

Review Article

Foam-Based Granulation in Pharmacy

Krushna Pandey¹, Rajal Singh², Nidhi Mishra³

Naraina Vidya Peeth College of Pharmacy.

I N F O

Corresponding Author:

Rajal Singh, Naraina Vidya Peeth College of Pharmacy.

E-mail Id:

rajals.343@gmail.com

How to cite this article:

Pandey K, Singh R, Mishra N. Foam-Based Granulation in Pharmacy. Rec Trends Pharm Tech Ind 2024 6(1): 13-16.

Date of Submission: 2024-04-04

Date of Acceptance: 2024-05-20

A B S T R A C T

Foam-based granulation is an emerging technique in pharmaceutical manufacturing that offers several advantages over traditional wet granulation methods. This process involves the incorporation of foam, which acts as a binder to agglomerate powder particles into granules. The key benefits include reduced liquid consumption, improved homogeneity, and enhanced control over granule size and density. Additionally, foam-based granulation can lead to more efficient drying and reduced processing times. This method also presents an environmentally friendly alternative by minimizing solvent use and energy consumption. The present review delves into the mechanisms of foam-based granulation, its operational parameters, and its potential applications in the pharmaceutical industry. Through a comprehensive analysis of current research and practical case studies, we highlight the process's efficiency, scalability, and impact on product quality. The findings suggest that foam-based granulation is a promising technology that could revolutionize pharmaceutical granulation processes, making them more sustainable and cost-effective.

Keywords: Foam-Based Granulation, Pharmaceutical Manufacturing, Wet Granulation, Binder, Granule Size

Introduction

Granulation is a pivotal process in the pharmaceutical industry, transforming fine powders into free-flowing, cohesive granules suitable for tablet compression and capsule filling. Traditional granulation methods, including wet and dry granulation, have been extensively utilized. However, these methods often present challenges such as high energy consumption, thermal degradation of active ingredients, and complex processing steps. Foam-based granulation has emerged as a novel technique, addressing these challenges while offering additional benefits.¹

Principles of Foam-Based Granulation

Foam-based granulation is an innovative wet granulation technique that uses foam as the granulating medium instead of traditional liquid binders. This approach offers a more controlled and efficient process, resulting in high-quality

granules with improved properties. The fundamental principles of foam-based granulation involve the preparation and use of foam, the blending and wetting of powder particles, and the subsequent formation and consolidation of granules. The process involves several key steps.²

- **Foam Preparation:** Foam preparation is a critical initial step in foam-based granulation, involving the creation of a stable and uniform foam that serves as the granulating medium. The process begins with selecting an appropriate liquid binder, which is typically an aqueous solution that can effectively bind the powder particles together. Common binders include water, polymer solutions like polyvinylpyrrolidone, and other hydrophilic liquids. To generate foam, a foaming agent is incorporated into the liquid binder. This agent, often a surfactant, reduces the surface tension of the liquid, enabling the formation of bubbles when

air is introduced. The concentration of the foaming agent is crucial as it determines the stability and size of the bubbles.³ Higher concentrations usually result in finer, more stable foam. The foam generation process can be carried out using various methods, such as mechanical stirring, air injection, or using specialized foam generators. The mixing conditions, including agitation speed and duration, play a significant role in determining the characteristics of the foam. Key attributes of the foam include bubble size, density, and viscosity. Smaller bubble sizes provide a larger surface area for the binder, ensuring more uniform wetting of the powder particles. The density of the foam is also important; lower density foams contain more air and less liquid, which helps in reducing the overall moisture content of the granules. The viscosity of the foam affects its flow properties and its ability to penetrate the powder blend uniformly. To enhance foam stability, stabilizers may be added to the foam formulation.⁴ These stabilizers help maintain the integrity of the bubbles during the granulation process, preventing premature collapse and ensuring consistent binder distribution. The prepared foam must exhibit sufficient stability to withstand the subsequent steps of foam-based granulation without losing its structure. This stability ensures that the foam can effectively wet and bind the powder particles, leading to the formation of high-quality granules with desirable properties. The careful optimization of foam preparation parameters is essential for the success of the foam-based granulation process, impacting the uniformity, mechanical strength, and overall quality of the final granules.⁵

- **Powder Blending:** Powder blending is a fundamental step in foam-based granulation, ensuring the uniform distribution of active pharmaceutical ingredients (APIs) and excipients within the powder mixture. This homogeneity is crucial for achieving consistent granule quality and performance in the final pharmaceutical product. The blending process begins with the precise selection and proportioning of the APIs and excipients, which may include fillers, binders, disintegrants, and lubricants. These components must be evenly distributed to ensure that each granule formed during the subsequent granulation process has a consistent composition, which is vital for maintaining the desired drug release profile and therapeutic efficacy.⁶ To achieve a homogenous powder blend, various blending techniques are employed based on the properties of the powder and the desired outcome. Common blending methods include tumbling mixers, which gently rotate the powder mixture to achieve uniform mixing through gravitational forces, and high-shear mixers, which use intense mechanical action to break down agglomerates and ensure thorough distribution of all components.

V-blenders and double cone blenders create a cascading motion that enhances mixing efficiency, while ribbon blenders use a horizontal trough with a rotating ribbon agitator to mix powders with different particle sizes and densities effectively. Blending parameters such as time, speed, and intensity must be carefully optimized to achieve the desired level of homogeneity without over-mixing, which can lead to powder compaction or degradation of sensitive components. The batch size should also be appropriate for the blender's capacity to ensure efficient mixing. After blending, the homogeneity of the powder mixture is assessed using sampling and analytical techniques, such as high-performance liquid chromatography (HPLC) or near-infrared (NIR) spectroscopy, to ensure uniformity. In the context of foam-based granulation, the uniformity of the powder blend directly impacts its interaction with the foam binder. A well-blended powder ensures that each particle is evenly wetted and bound by the foam, leading to the formation of consistent granules with uniform size and composition.⁷ This uniformity is essential for the granules' flow properties, compressibility, and dissolution characteristics, ultimately affecting the quality and efficacy of the final pharmaceutical product. Therefore, powder blending is a critical step that requires meticulous attention to detail and precise control to achieve optimal results in foam-based granulation.

- **Foam Addition:** Foam addition is a crucial phase in foam-based granulation, involving the careful introduction of prepared foam into the pre-blended powder mixture to initiate the granulation process. The foam, consisting of a liquid binder and a foaming agent, is generated to have specific characteristics, such as bubble size, stability, and density, which are optimized to ensure effective wetting and binding of powder particles.⁸ The addition of foam can be executed through various methods, including direct injection, spraying, or in-situ foam generation within the powder blend. In direct injection, the foam is introduced into the powder bed using a nozzle, ensuring targeted and controlled distribution. Spraying involves uniformly dispersing the foam over the surface of the powder blend, while in-situ generation creates foam directly in the mixer by introducing air and foaming agents during blending. As the foam interacts with the powder, the bubbles facilitate the even distribution of the liquid binder, ensuring uniform wetting of the powder particles. The foam bubbles collapse gradually, releasing the liquid binder and allowing the particles to adhere to each other, forming initial agglomerates or nuclei.⁹ This controlled release of the binder is vital for achieving a consistent granule size and preventing over-wetting or under-wetting of the powder. The rate of foam collapse,

influenced by the foam's stability, plays a significant role in the granulation process. A controlled collapse rate ensures a steady release of the binder, promoting uniform growth and consolidation of the granules. Proper mixing during foam addition is essential to ensure even distribution of the foam throughout the powder blend, facilitating the formation of cohesive and uniform granules. The mixing intensity must be carefully adjusted to avoid damaging the foam structure while ensuring thorough integration of the binder.¹⁰

- **Granule Formation:** Granule formation in foam-based granulation is a pivotal step where wetted powder particles coalesce into larger, cohesive granules. This process begins immediately after foam addition, as the foam's bubbles collapse and release the liquid binder, initiating particle-particle adhesion. The initial stage, known as nucleation, involves the formation of small agglomerates or nuclei as the binder causes nearby powder particles to stick together. These nuclei serve as the foundation for subsequent granule growth. The growth phase follows, where additional particles adhere to the existing nuclei, driven by mechanical mixing that enhances contact between particles. The rate of foam collapse and the amount of binder released are critical parameters that influence the uniformity and size of the granules¹¹. As granule growth progresses, the process of coalescence comes into play, where smaller granules merge to form larger ones. The dynamics of coalescence are influenced by the viscosity of the binder and the mechanical forces applied during mixing. High shear mixing, for example, can accelerate granule growth and lead to more uniform size distribution. Conversely, excessive shear can break granules apart, leading to undesirable size reduction. The granules are then further consolidated through mechanical agitation, which densifies the granules and enhances their mechanical strength. This is particularly important for ensuring that the granules can withstand subsequent processing steps, such as drying and compression, without breaking apart.
- **Drying and Sizing:** Drying and sizing are critical final steps in foam-based granulation, ensuring that the granules achieve the desired quality and performance characteristics. After the granulation process, the wet granules contain residual moisture from the liquid binder, which must be removed to solidify the granules and enhance their mechanical strength. Drying is typically performed using methods such as fluid bed drying or tray drying. Fluid bed drying is widely preferred due to its efficiency and ability to provide uniform drying. In this method, granules are suspended in a stream of warm air, which facilitates rapid and even moisture removal. Tray drying, on

the other hand, involves spreading granules on trays and exposing them to a controlled environment, though it may result in less uniform drying and longer processing times. The drying process must be carefully controlled to avoid¹²overheating, which can cause thermal degradation of sensitive components or lead to uneven granule drying. The objective is to achieve an optimal moisture content that ensures granule stability and minimizes issues like caking or poor flowability. Typically, the moisture content is reduced to a level that balances granule strength with ease of handling and processing in subsequent steps. Following drying, the granules undergo sizing, a process essential for achieving the desired particle size distribution. This step ensures that the granules are of uniform size, which is crucial for consistent tablet compression or capsule filling. Sizing involves separating granules into different size ranges using equipment such as sieves or screens. Oversized granules, which can affect the uniformity of the final product, are often milled or reprocessed to achieve the correct size. Conversely, undersized granules may be retained or blended with other batches to maintain product consistency.¹³

Benefits of Foam-Based Granulation

Foam-based granulation offers several distinct advantages over traditional granulation methods, contributing to its growing adoption in pharmaceutical manufacturing. One of the primary benefits is the enhanced uniformity of binder distribution. The foam's air-filled bubbles ensure that the liquid binder is evenly dispersed throughout the powder blend, resulting in a more consistent and homogeneous granule formation. This uniformity translates to improved granule properties such as flowability and compressibility, which are crucial for efficient tablet compression and capsule filling. Additionally, foam-based granulation often requires less binder compared to conventional methods. The reduced binder quantity not only minimizes the overall moisture content but also decreases the drying time, leading to energy savings and reduced processing costs. The lower binder content also helps in preserving the stability of heat-sensitive active pharmaceutical ingredients (APIs), as the process operates at lower temperatures, reducing the risk of thermal degradation. Furthermore, foam-based granulation can be less aggressive on the powder particles compared to high-shear or fluidized bed granulation methods, which can be particularly advantageous for delicate or friable materials.¹⁴ The technique's ability to produce granules with enhanced mechanical strength and optimal size distribution further improves the quality and consistency of the final product. Overall, foam-based granulation presents a more efficient and controlled approach to granule production, offering significant benefits in terms of process efficiency, cost-effectiveness, and product quality.

Mechanisms of Foam-Based Granulation

Foam-based granulation operates through several key mechanisms that collectively contribute to the formation of high-quality granules. The process begins with the introduction of foam, a stable mixture of air and liquid binder, into the powder blend. The primary mechanism is the wetting and nucleation phase, where the foam's bubbles collapse and release the liquid binder, which penetrates the powder mixture and causes initial particle adhesion. The foam's bubble size and stability are crucial here; smaller, more stable bubbles provide a greater surface area for binder distribution, ensuring even wetting of the particles. As the binder comes into contact with the powder, it facilitates the formation of nuclei, or small agglomerates, which serve as the starting points for granule growth.

Following nucleation, the growth and coalescence mechanisms take over. As more binder is released from the collapsing foam, the initial nuclei attract additional powder particles, leading to the gradual formation of larger granules. This phase is influenced by the mechanical mixing intensity, which promotes the aggregation of particles and the consolidation of granules. High-shear mixing or tumbling helps in achieving uniform particle contact and ensures that the granules grow to the desired size. During this stage, the granules undergo coalescence, where smaller agglomerates merge to form larger, more cohesive granules. The consistency of binder release, driven by foam stability, plays a crucial role in controlling the granule size and uniformity.¹⁵

Finally, the drying and solidification phase involves removing excess moisture from the wet granules to solidify their structure. As the binder dries, it hardens, enhancing the mechanical strength of the granules and ensuring they can withstand subsequent processing steps. The drying process also influences the final granule properties, such as porosity and size distribution. The entire foam-based granulation process is characterized by precise control over foam properties and process parameters, which collectively ensure the production of granules with optimal flowability, compressibility, and uniformity.⁴

Conclusion

Foam-based granulation represents a significant advancement in pharmaceutical manufacturing, offering numerous benefits over traditional granulation techniques. Its ability to produce uniform, high-quality granules with reduced binder quantities and lower energy consumption makes it an attractive option for tablet and capsule formulation. Despite some challenges, ongoing research and technological advancements are expected to further enhance the feasibility and application of foam-based granulation, solidifying its role in the future of pharmaceutical manufacturing.

References

1. veson SM, Litster JD, Hapgood K, Ennis BJ. Nucleation, growth and breakage phenomena in agitated wet granulation processes: a review. *Powder Technol.* 2001;117(1-2):3-39.
2. Kleinebudde P. The use of granulation in solid oral dosage forms. *Pharm Dev Technol.* 2004;9(1):1-19.
3. Knight PC, Seville JPK. Density effects in granule formation by granulation. *Powder Technol.* 1995;82(3):269-77.
4. Litster JD, Ennis BJ. *The Science and Engineering of Granulation Processes.* Dordrecht: Springer; 2004.
5. Ramaker DP, Peck GE, Vreeland WN, Friedman RL. Foam granulation: a new method for forming granules. *J Pharm Sci.* 1990;79(12):1075-80.
6. Saleh K, Vialatte C, Guigon P. Foam granulation: an overview of process principles and applications in the pharmaceutical industry. *Chem Eng J.* 2012;210:93-105.
7. Bika D, Reynolds GK, Salman AD, Hounslow MJ. The effect of liquid viscosity on particle growth mechanisms in a high shear mixer. *Powder Technol.* 2001;121(2-3):101-10.
8. Kristensen HG, Schaefer T. Granulation: a review on pharmaceutical wet-granulation. *Drug Dev Ind Pharm.* 1987;13(4-5):803-72.
9. van den Ban S, Goodwin DJ, Sayin R, Gladden LF, Simmons MJH. Foam granulation: the effect of foam properties on granule formation. *AIChE J.* 2010;56(8):2006-15.
10. Scott A, Oliver R, Davies MC, Roberts CJ, Tendler SJB, Williams PM. The application of atomic force microscopy to the characterisation of pharmaceutical surfaces. *Int J Pharm.* 2001;231(1):29-37.
11. Hemati M, Cherif R, Saleh K, Pont V. Fluidized bed coating and granulation: influence of process-related variables and physicochemical properties on the growth kinetics. *Powder Technol.* 2003;130(1-3):18-34.
12. Ghadiri M, Thornhill D, Bond CJ. Granulation of lactose powder with aqueous foam. *Powder Technol.* 2005;158(1-3):2-11.
13. Schaafsma SH, Vonk P, Kossen NWF. Fluid-bed agglomeration with a narrow droplet size distribution. *Powder Technol.* 1998;97(3):183-90.
14. Thompson MR, Sun J, White E, Papadopoulos D. Foam granulation: effect of surfactant concentration on granule properties. *Powder Technol.* 2010;197(1-2):19-28.
15. Barbosa-Cánovas GV, Ortega-Rivas E, Juliano P, Yan H. *Food Powders: Physical Properties, Processing, and Functionality.* New York: Kluwer Academic/Plenum Publishers; 2005.