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# FLUIDIZED BED GRANULATION WITH PVP K90 AND PVP K120

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## ABSTRACT

The characteristics and growth mechanisms of fluidized bed granules are dependent both on process variables and the grades of PVP binders used. Generally, an increase in the concentration, spraying rate and volume of binder solution caused an increase in granule size and a decrease in size distribution. These two factors will in turn affect the poured and tapped densities of granules. Granules prepared with PVP K90 solution appeared to grow by primary and secondary agglomeration to give an aggregate structure. Granules prepared with PVP K120 solution were formed through snowballing as the primary agglomeration process. This occurred at low binder solution concentration with secondary agglomeration taking place when the concentration of PVP K120 solution was increased.

## INTRODUCTION

Fluidization of starting powders in the presence of a suitable binder solution is a rapid means of achieving granulation. The properties, behaviour and choice of binder solution influence the process variables utilized for granulation and have profound effect on the final characteristics of granules produced [1-6]. This study aims to examine the effects of a low and a high molecular weight PVP on granulation.

## MATERIALS

Lactose (Pharmatose 200M, DMV, The Netherlands) was used as the feed material. The binders were polyvinylpyrrolidone, low (1,100,000) and high (2,000,000) molecular weight (PVP; Kollidon K90, BASF, Germany and Povidone K120, GAF, USA respectively).

## METHODS

### Granule Formation

Lactose powder, 400 g, previously sieved through 710 µm aperture size sieve, was granulated in a fluidized bed granulator (Niro Aeromatic, Strea 1, Switzerland) with PVP solution. Unless otherwise stated, the operating conditions used were: volume of binder solution 200 ml, atomizing pressure 0.8 bar, air volume 75-100 $m^3$/hr, inlet and outlet air temperature 60°C and 33°C, drying time 3 minutes and nozzle height from base plate 23.5 cm. The concentration and spraying rate for PVP K90 solution were 5% w/w and 15 g/min respectively while that of PVP K120 solution were 1.5% w/w and 12 g/min respectively.



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TABLE 1
Size Analysis Data and Formfactor Values of Granules

| Binder | Process Variables | | Mass Median Diameter (μm) | Span | % weight < 250 μm | Formfactor |
|---|---|---|---|---|---|---|
| PVP K90 | Conc (% w/w) | 3 | 560 | 1.82 | 14.0 | 0.805 |
| | | 5 | 560 | 1.49 | 4.9 | 0.846 |
| | | 7 | 1240 | 1.43 | 0.1 | 0.799 |
| | Spraying rate (g/min) | 9 | 425 | 2.44 | 16.8 | 0.638 |
| | | 12 | 450 | 1.87 | 16.8 | 0.691 |
| | | 15 | 560 | 1.49 | 4.9 | 0.846 |
| | Volume (ml) | 100 | 525 | 1.97 | 21.4 | -* |
| | | 150 | 535 | 1.64 | 13.5 | 0.861 |
| | | 200 | 560 | 1.49 | 4.9 | 0.846 |
| | | 250 | 670 | 1.19 | 0.2 | 0.871 |
| | | 300 | 675 | 1.24 | 0.4 | 0.904 |
| PVP K120 | Conc (% w/w) | 1 | 1175 | 2.00 | 23.5 | -* |
| | | 1.5 | 1490 | 1.19 | 7.0 | 0.963 |
| | | 2 | 1430 | 1.85 | 5.8 | 0.804 |
| | | 3 | 1740 | 1.31 | 0.1 | 0.775 |
| | Spraying rate (g/min) | 9 | 1205 | 1.77 | 7.8 | 0.859 |
| | | 12 | 1490 | 1.48 | 7.0 | 0.963 |
| | | 15 | 1675 | 1.19 | 2.4 | 0.951 |
| | Volume (ml) | 150 | 1465 | 1.57 | 9.8 | 0.940 |
| | | 200 | 1490 | 1.19 | 7.0 | 0.963 |
| | | 250 | 1385 | 1.31 | 1.9 | 0.942 |
| | | 300 | 1900 | 1.32 | 1.4 | 0.939 |

* Sphericity of granules was not determined as the modal size fraction contains granules of size less than 250 μm.

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Size Analysis and Sphericity

A nest of sieves (Endecotts, UK) of aperture sizes 250, 355, 500, 600, 710, 850, 1000, 1180, 1400, 1700, 2000, 2800, 3350 μm was used. Mass median diameter and span of each batch of granules were determined. Span is the ratio of size difference at 90th and 10th percentile to that of the mass median diameter.

Sixty granules, taken randomly from the modal size fraction of each batch, were subjected to formfactor determination (Imageplus, Dapple System, USA). The formfactor is defined as $4\pi$ X (area/perimeter$^2$). A value of unity indicates a perfect circle.

Poured and Tapped Densities

Granules were gently poured into a 100 ml preweighed graduated cylinder which was cut at 100 ml mark, levelled and weighed. Tapping was carried out using a mechanical tapping apparatus (Stampvolumeter, STAV 2003, Germany). The cylinder containing the poured granules was tapped for 1000 times or until there was no change in volume.

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Hausner ratio is the ratio of tapped density to poured density and measures the frictional condition in a moving powder mass. Carr index is the ratio of the difference of tapped and poured densities to tapped density and measures the degree of compaction.

### Friability and Crushing Strength Tests

A weighed granule sample of about 10 g was placed in a friabilator (Roche, Erweka, Model TA3R, Germany) with 15 steel ball bearings (average weight 0.88 g, average diameter 6.00 mm) and rotated at 30 rpm for 4 minutes. Friability index is the quotient in percentage of mass median diameters of granules after and before friability test.

Twenty five granules taken randomly from the size fraction of 710-850 µm were subjected to a crushing test using a tensile tester (Algol, Model 2252, Japan). The crushing force was applied at a rate of 2.975 mm/s. The load required to crush each granule was recorded with a digital force gauge (Aikoh, 9000 series, Japan) and the mean of 25 granules calculated.

### Viscosity Study

The kinematic viscosities of the binder solutions at 30°C, 40°C, 50°C and 60°C were determined using a suspended-level viscometer (Technico, No. 2, UK).

## RESULTS AND DISCUSSION

### Concentration Effect

The mass median diameter of PVP K90 granules remained the same at low binder solution concentrations (3% and 5% w/w) while those produced with higher binder solution concentration are of larger size. The proportion of fine particles from the latter batch was markedly reduced (Table 1). The granules with 7% w/w PVP K90 appeared to be made up of aggregates of small particles. This was attributed to the secondary agglomeration taking place during granulation, as a consequence of the high concentration used. A high concentration rendered a solution more viscous (Table 2). Earlier studies [7, 8] had shown that binder solutions of higher viscosity produced larger droplet size leading to an increase in granule size. The increase in binder solution concentration conferred strong liquid bridges between powder particles. Once formed, the bonds were strong enough to resist breaking up forces generated by the fluidization process. Thus, such formed nuclei were more susceptible to further size growth with a greater tendency towards the formation of aggregates. This observation is supported by the presence of the small fraction of particles below 250 µm and a low span value of 1.43 which indicated a narrower size distribution of granules in comparison to those granulated by lower concentration of PVP K90 binder solution. These small particles were exhausted in the granule growth by adhering together or to formed nuclei. The formfactor value of these granules deviated significantly from unity. This is a further indication of the formation of aggregates. Granule strength increases with the concentration of binder solution due to the higher content of binder in the liquid bridges which when dried formed strong bonds within granules (Table 2).

There is a trend towards a lower Hausner ratio and Carr index with increasing PVP K90 solution concentration (Table 2). Low concentration PVP K90 solution produced granules of wider size distribution as indicated by the larger span value. Thus, closer packing was possible with smaller granules occupying the spaces left by the larger granules. With increasing binder solution concentration up to 7% w/w, irregular granules or aggregates were produced. These granules packed at very low apparent densities. This gave rise to smaller Hausner ratio and Carr index.

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TABLE 2
Packing and Mechanical Strength of Granules and Viscosity Data of PVP Solutions

| Binder | Process Variables | | HR | CI | FI (%) | CS (N) | Viscosity (centistoke) | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | 30°C | 40°C | 50°C | 60°C |
| PVP K90 | Conc (% w/w) | 3 | 1.155 | 0.134 | 73.2 | 0.22 | 75.6 | 54.4 | 39.9 | 29.0 |
| | | 5 | 1.119 | 0.107 | 80.4 | 0.36 | 189.7 | 135.8 | 96.0 | 68.2 |
| | | 7 | 1.103 | 0.093 | 91.1 | 0.55 | 406.4 | 285.3 | 200.5 | 140.8 |
| | Spraying rate (g/min) | 9 | 1.174 | 0.148 | 83.5 | 0.30 | | | | |
| | | 12 | 1.163 | 0.140 | 81.1 | 0.27 | | | | |
| | | 15 | 1.119 | 0.107 | 80.4 | 0.36 | | | | |
| | Volume (ml) | 100 | 1.161 | 0.138 | 34.3 | 0.13 | | | | |
| | | 150 | 1.132 | 0.116 | 83.2 | 0.20 | | | | |
| | | 200 | 1.119 | 0.107 | 80.4 | 0.36 | | | | |
| | | 250 | 1.105 | 0.095 | 93.3 | 0.57 | | | | |
| | | 300 | 1.086 | 0.079 | 96.3 | 0.62 | | | | |
| PVP K120 | Conc (% w/w) | 1 | 1.135 | 0.119 | 17.0 | 0.07 | 41.1 | 30.3 | 22.0 | 16.6 |
| | | 1.5 | 1.089 | 0.082 | 61.1 | 0.11 | 73.4 | 54.2 | 39.4 | 29.2 |
| | | 2 | 1.089 | 0.080 | 74.8 | 0.21 | 113.6 | 84.2 | 60.0 | 43.7 |
| | | 3 | 1.073 | 0.069 | 85.1 | 0.37 | 251.4 | 189.0 | 133.2 | 97.5 |
| | Spraying rate (g/min) | 9 | 1.121 | 0.108 | 57.3 | 0.15 | | | | |
| | | 12 | 1.089 | 0.082 | 61.1 | 0.11 | | | | |
| | | 15 | 1.073 | 0.068 | 66.9 | 0.18 | | | | |
| | Volume (ml) | 150 | 1.101 | 0.091 | 24.2 | 0.10 | | | | |
| | | 200 | 1.089 | 0.082 | 61.1 | 0.11 | | | | |
| | | 250 | 1.089 | 0.082 | 59.2 | 0.20 | | | | |
| | | 300 | 1.059 | 0.055 | 76.3 | 0.32 | | | | |

HR: Hausner ratio CI: Carr index FI: Friability index CS: Crushing strength

Different mechanisms of size growth are observed for granulation with PVP K120 solution. Snowballing as the primary agglomeration process predominated at low binder solution concentration and secondary agglomeration occurred at higher binder solution concentration. The useful range of concentration that was able to produce granules of suitable size and size distribution was narrow. A concentration of 1% w/w PVP K120 solution resulted in a large proportion (23.5%) of particles less than 250 µm (Table 1). Low concentration of PVP K120 solution has less adhesive action and results in weaker bonding of particles. This was reflected in the smaller friability index and crushing strength values obtained (Table 2). Granule formation in a fluidized bed is a balance of size enlargement and reduction. Weak liquid bridges on the surfaces of feed material would not be able to hold the powder making up a particle and thus allowing size reduction process to predominate. A further reduction in binder solution concentration may prove to be too dilute for exertion of any binding effect on the feed material. This very low concentration of PVP K120 solution caused caking at the base of fluidized bed granulator because of the high solubility of lactose.

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Majority of the granules that did form with the low concentration PVP K120 solution were from the larger size range. The span value of 2.00 which was relatively larger than the other batches indicated a wide size distribution and thus favoured a larger Hausner ratio and Carr index (Table 2). Formfactor value of these granules was not determined as the modal size fraction fell in the region of fine particles (< 250 µm) which may not give meaningful results. An increase in the concentration of PVP K120 solution to 1.5% w/w significantly reduced the proportion of particles less than 250 µm and the span value although the granule mass median diameter was increased. These granules had formfactor value approaching unity. These round granules may be formed by snowballing process which explained the size and shape of granules. In snowballing mechanism, many fine particles are involved in the layering process onto formed nuclei. This size growth occurred towards the last stages of granulation process and the size growth at this stage was rapid. It, however, did not lead to the formation of aggregates which could be brought about by secondary agglomeration. These granules being spherical, packed well but with less fine particles to occupy the intergranular spaces which led to a lower Hausner ratio and Carr index than that of granules produced by a lower binder solution concentration. A further increase in the concentration of PVP K120 solution to 2% w/w caused a slight drop in the mass median diameter of granules. At this concentration, secondary agglomeration played a major role. The binder solution concentration was sufficient to bind powder particles together to cause aggregation but yet not strong enough to maintain the aggregate structure. This resulted in a breakdown of aggregates giving rise to a smaller mass median diameter.

The size reduction process during continuous fluidization was greatly reduced when PVP K120 3% w/w solution was employed for the granulation process. The agglomerates formed were strong but irregular in shape with formfactor value greatly deviating from unity, confirming size enlargement by secondary agglomeration. Mechanical stress during fluidization was not strong enough to overcome the strong liquid bridges formed between particles. Friability index and crushing strength values were high. When the same concentration (3% w/w) of PVP K90 and PVP K120 binder solutions was compared, the mechanical strength of granules granulated with PVP K120 was greater. This was attributed to the greater binding power of PVP K120 and was reflected by the viscosity profiles at all temperatures (Table 2). The more viscous PVP K120 3% w/w solution prevented flow of binder solution on primary particle to allow a size enlargement by layering process. Instead, the more localised binder solution permitted adherence of particles and powder material onto localised spots thus creating aggregates comprising small particles. Coupled with the increase in droplet size due to the increase in binder solution viscosity, non-spherical granules were produced. These non-spherical granules packed poorly with much interlocking and gave small Hausner ratio and Carr index.

## Spraying Rate Effect

The increase in spraying rate of both types of PVP caused a corresponding increase in the granule size (Table 1). A high spraying rate allows a greater number of droplets to be sprayed onto powder material per minute. This resulted in an increased number of liquid bridges and hence a larger granule size. The continuous impingement of binder liquid permitted a greater possibility of powder or small particles to meet and adhere to each other in an attempt to form a larger particle. With a slow spraying rate, binder solution evaporated rapidly per unit time. Binding of particles is then not promoted. In addition to this, the longer granulation time exposed granules to attrition forces resulting in smaller size granules. Size and shape of granules are affected by the change in the spraying rate, with higher spraying rate producing larger granules which when packed leave much intergranular spaces. On the other hand, granule strength did not present a consistent pattern when the spraying rate was varied (Table 2). Instead, the change is more obvious when the concentration or volume of binder solution was varied as these directly determined the amount of granulating binder used for each process.

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Volume Effect

Variation in binder volume was found to affect granule size though not to a very large extent (Table 1). In the case of PVP K90 solution, there was an increase in the granule size although small with increase in the binder volume. Formfactor values of these granules remained favourable. In the case of PVP K120 solution, the increase in the binder volume from 150 to 250 ml produced granules that were similar in mass median diameter. This is possibly due to the longer granulation time associated with the larger volume used which would probably negate the effect of the increased volume. Longer granulation time would mean granules were subjected to a greater attrition effect. A higher volume of 300 ml was too large for the powder load and allowed a large increase in size not withstanding the effect of process time. The effect of volume on granule strength and packing properties was similar to that of concentration (Table 2).

The conditions used for granulation with the two types of PVP were not directly comparable due to their different binding properties which would require different processing parameters for granulation to occur successfully. However, they served to illustrate the change in the granule characteristics as well as offered some insight into granule growth resulting from the two molecular weights PVP at different process variables of granulation. One interesting aspect of granulation with PVP K120 was that with the correct concentration, the granules produced have formfactor values approaching unity which indicates a collection of generally spherical granules which may have come about through snowballing process. Spraying rate and volume of binder solution did not seem to affect the sphericity of granules as much as the concentration effect. The majority of K120 granules formed were, however, either very fine or very large. There was a narrow range of PVP K120 concentration that can be used for production of granules. Beyond this range, granulation process was found to produce quite unsatisfactory granules, being too fine or of aggregate nature.

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