Study on Basic Model and Application of Fluidized Bed Granulation Technology

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Abstract. Fluidized bed granulation is a modern industrial process, it plays an important role in the manufacture of many-particle products. Fluidized bed granulation operation has low requirements on particle size and shape. Fluidized bed granulation makes the manufacturing cost of drugs as low as possible so that more diseases can be cured by drugs. But there are still some shortcomings in practical use, which affect the final use effect. This paper will summarize the development of fluidized bed granulation in pharmaceutics and analyze the optimization of the fluidized bed granulation process. This paper summarizes the results of previous studies and compares the data in previous studies to get specific advantages and disadvantages of traditional fluidized bed granulations compared with FHMG. It is found that there are many factors affecting the process effectively in the process of fluidized bed granulation, so it is necessary to optimize the process of fluidized bed granulation according to the factors, improve the rationality of process parameters, and improve the effect of granulation.

Keywords: Fluidized Bed Granulation · FMHG · Oral Drug Delivery · Boiling Granulation

1 Introduction

At present, fluidized bed granulation is a common technology in industrial production, which not only has remarkable characteristics and advantages but also can effectively improve the production quality and efficiency of products. However, the application of the fluidized bed granulation process will be affected by many factors, resulting in its application effect being greatly reduced. In order to ensure that the function of fluidized bed granulation can be effectively played, it is necessary to take effective optimization measures according to its current situation and strengthen the understanding of the effect of fluidized bed granulation. In order to develop the potential application value of this technology, more and more researchers have carried out in-depth research on its granulation mechanism, influencing factors and practical operating conditions. However, fluidized bed granulator operation has a high demand for technology, which is often affected by atomization characteristics of materials, operating conditions of equipment and fluidization process, this paper summarizes the disadvantages and provides some

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feasible methods. In this paper, four basic fluidized bed granulation technologies and new granulation technologies are explored, and their advantages and disadvantages are summarized and listed by comparison. As the epidemic continues to rage around the world and a large number of basic drugs are in short supply, the advantages of flowed granulation will be amplified and more widely used in the pharmaceutical industry to better overcome its shortcomings and make it more efficient, which will greatly improve the guarantee of people's life.

2 The Introduction of Fluidized Bed Granulation

2.1 Fluidized Bed Granulation Process

Spray fluidized granulation as a way of granulating technology is atomized into droplets will melt or solution, suspension, injection to the basic curing or drying particle fluidization movement (or grain), particle surface coated with the melt or solution, suspension, after appropriate time curing or drying, particles grew up for larger nuclear particles, so repeated several times, Finally, granular solid materials with a certain size range are formed and discharged as finished products. As a particle processing process, granulation is related to almost all solid preparations. The growth and granulation process of coating is shown in Figs. 1 and 2 and illustrated by legen. In Fig. 1, A represents spray drying, B coating, and C coalescence. In Figs. 2, 1 represents adhesive spray, 2 powder supply, and 3 sprays.

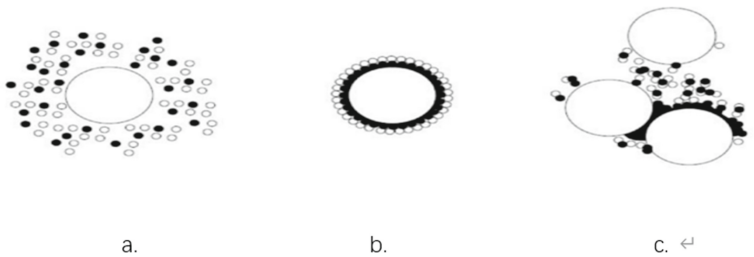

Fig. 1. Particle adhesion state [5]. *Source* Zhou yunzhen, Tian bing, Pharmaceutical & Engineering Design 2011, 32(4). The content cited is with permission of Zhou Yunzhen and Tian Bing

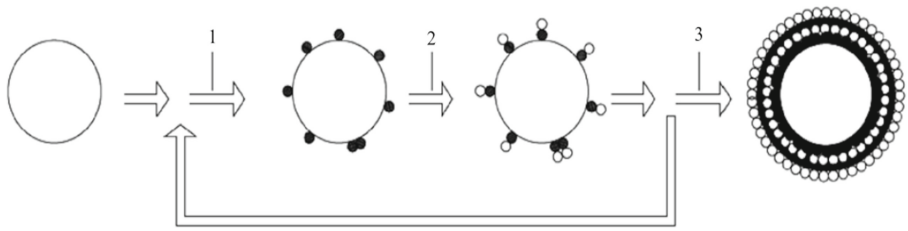

Fig. 2. Powder coating model [5]. *Source* Zhou yunzhen, Tian bing, Pharmaceutical & Engineering Design 2011, 32(4). The content cited is with permission of Zhou Yunzhen and Tian Bing

2.2 Working Principle of Fluidization Granulation

It works by suspending the powder with airflow, even if the powder is fluidized, and then spraying it into a binder to condense the powder into particles. Mixing, pelleting, drying, and other operations can be done in one unit because the temperature of the airflow is adjustable. A fluidization granulator is generally composed of an air preheater, compressor, blower, fluidization chamber, bag filter, etc. The gas distributor is usually a porous inverted vertebra covered with a 60–100 mesh stainless steel screen. The upper part of the fluidization chamber is provided with a bag filter and a recoil device or vibration device to prevent the bag filter from being blocked. When working, the filtered air is sent to the air preheater by the blower. After preheating to the specified temperature, it enters the fluidization chamber from the bottom through the gas distributor and the secondary jet air inlet to fluidize the material. Then, the adhesive is sprayed into the fluidization chamber, and after continuing fluidization and mixing for several minutes, the material can be discharged [1,2]. Hot and humid air is removed by a bag filter and discharged. The particles obtained by the fluidization granulation mechanism are mostly 30 ~ 80 mesh, the shape of the particles is relatively round, and the fluidity of the tablets is also good, which is very beneficial to improving the quality of the tablets. Because fluidization granulator can complete a variety of operations, simplify the process and equipment, the production efficiency is high, production capacity is large and easy to realize automation, suitable for wet or heat-sensitive material pelleting. The disadvantage is that power consumption is larger. In addition, the density of materials should not differ too much, otherwise, it will be difficult to fluidize granulation. Sometimes the spray of molten or solution, suspension droplets, not in contact with other moving particles, has been solidified or dry, the formation of new nuclear particles. According to the particle number balance, the particle growth rate can be obtained to determine the required residence time and the height of the thick phase zone in the fluidized bed. The atomizing device mainly has two kinds of airflow nozzle and pressure nozzle, among which the pressure nozzle is less used (Fig. 3).

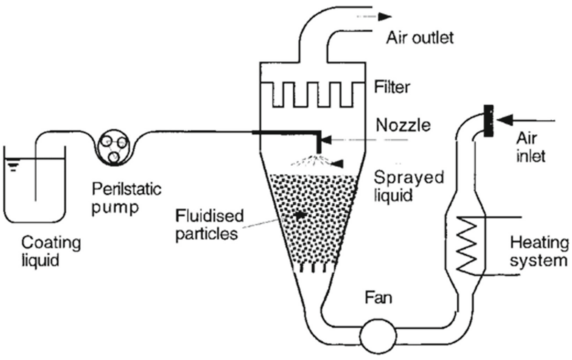

Fig. 3. Fluidized bed spray granulator [3]. *Source* Zhang Dong-li, HAO Dong-sheng, SHU An-qing, ZHANG Wei-Wei, CHEMICAL INDUSTRY AND ENGINEERING. Vol.22 No.4. The content cited is with permission of Zhang Dong-li, HAO Dong-sheng, SHU An-qing, ZHANG Wei-Wei

2.3 Advantages and Disadvantages of the Fluidized Bed Spray Granulation

Compared with other granulation methods, fluidized bed spray granulation has unique advantages:

(1) Can be in the same equipment to achieve mixing, granulation (coating or agglomeration), drying, cooling and other operations, from the liquid material one step into dust-free particle products, the average particle size is generally 0.3–3 mm (there are also larger particles, such as urea fluidized bed spraying granulation, its particle size can reach 2–8 mm).
(2) Due to the intense agitation and mixing of gas and particles in the bed, the bed temperature is uniform, the gas-solid contact area is large, and the heat and mass transfer rate is high.
(3) Simple process, compact equipment, large production capacity. Fluidized bed spraying granulation also has some shortcomings:

At present, the defects of fluidized bed spray granulation technology are:

(1) The air distribution in the bed is not uniform, many gases pass through the bed in the form of bubbles, and the entrain phenomenon is serious due to bad operation.
(2) Due to the violent collision between particles will cause particles to be broken and produce fine powder, so it requires high efficiency of fine powder recovery equipment.
(3) Once the amount of spray is too much, it is easy to cause a large range of agglomeration between particles, rapid deterioration of fluidization state, resulting in gas short circuit and dead bed. Fluidized bed spraying granulation is an organic combination of fluidization, spray and drying technology. It has been widely used in the pharmaceutical industry with the batch operation and the chemical industry with continuous operation

3 Basic Fluidized Bed Granulation Methods

3.1 Spray Granulation in Fluidized Bed

In fluidized bed spray granulation, the air is often treated as fluidized gas, which is preheated and then transported to the bottom of the fluidized bed with a distribution plate, so that the granulated solid powder presents a fluidization state. The liquid feed is generally sprayed into the fluidized bed through a double-fluid nozzle, and the nozzle is required to operate flexibly and is not prone to blockage. If the gas is hot, the blockage should be paid special attention to when atomizing the crystal liquid [3]. For the liquid coating on the surface of particles, in order to make it can effectively dry, the countercurrent method of gas and solid particles is generally used to make the particle size distribution of the product have good uniformity [4]. At the same time, fluidizing gases need to be kept fast enough to ensure that large particles move strongly enough to avoid clumping.

3.2 Granulation in Spray Fluidized Bed

Spray fluidized bed granulation has a high similarity with the spray granulation of fluidized bed, which is mainly to spray the material liquid that can be pumped and atomized into mist, and then spray it onto the hot particles in the bed for drying, and directly generate the corresponding solid particles. In the process of particle production, there is no need for bed agitation. It combines the advantages of a common fluidized bed and a standard spray fluidized bed. It can not only deal with large particle materials, but also has good gas-solid contact and mixing effect of common fluidized bed, so it is often used in the production of large particle products.

3.3 Vibrating Granulation in Fluidized Bed

Vibrating granulation can be accomplished by rotating disc, rotating cylinder and other vibrating fluidized beds. In the granulation process, the equipment is a fluidized bed for gas vibration if gas is used as a carrier for heat and material transfer. Fluidized bed vibrating granulation has high granulation intensity and high granulation speed, and the product quality is very good, some fine powder which is difficult to fluidization process can also be successfully granulated, so it avoids the consumption and waste of resources and has a high economy. This method is often used in pharmaceutical and food granulation production.

3.4 High Speed, Supercritical Fluid Granulation

The high-speed and supercritical fluid process is a process in which the supercritical fluid expands rapidly through a fine nozzle. In the process of its expansion, temperature, pressure, sudden changes, can lead to solute the actual degree of supersaturation jump, if the solution by single-phase, will be lots of precipitation of micronucleus, within a very short time microkernel can grow rapidly, and some even granularity of sub-micron and nanometer level microparticle type. It can be found by observing the pictures of fine particles obtained in the experiment that the particles show uniform growth, and the coating of granulation is accumulated layer by layer [5]. This granulation method can be effective.

Control particle size, but there are also many problems in industrial production practice, such as fluid spraying at high speed, there will be a large power consumption; The lowest temperature of the nozzle during operation should reach 70–80°C, so it has high requirements for the strength and high-temperature resistance of equipment materials [6].

4 Innovative Application of Fluidized Bed Granulation

4.1 Fluidized Hot Melt Granulation (FHMG)

Traditional granulation methods, such as wet and dry granulation, have a number of well-known disadvantages, including long process times, multi-unit operations, potential loss of drug activity during production, inherent difficulties in drug powder compression, uneven and unstable flow during production, and often high processing costs. In

comparison, fluidization hot melt granulation is a relatively undeveloped technique for pharmaceutical powder granulation that may provide an alternative method. For example, this method does not involve the use of solvents, thus negating the problems associated with hydrolysis and water removal during the process, which are often associated with the use of aqueous granulation fluids. In addition, and need a lot of unit operations, compared to traditional wet granulating FHMG can be completed in one step, in addition, the production of grain has been shown by the FHMG process with a high level of mobility and compressibility, conducive to the production of solid dosage forms[7]. Similar to other melt granulation techniques, FHMG is a process for agglomerating pharmaceutical powders using low melting point pharmaceutical materials as binders rather than traditional liquid binders. Our previous work has shown that agglomeration formation occurs through distribution, immersion, or a combination of the two during FHMG. The distribution mechanism is that the molten binder is first dispersed on the surface of the particles, and then dispersed on the surface of the particles as a result of agglomeration, thus forming particles. Impregnation, by contrast, begins with the binder particles, which are the core of the aggregate to which finer particles are attached and embedded. From a binder core size control aggregate growth perspective, the growth has a certain appeal, immersion and immersion grow grain microstructure is a layered structure, has great potential for pharmaceutical applications.[7].

4.2 Boiling Granulation

Boiling granulation is Powder material into the hopper closed container, due to the action of hot gas flow, so that the powder suspension fluidization circulation flow, to achieve uniform mixing, at the same time, spray into the fog binder wet container powder, powder condensed into loose small particles, particles. The powder material used for boiling granulation is poured into the fluidized bed, and the cold air enters from the rear heating chamber of the main engine. After filtration by a filter, the powder is heated by the heater to the inlet temperature ($\geq$90°C), and the powder is fluidized in the fluidized bed [8]. Will dissolve the mixture at the same time dope solution by the gear pump into the two-fluid atomizer, solution after atomizer atomized spray to the fluidization of material and particle interaction bridge gathered granulating and grew up, after the evaporation of moisture by induced draft fan out of the closed[9].

There are some of the characteristics of Boiling granulation:

(1) Through boiling powder material granulation, improves the fluidity of drug particles, reduce powder flying;
(2) Due to the large surface area of fog droplet groups, the drying time of materials is relatively short (in seconds). [10]
(3) In the high-temperature airflow, the temperature of the surface wetting material does not exceed the wet-bulb temperature of the dry medium, because of the rapid drying, the temperature of the final product is not high, so boiling drying is especially suitable for heat-sensitive materials;
(4) Easy to change operating conditions, can better adjust or control the product quality indicators, such as particle size distribution, product shape, moisture content;

(5) The mixing, granulation, and drying process of raw materials can be carried out at the same time, greatly shortening the boiling granulation time;
6) Boiling granulation process parameters are stable, high repeatability, suitable for continuous batch production.

5 Conclusion

This paper describes the principle and technology of fluidized bed granulation and summarizes four basic fluidized bed granulation methods. Two new granulation techniques, hot-melt granulation and boiling granulation, were introduced and compared with previous granulation methods. The application of the new fluidized bed granulation technology to the pharmaceutical industry will greatly reduce the initial cost and better protect people's health. The data referenced in this article is limited and incomplete in many aspects. In recent years, the application of fluidized bed granulation technology can supplement the shortcomings of its application.

References

1. Xu Yiyong. Optimization analysis of fluidized bed granulation process. Machinery and equipment. 2021 vol 1
2. Xie Zhiyong. Discussion on spray granulation drying technology. Xinjiang Institute of Nonferrous Metals. 2020 vol 1
3. Zhang Dong-li, HAO Dong-sheng, SHU An-qing, ZHANG Wei-Wei. Progress in fluidized bed spray granulation technology. CHEMICAL INDUSTRY AND ENGINEERING. Vol.22 No.4
4. Xu Qing hu Ya Jun an Feng Ye Jingsheng . Research and development of atomization granulation technology. GM in Petroleum & Chemical Industry. 2009 vol 6
5. Zhou Yunzhen Tian Bing. Related factors affecting fluidized bed granulator. Pharmaceutical & Engineering Design 2011, 32(4)
6. H. Zhai, D. S. Jones, C. P. McCoy, A. M. Madi, Y. Tian, and G. P. Andrews. Gastroretentive Extended-Release Floating Granules Prepared Using a Novel Fluidized Hot Melt Granulation (FHMG) Technique. 2014, 11, 3471−3483
7. Zhai, H.; Li, S.; Andrews, G.; Jones, D.; Bell, S.; Walker, G. Nucleation and growth in fluidised hot melt granulation. Powder Technol. 2009, 189 (2), 230−237
8. Walker, G.; Bell, S. E. J.; Vann, M.; Jones, D. S.; Andrews, G. Fluidised bed characterisation using Raman spectroscopy: Applications to pharmaceutical processing. Chem. Eng. Sci. 2007, 62 (14), 3832− 3838
9. CAI Jian, Du Haihong, Zhao Longlong. Problems and solutions of boiling pelletizing process. Chemical Engineering & Equipment. 10.2021 178–180
10. Yu Caiyuan, Wang Baohe, Wang Xizhong. Spray drying technology [J]. 2013(6).