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Fluid Bed Granulation

A modern, economic method for tabletting and encapsulation

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Summary

With fluid bed granulating, the powder to be granulated is mixed in a fluid bed granulator by whirling in a current of air, sprayed with the granulating liquid in the air vortex and the resultant granulate dried in the same work process.
By means of fluid bed granulating the overall manufacturing procedure of tabletting or encapsulation is considerably simplified and shortened. This procedure has substantial advantages from a manufacturing and economic point of view (increase in productivity, decrease in costs).

The manufacture of mixtures, ready for tabletting or filling into capsules can be considerably shortened and simplified by making special use of suitable methods and machines. Apart from direct compression or direct filling the more customary procedures of moist or dry granulation are of importance. The three essential phases, i.e. mixing, agglomerating and drying, naturally require several steps in which separate machines are employed. As opposed to this multiphase preparation of tabletting or capsule filling mixture ("input") we have one single phase of compressing or filling into capsules ("output"). The possibilities of increasing productivity by employing more and more efficient tabletting or capsule filling machines remains limited, as long as the "input" demands a complex work process.

The starting point of our galenical-technical development was therefore to shorten and decrease the number of steps necessary for granulating. "Input" and "output" should be synchronized to such an extent that both processes should keep in step with each other. The stream lining of a manufacturing process may well be interesting "per se" and may have a certain value from the point of view of organisation. According to the existing conditions the focus of our development is concentrated however on productivity increase with simultaneous reduction of manual working time.

After the good results obtained with fluid bed driers*) for many years in our manufacturing department it was natural to develop on the basis of this apparatus a single stage granulating method. Our investigations showed that the mixing effect in the air vortex, even with different particle sizes of powders, is perfect. Therefore we had only to search for an appropriate method of spraying the powder mixture in the fluid bed in order to carry out in the same apparatus the phases which lie between mixing and drying.

A fluid bed drier with a capacity of 30 kg. has been adapted to our ends by the following three essential modifications:

i) Installation of a suitable spray system through which the spray liquid is fed into the particle deceleration zone.

ii) A modified filter which prevents the sticking of the freshly sprayed particles in the filter sacks.

iii) Mounting of an intermediate cylinder between container and filter in order to enlarge the particle deceleration zone.

With this modified fluid bed drier the technological problems were solved in cooperation with the manufacturer. We are at present working with a fluid bed granulator with a capacity of approx. 150 kg. from the same firm. This apparatus was built according to our recommendations as a prototype and is now standard manufacture. From a galenical point of view suitable spray liquids as well as suitable formulae for excipients in powder form had to be developed. The outcome was all the more gratifying as we succeeded in employing a standard excipient composition and a standard method for all the products on which we worked. Slight modifications were only necessary in a few cases. The excipients are, apart from bulking agents, binders, anti-sticking substances, lubricants, disintegrating agents and the granulating liquid.

This technical and galenical development makes it possible to condense all the necessary phases of granulating into one single work process in one single apparatus. The usual operations of conventional granulating are compared with fluid bed granulation in table 1. The comparison shows that alone the time required for drying a conventional granulate in the fluid bed drier suffices to carry out the full process of fluid bed granulating, i.e. to prepare the entire, agglomerated and dried mixture ready for tabletting. Most of the manual work is eliminated, in particular reloading and cleaning of several machines. The acceleration of granulating as well as the possibility of rationalizing the entire production procedure by a universally applicable standard procedure bring about a productivity increase, a decrease in costs as well as an increase in the safety factor.

Apart from these advantages gained from rationalising the manufacturing process the galenical qualities must not be forgotten. In the first place we wish to mention the homogeneous distribution of the active ingredients and the uniform particle size of the granules which are spherical. These characteristics, together with excellent flow properties, have a favourable effect on the accuracy of dosage. The fluid bed effect of the apparatus produces an equilibrium between the lighter and heavier powder particles which eliminates the danger of separation. Even if the fraction of active principle is small, an optimum distribution is obtained by e.g. dissolving or suspending the active ingredient in the spray liquid and adding it in this way to the entire tabletting mixture. Admixing of the external phase is eliminated.

Further advantages of fluid bed granulating in manufacture result from the possibility of avoiding complications which might occur with conventional granulation causing a considerable loss of time. For "problematic" granulates (in respect of granulating as well as compressing) fluid bed granulation can be tried with advantage.

The compressing properties of numerous granulates prepared by us by fluid bed granulation was perfect.

The following description of the process is designed to show the technique of fluid bed granulation:

The active ingredients and the excipients are weighed into the container of the fluid bed granulator. The

*) Manufacturer: Fa. W. Glatt, 7859 Haltingen, West-Germany.

powder is mixed in the apparatus by means of an air vortex for about 2 minutes. The granulating liquid is then sprayed for about 10 minutes. The resulting granulate is subsequently dried for approx. 30 minutes. The granulate remains throughout the process in the fluid bed granulator and is continually whirled in a current of air at e.g. 40° C. The granulate can be immediately compressed to tablets, cores, or encapsulated.

Air temperature, spraying rate, volume of air inducted and exhausted, drying time, type and concentration of binder, time and composition can vary for individual preparations. Through the variation of the individual conditions the required particle size can be obtained. Control of the quality of the granulate during fluid bed granulation is easily possible through the built-in window of the container or by interruption of the process.

The use of the fluid bed granulator is not limited to the production of tabletting and capsulating mixtures. Granules as dosage forms also enter into consideration or e.g. the stabilisation (coating) of sensitive active ingredients in powder form or the dispersion of fluid active principles.

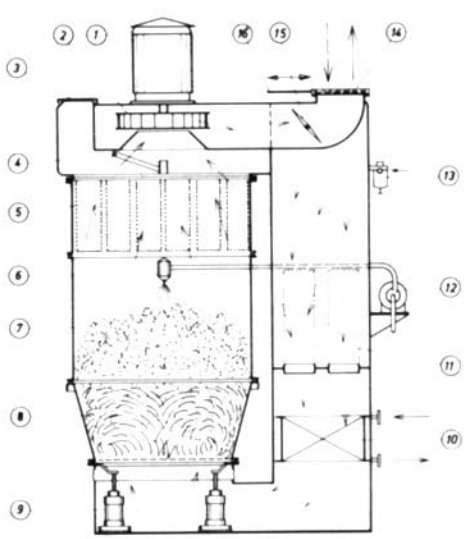
Fig. 2 — Fluid bed granulator WSG 120 opened (Manufacturer's photo: Fa. W. Glatt, 7859 Haltingen, West-Germany).

Table 1: Comparison between conventional granulating and fluid bed granulation.

Work processes		Apparatus		Approx. time consumed for fluid bed granulation e.g. for 100 kg. batches
Conventional Granulation	**Fluid bed Granulation**	**Conventional Granulation**	**Fluid bed Granulation**	
Weighing	Weighing	In mixing vessel	In "WSG"*) container	According to mixture
Mixing	Combinded (manually or automatically controlled)	Mixer	"WSG"*)	approx. 1–2 min.
Wetting, Kneading		Mixer-Kneader	In "WSG"*) by spraying	approx. 10 min.
Granulating		Granulator	—	—
Drying		Fluid bed drier or conventional drying oven	"WSG"*)	approx. 30 min.
Breaking		Mill or oscillator	—	—
Admixing the external phase		Mixer or granulate mixer	—	—
Sieving of fines	—	Sieving apparatus	—	—

*) WSG = Fluid Bed Granulator.

Fig. 1 — Fluid bed granulator WSG 120 closed (Manufacturer's photo: Fa W. Glatt, 7859 Haltingen, West-Germany).



1 motor
2 fan
3 excess pressure valve
4 knocking-off device
5 special round filter
6 streamlined nozzle mounting
7 particle deceleration zone
8 container
9 pneumatic lifting and sealing jack
10 air heating unit
11 pre-filter
12 dosing pump
13 connection for compressed air
14 air inlet and outlet ducts
15 air exit butterfly
16 air entry valve

Fig. 3 — Working plan of fluid bed granulator unit, type WSG 120 (Fa. W. Glatt, 7859 Haltingen, West-Germany).