimation of drugs in bulk and is in tablet dosage forms, the method is economical, rapid and do not require any sophisticated instruments. This review also describes about the techniques used for preparation of wet granulation and also describes about stages of granules development. A judicial selection of appropriate technology for carrying out the granulation processes the key to achieve a targeted granulation and final product parameters. in depth knowledge of the processing techniques and their merits and demerits is required to adopt during development stage of product.

KEYWORDS: Wet Granulation, Binder Solution, Nucleation, Coalescence, Granules.

INTRODUCTION'[1,2]

Pharmaceutical wet granulation (WG) is a size-enlarging procedure used to change the initial material's properties such as flow, density, binding, compression, disintegration, and other qualities. The wet granulation procedure is a standard process used in the production of solid dosage forms like tablets and capsules. It normally entails a number of laborious processes. But because the product is no longer visible or accessible during the process in the one-step "one-pot" operation, these novel approaches may likewise amplify possible issues in process control. Because they affect the process and product quality, it is important to detect these aspects at the bench level before automated processing starts. This will allow for proper control. A better understanding of pharmaceutical manufacturing processes and more precision in regulating crucial factors are now necessary due to recent advances in the

pharmaceutical sector. The Food and Drug Administration now requires the idea of "validation" as a part of the creation of new pharmaceutical goods. It is vital to measure how various variables affect the process and the final products, as well as to offer evidence of how those final products might be impacted during the process. In addition to providing proof of how those ultimate goods may be impacted during the process, it is critical to measure how different variables affect the process and the final products. It is crucial that the quality and effectiveness of the dosage form are not compromised as products move from the developmental stage to the production scale, such as from the granulation stage to the manufacturing of tablets or capsules, or when technologies are transferred. Therefore, research and case studies are being conducted to.

Mechanism of Wet Granulation'[3]

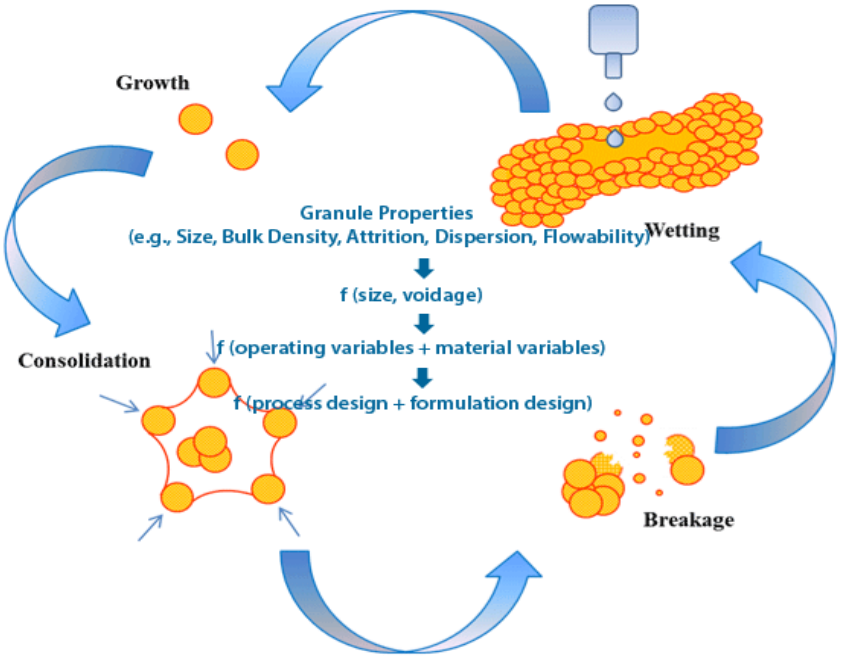


FIGURE [1] Mechanism of Wet Granulation'.[3]

Characteristics of an ideally drug delivery system'[3]

- Each component of the formulation needs to be evenly distributed throughout the granules.
- To guarantee reproducible flows, which in turn provide constant tablet weight throughout the batch, a suitable granulation should have a shape that is as close to spherical as possible.
- The hopper must not experience the separation of granules with different sizes or densities as a result of machine vibration.

- To lessen die-wall friction, granules should have good disintegration characteristics and lubrication.
- The fines in the granules should be enough to fill any gaps left by the coarse granules for enhanced compression properties.

Reasons for granulation

Granulation causes: Powder mixtures are transformed into granules for a variety of reasons.

1. To enhance the flow properties of powder mix.
2. To prevent segregation of powder components during tablet ting or storage.
3. To reduce the incidence of dust production.
4. To reduce cross-contamination and hazard associated with the generation of toxic dust that may arise during manufacturing processes.
5. To improve the compression characteristics of drug substances.

Special features of Wet Granulation

1. Wet granulation is used to form agglomerates of a certain particle size from single powder ingredients.
2. Processes like wet granulation are required in order to achieve a homogenous.
3. Compressible "mixture" of the single components of a solid oral dosage form for aqueous and solvent based wet granulation.

Advantages of Wet Granulation

a. Enhance the powder's flowability, cohesion, and compressibility to make it easier to compress.
b. Lower binder concentration due to the layer of a binder surrounding the powder particles, as well as lower pressure and energy compared to dry granulation.
c. May be utilized for strong, heat-insensitive drugs with high doses of compressibility. keeping the distribution uniform for low dose
d. The prepared compacted tablets' hardness, disintegration, dissolving, correlation, and preparation.
e. Due to the moisture in the previously used water, hydrophobic drugs dissolve more quickly.
f. Maintaining good content homogeneity because particle segregation is prevented because each granule has the same density as a different component of the powder mixture.

Disadvantages of Wet Granulation

a. The intimate mixing of water with the formulation components is a drawback of both low and high shear granulation.
b. Heavy energy consumption
c. Less important factors to consider are the binder's selection and addition technique as well as the impact of temperature and drying time on the distribution of the drug within the solid mass. Water makes it stable.
d. Although wet granulation exists,
e. There are still numerous intrinsic drawbacks to the wet granulation method.

Techniques for preparing Wet Granulation[5]

- By traditional sieving method
- By using extrusion granulation technique
- Dry and wet mixing method of binder solution

Traditional sieving method

1. Low shear granulation'[9]

1. The medication and intragranular excipients are granulated with a binder solution in this method, which uses low speed planetary or trough mixers. The resulting wet mass is screened to create discrete granules, which are commonly dried in a tray drier.

2. Extra granular excipients are blended with the dry granules, they are lubricated, and they are compressed after being rescreened or milled to the appropriate size.

3. The mixer's base has a high-speed "chopper" that continuously chops up the moist mass as granulation takes place.

4. Compared to low shear granulation, this combination allows for very efficient mixing of the components and the use of less water.

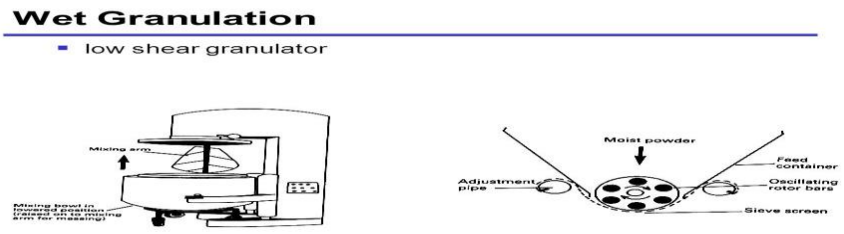
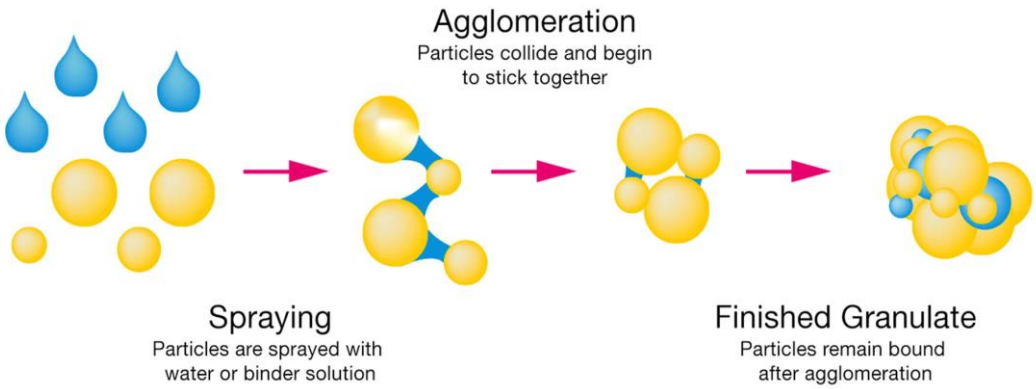


FIGURE [2] Illustration of granule growth by Low shear granulation'.[9]

2. High shear mixer'[10,11]

1. Pharmaceutical businesses frequently use high shear mixtures for blending and granulation.
2. The impeller in this sort of equipment rotates at a high speed (about 50–100 rpm), which propels the particles into motion. A chopper is also part of the apparatus, and it rotates between 1500 and 4000 rpm.[10]
3. A high shear mixer granulator is a closed vessel, and the amount of handling required is minimized because the created granules may typically be delivered to a fluid bed dryer in a closed system.
4. The broad application of high shear granulation to virtually any formulation is one of its main benefits.
5. The amount of mixing done can quickly cause over-granulation, which has negative impacts on the ability of granule tablets.

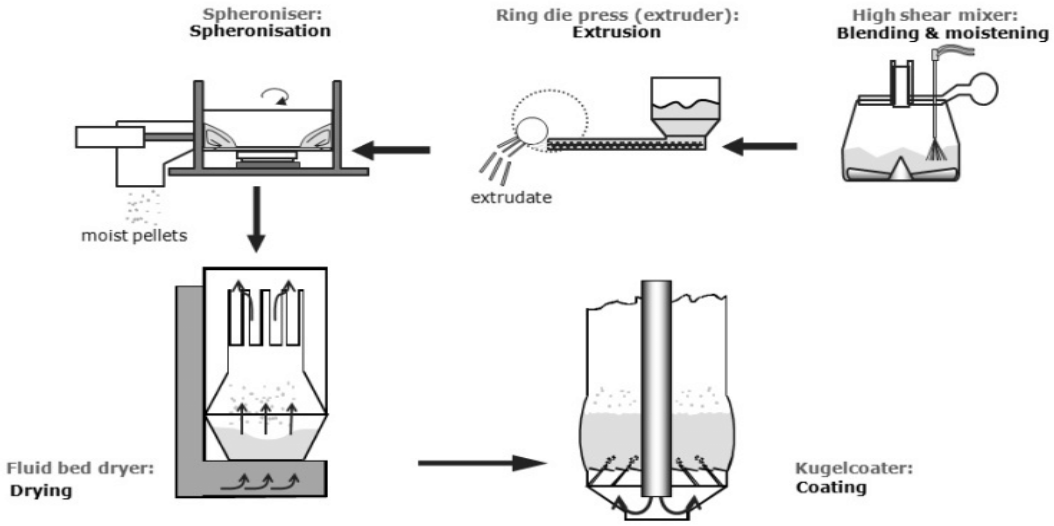


FIGURE[3] Illustration of granule growth by High shear mixer method.

3. Extrusion granulation method

1. The pharmaceutical sector uses wet granulation frequently because it enhances the flow characteristics, homogeneity, and compressibility of the powder mix.
2. Traditionally, batch wet granulation procedures use high shear mixers and fluidized bed granulators.
3. The methods employed for solid agitation and the mechanism of granule formation in these two procedures are different from one another.

4. of late It should be highlighted that adopting a continuous granulation process can prevent scale-up issues with batch granulation techniques since the same machinery and identical process parameters can be used for small-scale and large-scale manufacturing.
5. Continuous and uniform mixing and granulation of powders that can be utilized right away for tableting are necessary for a completely continuous tableting process, which begins with the dispensing of the individual formulation components and ends with the packing of the tablets.
6. Extrusion, fluid bed agglomeration, instant agglomeration, and spray drying are all continuous wet granulation processes, albeit at the moment extrusion is the most used for pharmaceutical purposes.



FIGURE[4] Illustration of granule growth by extraction method.

Dry and wet mixing method of binder solution

1. Rather from being compacted, wet granulation is created by adhering the particles with an adhesive. As more liquid is poured, bridges between the particles form and the tensile strength of bonds increases.
2. A mixture of dry primary powder particles is massed using a granulating fluid during wet granulation. The fluid should not be poisonous and contains a solvent that can be eliminated by drying.
3. Water, ethanol, isopropanol, and ethylene chloride are common solvents that can be used singly or in combination.

4. The granulation liquid can be employed on its own or—more frequently—as a solvent with dissolved, suspended, or gelatinized binder.
5. When the granule is dry, this is done to guarantee particle adherence.

Process details: convetional wet granulation

Theoretical Aspects

According to Iveson[3] there are fundamentally only three stages of process, which determines the wet agglomeration behaviour:

- Wetting and nucleation;
- Consolidation and growth and finally
- Breakage and attrition.

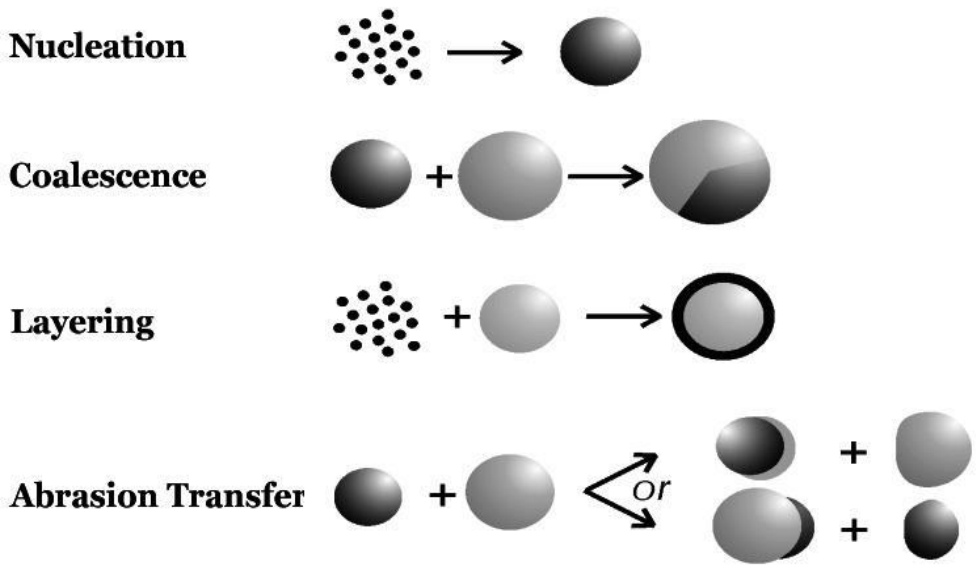


FIGURE [5] Illustration of granule growth by nucleation and by coalescence.[4]

These processes frequently occur simultaneously in the granulation apparatus, making it challenging to investigate how each phenomenon affects the agglomeration properties.

The particles must be wetted in order for nucleation to occur. the beginning agglomeration creation. According to Hapgood[5], the following factors influence the nucleation rate:

• Wetting thermodynamics

• Drop penetration kinetics and

• Binder dispersion.

"The liquid delivery parameters[6] and powder mixing[7] depend on the binder dispersion in the mass of powder."

All of the elements involved in the wet granulation method, the oldest and most common way to create granules, form a three-phase system consisting of:

•Dispersed solid

• Granulation liquid and

• Air.

Even though intermolecular attraction interactions, van der Waals forces, and electrostatic forces also play an early role, the liquid bridges that form between the solid particles are the primary cause of the cohesive force that acts during the moist agglomeration process.

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Newitt and Conway-Jones[8] and Barlow[9] describe the addition of granulation liquid to the bulk of powder in a sequence of four states known as "Pendular," "Funicular," "Capillary," and "Droplet or Suspension," which are schematically represented in (Figure 2).

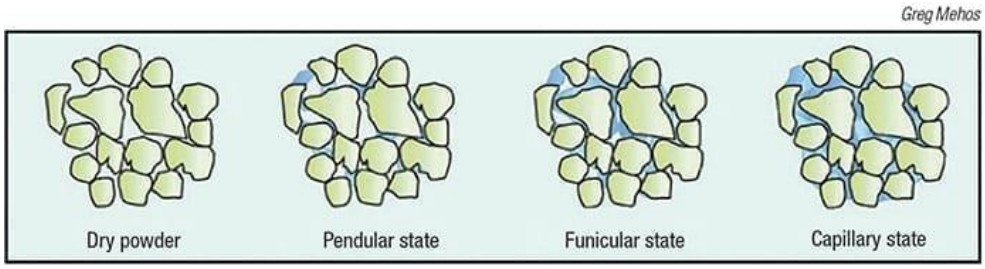

FIGURE [6] States of liquid content in an agglomerate during wet granulation.[4]

Liquid film forms on the powder surface when liquid is initially applied to the medication powder. At the site of contact, discrete liquid bridges are then constructed. Surface tension and capillaries produce the cohesive force during this stage, which is referred to as the "Pendular State." Air is still present between the particles. The air no longer forms a continuous phase in this so-called funicular state. All inter-particle gaps are filled when the water content rises more.

At this stage, known as the Capillary State, the particles are held in place by capillary pressure and interfacial forces at the granule surface. At this moment, the granules are at their strongest. Additional liquid addition creates solid particles that are entirely engulfed in liquid, giving rise to the droplet state.

At this stage, the system only consists of a scattered solid phase and a liquid phase. Once the granulation process is complete, the liquid is removed by drying, but multiple bonding mechanisms still keep the granules together.

CONCLUSION

The Main aim of this Review article was to describe reasons to prepare wet granulation, mechanism of granulation, advantages and disadvantages of wet granulation. This review also describes about the techniques used for preparation of wet granulation and also describes about stages of granules development.

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