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Short communication

Fluid bed granulation – theoretical and practical approach

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Introduction

Granulation is the process of agglomeration of a powder mixture, which results in the enlargement of the particles. Fluid bed granulation is a wet granulation technique widely used in pharmaceutical technology to convert fine, often poorly flowing powders into free-flowing, compressible granules suitable for tableting and capsule filling (Shanmugam, 2015). In a fluid bed granulator, an upward flow of conditioned air fluidizes the powder bed while a binder solution is sprayed, causing particles to adhere and grow into granules that are subsequently dried in the same equipment.

Principles of fluid bed granulation

In fluid bed granulation, the product container holds the powder blend on a perforated distributor plate, through which process air is introduced to achieve a stable fluidization regime. Fluidization quality is typically controlled by adjusting inlet air flow, temperature and humidity to maintain particles in a suspended, vigorously mixing state without elutriating excessive fines or causing dead zones. A binder solution is atomized through one or more nozzles (usually top-spray for classical granulation), producing fine droplets that impact the fluidized particles and form liquid bridges between them. The same air stream that maintains fluidization also provides the thermal energy necessary to evaporate the granulation liquid and solidify the bonds, so that drying and granule formation occur in a single, integrated unit operation (Bouffard et al., 2005).

Typical process parameters were considered: inlet air temperature, air flow rate, product (bed) temperature, atomization air pressure, binder spray rate, binder concentration and spray time, as well as critical quality attributes such as: granule size distribution, flow properties, moisture content and tablet performance (Wu et al., 2017). Depending on the specific equipment design, different configurations can be used, including top-spray fluid bed granulation for conventional agglomerates, bottom-spray (Wurster) systems for coating and layering, and rotor/tangential-spray inserts for pelletization or powder layering applications.

Mechanism of granule formation, critical process parameters and influence on granule quality

The mechanism of fluid bed granulation involves several overlapping stages: wetting and nucleation, coalescence and growth, consolidation, breakage, and drying. When the atomized binder droplets contact fluidized particles, small nuclei are formed; these then collide with other wet or partially dried particles, leading to growth either by coalescence (agglomeration) or by surface layering, depending on the balance between wetting and drying (Cronin et al., 2020). If drying is very fast relative to wetting, the dominant mechanism becomes layering: droplets or dissolved solids deposit on particle surfaces, so that individual particles grow by successive shells with limited agglomeration (Becher and Schlünder, 1997).

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When liquid bridges persist for longer times and binder strength is high, collisions of wet particles produce larger agglomerates that may compact and densify before drying, yielding more porous, irregular granules.

Process monitoring and control

Fluid bed granulation can be highly sensitive to operating conditions and formulation variables. Higher inlet air temperatures and air flow rates enhance drying and can reduce granule size by limiting the time for wet coalescence, but excessive drying may cause spray-drying of fines, poor binder efficiency and wide size distributions. Binder type and concentration influence liquid bridge strength and viscosity: more viscous or higher-solids binders typically increase granule size and mechanical strength, but they may also increase the risk of overwetting, defluidization and formation of large, undesired agglomerates. Spray rate and atomization pressure must be balanced: low atomization pressure can produce large droplets that overwet the bed, whereas too high pressure yields very fine droplets that may dry before effective wetting occurs, reducing granulation efficiency (Bouffard et al., 2005; Medarević et al., 2012). Accurate control of liquid binder addition is critical to achieving consistent granule quality. Two key components that enable this control are the peristaltic pump and the flow meter. A peristaltic pump transports binder solution through flexible tubing using rotating rollers. As the rollers compress and release the tubing, fluid is pushed forward in a controlled manner. A flow meter measures the rate of liquid flow through a system. In fluid bed granulation, it is used to monitor the actual binder flow rate delivered to the spray nozzle.

Conclusion

Fluid bed granulation is a versatile and widely used wet granulation technique that combines fluidization, spraying and drying in a single, efficient operation to produce free-flowing, compressible granules for solid dosage forms (Shanmugam, 2015). Both the critical material attributes (CMAs) of the raw materials and the critical process parameters (CPPs) have a significant impact on the final granule properties during fluid bed granulation. Therefore, both must be carefully monitored and controlled throughout the production process. Advantages of fluid bed granulation include improved mixing, uniform granule formation, reduced processing time, and lower risk of contamination due to its closed system design. However, challenges such as equipment cost, process complexity, and sensitivity to formulation and operational variables must be addressed. The goal is to produce granules with appropriate characteristics that will further influence product quality, flowability, compressibility and manufacturability.

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