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GRANULATION IN A FLUIDIZED BED II

EFFECT OF BINDER AMOUNT ON THE FINAL GRANULES

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ABSTRACT

There are many parameters affecting the properties of the final granules prepared in a fluidized bed. In this study one of the product parameters, quantity of the binder, has been studied for its effect on the final granule size, size distribution and friability.

Determination of granule size change as a function of binder quantity leaded us to study the growth mechanisms during fluidized bed granulation. Two mechanisms are suggested;

1) Snowballing of primary granules (nuclei).

2) Agglomeration of primary granules.

It has been shown that there is a critical amount of binder at which the formation of the primary granules

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comes to an end if more binder is added to the system. Then granule growth occurs by agglomeration of the primary granules. The physical properties of the granules formed before and after this critical binder concentration varies significantly.

INTRODUCTION

The process known as fluidized bed granulation has been extensively used for wet granulation since the early 1960's. It involves the spraying of a binding solution on to powders suspended in an upward moving stream of air.

This technique appears at first sight attractive, because all the multistage operations of conventional wet granulation can be performed using a single piece of equipment, thus reducing both time and labor costs. Comparison of this technique with conventional processes has been discussed in detail elsewhere (1,2).

The application of fluidized bed granulation in the pharmaceutical industry has, however, only been partially successfull. This occured as a result of the large number of existing formulations which could not be easily transferred to the new process without lengthy and expensive redevelopment work. Such redevelopment is necessary due to the existance of many different operating parameters for fluidized bed granulation, all of which can affect the properties of the final granules. Aulton and Banks (3,4) classified the possible variables during fluidized bed granulation into three groups;(a) apparatus parameters;(b) process parameters; and (c) product parameters. This classification is an extension of earlier suggestions made by Ormos et al (5) and Schaefer and Worts (6). A subsequent review by Aulton and Bank (4), however, indicated considerable controversy concerning the parameters involved. Devay et al. (7) recently attempted to optimize the operational parameters involved in this technique, with only marginal success.

Among the so-called product parameters, the amount of binder can be considered as one of the most important variables. This affects most specificially the size and friability of the resulting granules. Several investigators have shown that increasing the binder content of the granules causes a rise in granule size (8-11). Ormos et al (5) found that the mean size of the granules is mainly determined by the overall amount of the binder present, being independent of the relative amount of binder, feed rate and concentration of the granulating liquid. However, little explanation was given in these studies concerning the type of relation and mechanisms of granule growth. The purpose of the present study was to investigate the possible changes in fluidized bed granule properties caused by an increase in the amount of binder present. We hope also to determine the granule growth mechanisms occuring during fluidized bed granulation which are found with these changes.

EXPERIMENTAL

The materials used to prepare the granules were lactose[2], starch[3] and polyvinylpyrrollidone[4] (PVP). The following fomulations were employed for al batch granulation operations:

Component	Percent by weight
Lactose	74% - 88%
Starch	10%
PVP	16% - 2%

The amount of starch was, therefore, kept constant in all formulations. The variation in the quantity of the binder, PVP, was achieved by replacing an equivalent amount of lactose. As suggested by Alkan and Ulusoy (12) the binder was added to the premixed starch and lactose powders as a 7.5% w/w ethanolic solution.

The equipment employed for granulation has been described in detail elsewhere (12). Granulation was carried out on 288g of the powder mixture of lactose

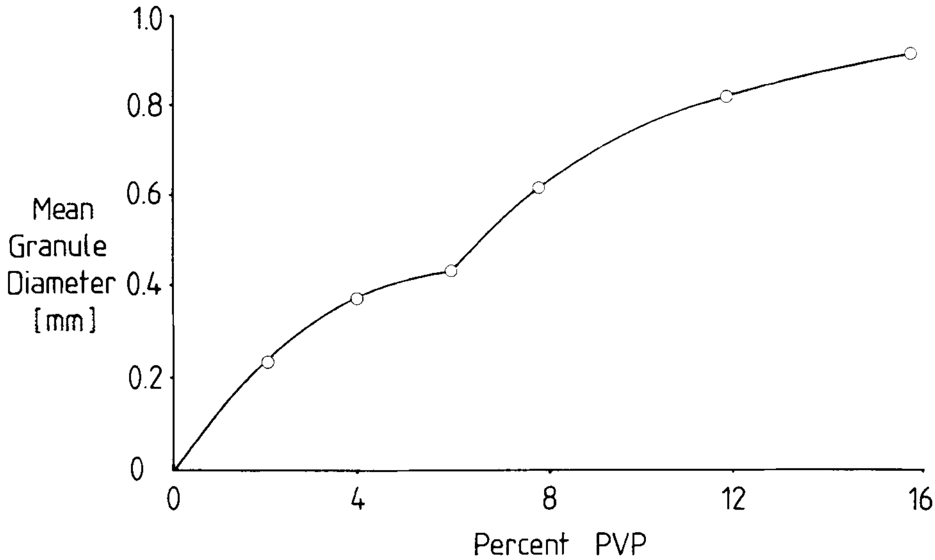

FIGURE 1

EFFECT OF BINDER AMOUNT ON MEAN GRANULE DIAMETER

and starch. The granulation parmeters were kept constant for all batches as follows:

Inlet air temperature:	303°K
Fluidization air flow-rate:	25-50 $m^3 s^{-1}$
Air pressure to the nozzle:	9.8 N cm^{-2}
Dome position on the nozzle:	5
Granulation fluid flow-rate:	25 $cm^3 s^{-1}$
Binary nozzle position:	18 cm from powder surface.

The mean sizes of the prepared granules as well as their friabilities were determined as described before (12).

TABLE 1

CHANGE IN MEAN GRANULE DIAMETERS WITH THE AMOUNT OF BINDER

% PVP	Mean Diameter (mm): Arithmetic	Geometric	S.D. from Mean
2	0.243	0.210	2.35
4	0.383	0.477	1.75
6	0.434	0.490	1.69
8	0.626	0.615	2.73
12	0.813	0.840	2.80
16	0.920	0.960	2.63

Effect of Binder Amount on Granule Mean Diameters.

RESULTS AND DISCUSSION

An increase in the amount of binder in the formulations caused the mean size of the granules to rise, as can be clearly seen in Figure 1. The change in mean size is more noticable with small amounts of binder i.e., up to a concentration of 6% PVP. Table 1 shows this change together with the geometric mean diameters and their standard deviations (S.D.) as determined from the log-probability plot of the sieve analysis data. The standard deviations indicate that the size distribution of the granules is narrowest with a binder concentration of 6%.

Figure 2 shows the granule size-distribution plots. A normal, narrow distribution was obtained for the formulation containing 6% PVP, whereas the other formulations showed wider distributions and were more close to a log-normal type.

Table 2 indicates how the granule friability decreases with increasing amount of binder, correspondent to a rise in the friability index (13). Less friable granules were formed as the binder concentration increased, an observation which is in agreement with previous reports (5,12). However, there is a limit for this increase in friability index, which in this case occured after a concentration of 6% binder.

The results show that there is a critical amount of binder at which the properties of the granules change during fluidized bed granulation. It is 6% w/w for the experimental conditions investigated in this study. This may be due to a change in the mechanism of formation of the granules in the process. The change with amount of binder in the quantity of granules having a specific size fraction may offer an

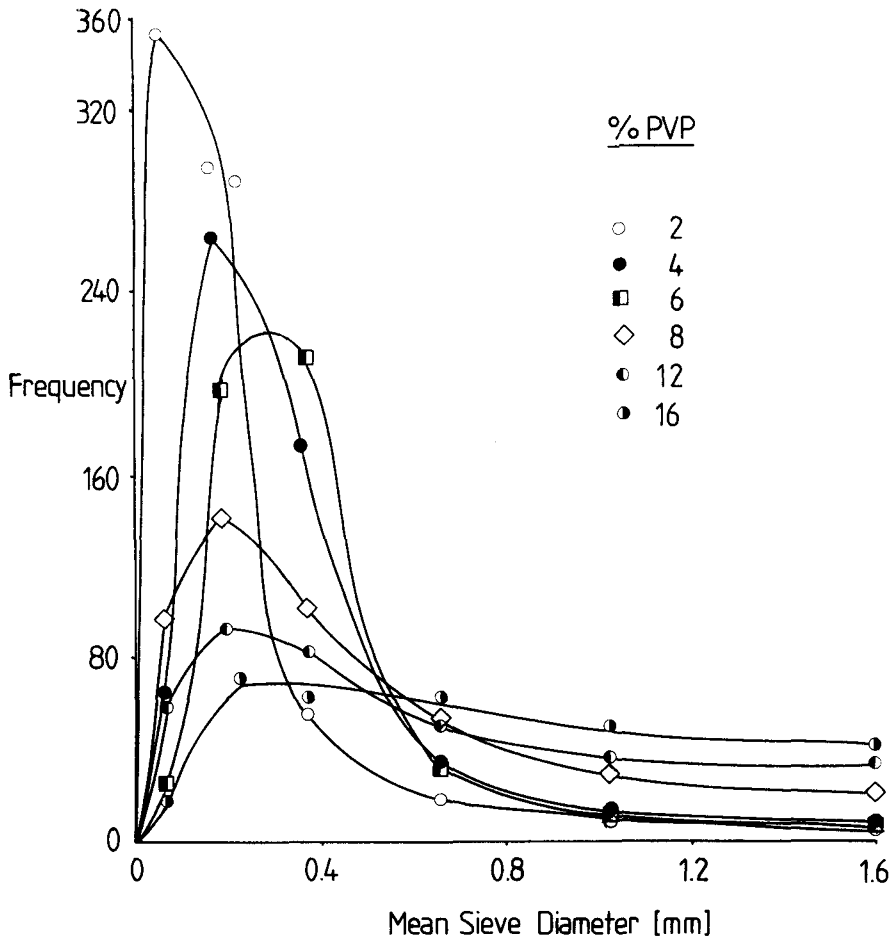

FIGURE 2

SIZE DISTRIBUTIONS OF GRANULES

explanation for these observations. In Figure 3, changes in the % weight of both small and large granules with binder amounts are shown. It can be see that the quantity of large granules (1.25 - 2.00 mm) i very small up to 6% of binder. Above this

TABLE 2

CHANGE IN GRANULE FRIABILITY WITH THE AMOUNT OF BINDER

% PVP	Friability Index
2	54.05
4	68.86
6	71.73
8	77.96
12	78.08
16	77.54

Effect of Binder Amount on Friability of Granules.

concentration of PVP, the formation of big granules increases very rapidly and reaches a quantity as high as 30% of the total amount. Figure 3 also shows that the amount of fines (0.125 mm) decreased very quickly as the binder concentration increased to 6%; after this, however, there was a gradual decrease in these quantities. The slight increase in fine amounts just after 6% PVP may be explained from the abrasion effects

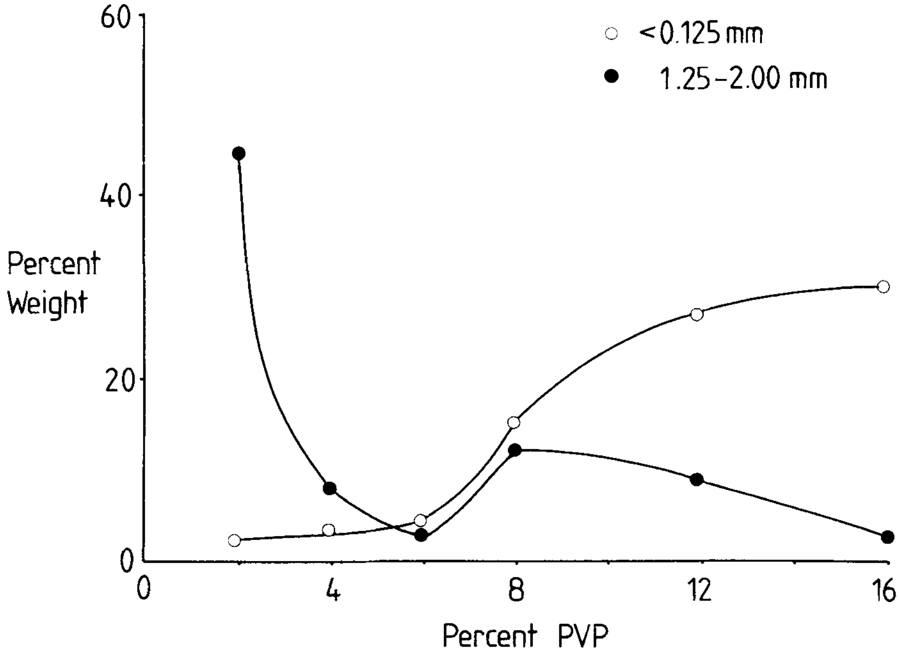

FIGURE 3

EFFECT OF BINDER AMOUNT ON PERCENT WEIGHT FRACTION

of the fluidizing air during transition from one granulation mechanism to another. From these results it is obvious that a marked difference occurs in properties of the granules at a binder concentration of approximately 6%. This can be explained by postulating a change in the granulation mechanism around this binder concentration.

Granules can be formed in a fluidized bed by two mechanisms. These are shown schematically in Figure 4. The first mechanism ('snowballing') involves the

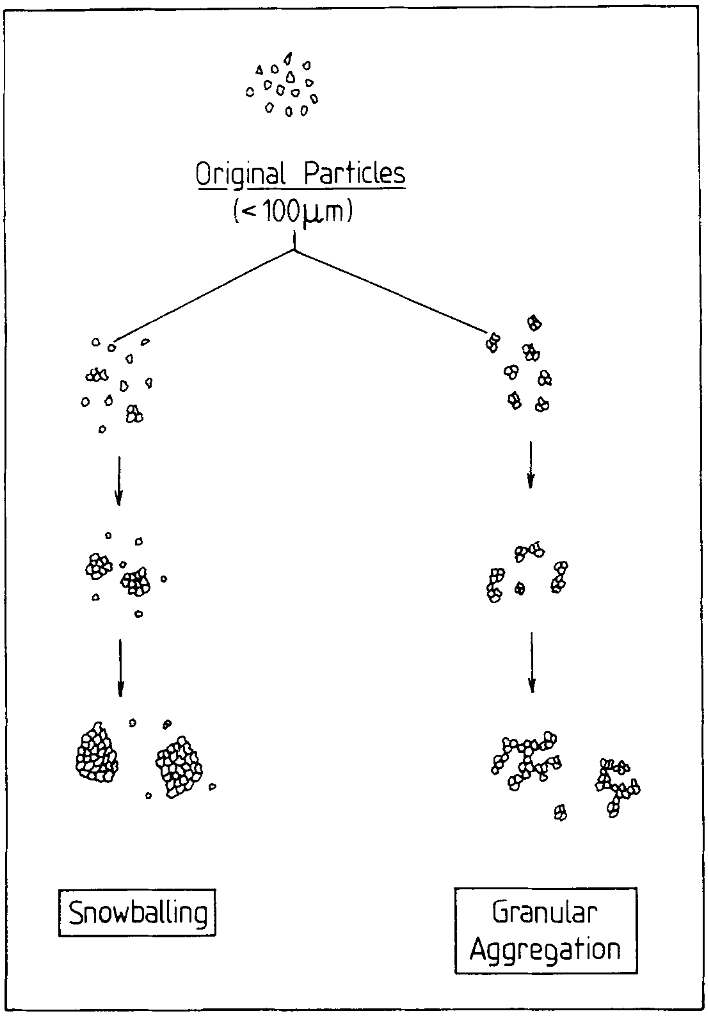

FIGURE 4

GRANULATION MECHANISMS

initial formation of primary granules by the aggregation of a few individual particles (nuclei). These subsequently grow by the adhesion of the other individual particles onto the surfaces of the nuclei. The second mechanism involves the formation of large granules by the direct agglomeration of the primary granules with each other. The rate of growth of granules with this second mechanism should be higher than that occuring with snowballing. This corresponds to the regression analysis of the semilogarithmic plot of Figure 1, which yields two straight lines. The rate of growth of the second mechanism (0.145) was twice that of the first (0.071), as indicated by the slopes of the regression analysis. Microscopical observation of granules supported this idea of their formation by two different mechanisms; those formed by the second mechanism possesed a much rougher surface than those prepared by the first, as would be expected.

It can be suggested that the second mechanism was responsible for the formation of the large granules at concentrations of above 6% PVP, whereas the first mechanism predominated during the formation of primary granules upto 6% PVP. This critical amount of binder appears to be the optimum amount required to form even and narrowly-distributed granules. Under the conditions used in these studies, concentrations above this optimum quantity of binder cause the primary granules to agglomerate, producing a marked change in the physical properties of the final granules. However, if the concentration of binder is reduced to less than 6%, an insufficient amount exists to bind all of the individual particles together.

The maximum mean size of the primary granules which can be formed under the studied conditions is 0.434 mm. This can be determined from Figure 3 from the value corresponding to 6% binder concentration.

CONCLUSION

During fluidized bed granulation the amount of binder can affect the properties of the final granules e.g., mean size, size distribution and friability. Also the granulation mechanism can change with change in amount of binder present in the formulation. The optimum amount of binder should be that which is necessary to bind individual powder particles together to form primary granules by the snowballing mechanism. In this fashion the granules have the smallest size distribution and friability. An excess of binder is unadvisable, since it can change these desired properties and also increase production time and cost.

FOOT NOTES

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