

The influence of a Swinging Bowl on Granulate Properties

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The influence of the use of a swinging bowl on drying times and granulate properties of a low-binder formulation was studied.

One large batch of granulate was prepared in a high-shear mixer (GRAL 600) and divided into sub-batches that were dried under vacuum in a high shear single pot processor (ULTIMA 25), either using the swinging bowl or not.

Drying time, particle size distribution, flowability, poured and tapped bulk density, Carr's Index and Hausner ratio of the granulate dried with the 2 different methods are compared.

The results show that using the swinging bowl during drying speeds up the drying process, improves the particle size distribution, leading to better flowability and bulk density results.

Single pot processing with the use of the swinging bowl can thus present a solution for contained processing of low-binder formulations.

In view of the current trend of keeping production processes as contained as possible, many old production processes have to be reviewed. There are still a lot of formulations developed for older production techniques like granulation in planetary mixers and drying in ovens. Usually these formulations contain only a small amount of binder, or a very weak binder. When these old formulations have to be

processed in a more contained and more modern way, problems may arise due to the fact that these granulations are very weak and easily broken down by mechanical action.

Single Pot processing, or mixing, granulation and drying in the same high shear mixer, is becoming more and more popular to produce in a contained way. However, a possible disadvantage of

single-pot processing techniques is the fact that it can be difficult to process weak granulates due to the necessary action of the mixer arm during the drying process, which causes attrition.

Weak granulates that have to be dried under vacuum, without the use of microwaves, are particularly susceptible to this detrimental action. In case of high moisture content, a pure vacuum drying process can take several hours, and the mixer has to be used frequently to obtain a good contact with the heated wall of the bowl, from where the evaporation energy comes.

As an alternative to the use of the mixer arm for bringing the product into contact with the heated wall, the movement of a swinging bowl can be used.

This study is aimed to investigate the influence of the use of the swinging bowl (without use of the mixer arm) on drying times and granulate properties of a low-binder formulation.

Method

Wet granulation. To obtain comparable results with regard to particle size distribution, one large batch of a PVP placebo was granulated on a GRAL 600 (Collette NV, Wommelgem, Belgium).

Table I: Composition of the PVP placebo

Material	Quantity	Supplier
Lactose (min. 98% < 150 µ)	139.2 kg	(DMV, Holland)
Corn Starch	15.6 kg	(generic brand)
PVP K30	5.04 kg	(BASF, Germany)
Water	±18.5 kg	

All ingredients were added dry into the bowl and were mixed for 3 minutes at a mixer speed of 95 rpm. The water was added via the liquid addition system of the machine, consisting of a pressure vessel (at 4 bar) and a flat-spray nozzle with a flow rate of 8 litres /min at 2 bar (Delavan, UK) with the mixer at 95 rpm. The chopper was activated at low speed (1350 rpm) after 1 minute of liquid addition. The total time of liquid addition and wet mix (to distribute the water homogeneously) was 5 minutes with mixer and chopper at the above settings. For the granulation, the mixer speed was increased to 135 rpm and the chopper was kept on low speed. Granulation took 8 minutes.

The product was discharged from the bowl through a 2 mm wet mill (Quadro, Canada) and then divided into 8 sub-batches of 6.660 kg each. Seven sub-batches were dried in an ULTIMA 25 (Collette NV, Belgium) and one in a tray dryer (Vismara, Italy).

Drying of the granulate

Three different drying methods were applied on the batches:

Tray drying: 1 batch of the PVP placebo was dried for approximately 16 hours on a tray at an approximate temperature of 40°C. This batch represents the reference for the particle size distribution of the granulate after granulation.

Vacuum drying without use of the swinging bowl: 3 batches

Vacuum drying with use of the swinging bowl: 4 batches

The drying conditions for the 2 vacuum drying procedures are summarized in Table II.

Table II: Parameters used during drying

Parameters	Vacuum drying without swinging	Vacuum drying with swinging
Temperature jacket (°C)	50°C	50°C
Temperature chiller (°C)	1°C	1°C
Vacuum	0 mbar	0 mbar
Mixer function	ON	OFF [†]
Speed	50 RPM	/
ON / OFF (flip/flop) mode	- T0 - T15: 20" / 20" - T15 - T30: 20" / 60" - T30 - T60: 20" / 40" - T60 - T75: 20" / 60" - T75 - end: 10" / 60"	/
Chopper function	ON	OFF [†]
Speed	600 RPM	/
ON / OFF (flip/flop) mode	OFF (chopper follows the same settings as mixer)	/
Swinging function	OFF	ON
Position	/	Position 2 (75°)
Mixer left / right (x / y)*	/	- T0 - T30: 5 / 0 - T30 - T60: 10 / 0 - T60 - T75: 0 / 0 - T75 - end: 15 / 0 - Mixer time = 2"

[†] When swinging is used, the mixer and chopper functions are switched off, but are automatically activated during swinging (see mixer left/right). * This function will activate the mixer at a speed of 50 rpm and the chopper at a speed of 600 rpm every xth time the bowl reaches its maximum position (in this case 75°) on the left side and every yth time the bowl reaches its maximum position (in this case 75°) on the right side.

They are kept the same for both methods with regards to jacket temperature, chiller temperature, pressure in bowl and mixer and chopper speed. The difference between the 2 methods lies in the use of the swinging bowl or not, and in the frequency of use of mixer and chopper.

The vacuum drying method without use of the swinging bowl, utilizes the "flip/flop" for the mixer and chopper with setpoints between 20 seconds on / 20 seconds off, and 10 seconds on / 60 seconds off (this means that the mixer and chopper will be activated during 20 seconds / 10 seconds respectively and then stopped for 20 seconds / 60 seconds, respectively)

The vacuum drying method with use of the swinging bowl utilizes the "Mix left/right" function, with setpoints between 5/0 and 0/0, with mixer time 2 seconds. This means that the mixer and chopper will be activated for 2 seconds every 5th / 0th time, respectively, the bowl reaches its left extreme position and never (in both cases) when the bowl reaches the right extreme position.

The difference between these 2 methods with regards to frequency of use of mixer and chopper can be seen in figure 1a and 1b.

In both methods, the granulate was mixed for 30 sec. at a mixer speed of 100 rpm and a chopper speed of 1500 rpm before drying, in order to homogenize the product and to avoid influences by the storage time.

Every 15 minutes the process was stopped to take a sample. The sample was taken every time at the same place (the middle of the bowl) from the top layer of product.

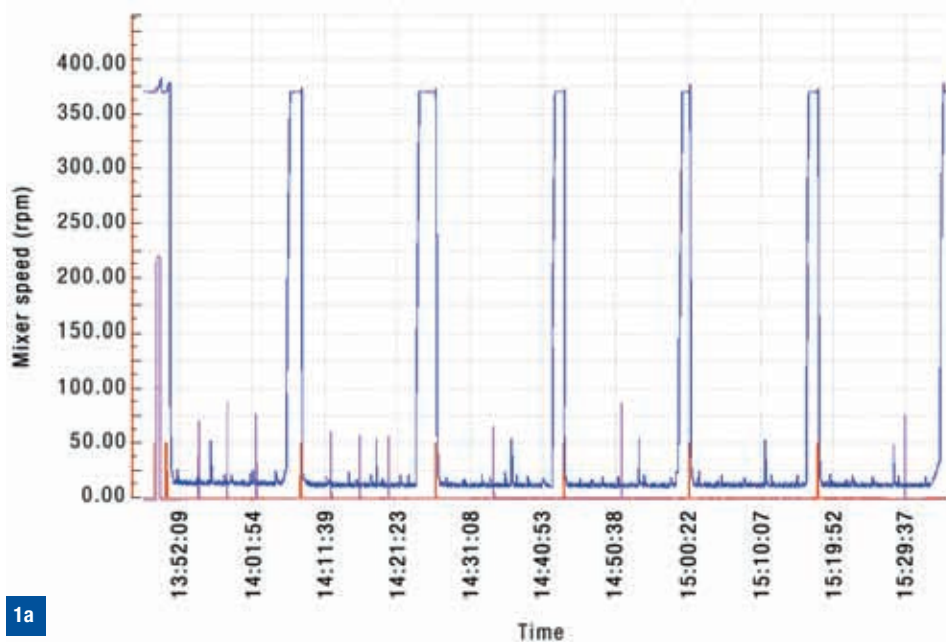
Seven grams of each sample were analyzed on a Halogen Moisture Analyser (type HR73, Mettler-Toledo, Germany) at a temperature of 105°C with an endpoint of 10 minutes.

Drying was continued for each batch until the moisture level was below 2% w/w.

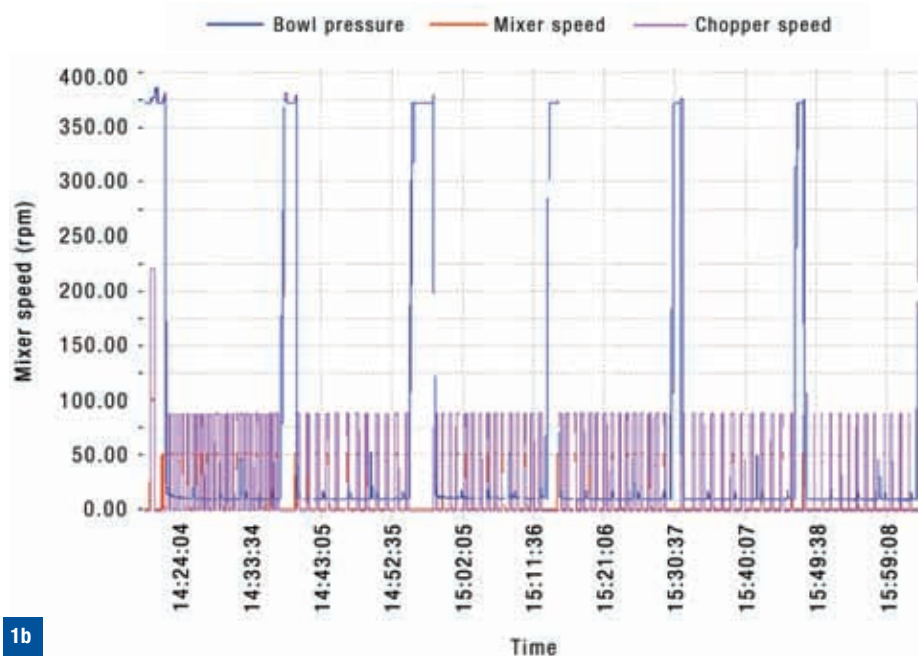
Granulate properties

When the granulate was dry, sieve analysis was done with a set of sieves with the following mesh sizes: 1000 µm, 850 µm, 500 µm, 250 µm, 150 µm, 75 µm, 38 µm (Retsch, Germany). Each batch was passed through a 2000 µm sieve and three 100 g samples of each batch were shaken on a shaker (Retsch, Germany) for 10 minutes. The amount of particles on each screen was measured.

Figure 1: Use of mixer and chopper during drying (a) with swinging bowl; (b) without swinging bowl



1a



1b

Flowability of the granulate was investigated by measuring the flow rate of 100 g of granulate through a normalised hopper with the following dimensions (1):

- upper diameter:
 - external / internal: 132 / 128 mm
- diameter of the outlet:
 - external/ internal: 12 / 8 mm
- Height of the outlet: 125 mm
- Total height: 235 mm

Both the granulate alone and the granulate mixed with 0.5% magnesium stearate in a GRAL 10 high shear mixer (Collette NV, Belgium) for 90 seconds at speed 1 (420 rpm), were tested.

The procedure used is as follows:

- the outlet of the hopper is blocked

- the sample of 100 g is introduced into the hopper, taking care that the outlet is completely filled
- a timer is started at the exact moment when the block of the outlet is taken away and stopped when the whole sample has flown out of the hopper.

The bulk density of a 100 g sample of each batch, before and after addition of 0.5% magnesium stearate, was tested using a poured and tapped bulk density measurement device (J. Engelsmann AG, Germany). A volume measurement was taken before tapping (poured bulk density) and after 500 taps (tapped bulk density). From this volume measurement, the poured and tapped bulk density was

calculated as well as the Carr's Index (CI) and the Hausner ratio to evaluate flowability and compressibility.

The Carr's Index is calculated according to the following formula (2):

$$CI(\%) = 100 * (d_t - d_u) / d_t$$

Where

d_t = tapped bulk density

d_u = poured bulk density

CI is thus a measure of the percentage of compressibility and can be interpreted in the following way: the higher the compressibility, the poorer the flowability (3). According to Carr, an excellent flowability can be expected when the index is 5 to 15 % (2).

The Hausner ratio is the ratio between tapped bulk density and poured bulk density and is an assessment of interparticulate friction. According to Stamm and Mathis, this ratio should be below 1.6 to be able to produce suitable tablets (4).

Results and Discussion

Influence on drying times. The first striking result from this comparison was that the drying times for the batches dried under vacuum with use of the swinging bowl were on average 15 minutes shorter than those for the batches dried without use of the swinging bowl (see Figure 2).

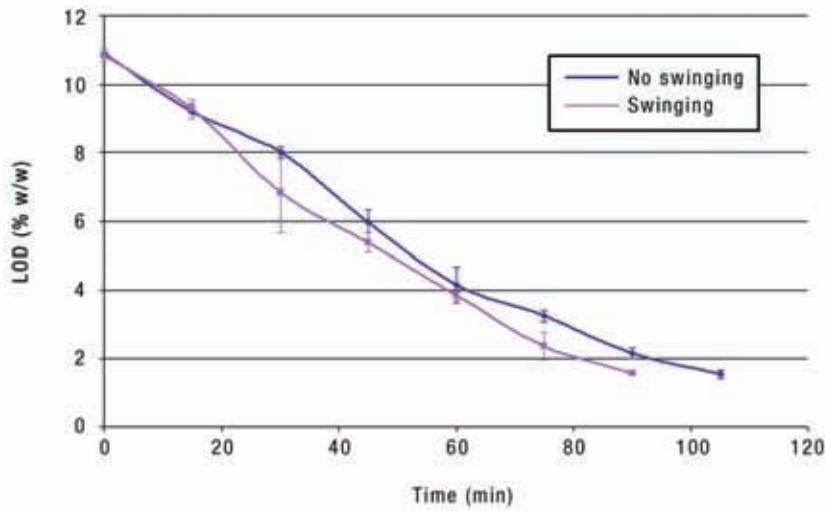
In trying to determine whether this difference in drying time is significant, a hypothesis test was done on the difference of the mean Loss on drying (LOD) after 90 minutes drying.

This point was chosen because, at that point, the LOD of all batches dried using the swinging bowl was below 2% w/w, which was determined as the endpoint for drying, while none of the LODs of the batches dried without using the swinging bowl was below the 2% w/w limit.

The hypothesis test shows that the null hypothesis, that the means of the LOD are the same, can be rejected at the 1% significance level ($p=0.00085$). This means that there is a significant difference between the average LOD after 90 minutes drying of the batches dried using the swinging bowl and the average LOD after 90 minutes drying of the batches dried without using the swinging bowl, while no difference could be found between the average LODs of these batches at the beginning of drying ($p=0.189$).

As the difference in average LOD is significant at 90 minutes of drying, it is safe to

Figure 2: Comparison of drying times for vacuum drying with and without swinging bowl. Limits of error for each point = 2 x standard deviation for that point. (LOD = Loss On Drying.)



assume that the difference in drying times is also significant.

This result is especially striking if the frequency of use of the mixer arm is taken into account. Trials have shown that the speed of drying decreases when the frequency of use of the mixer arm decreases (5). In Figures 1a and 1b, it can be clearly seen that the frequency of use of the mixer (and the chopper) was much lower for the batches dried with the swinging bowl compared to the batches dried without swinging bowl, thus one would expect a longer drying time for first batches.

The shorter drying time for the batches dried using the swinging bowl is due to the fact that the available area for energy transfer between the heated wall and the product is much larger when using the swinging bowl (even without the use of the mixer arm), then when using a static bowl and the action of the mixer arm to bring the product into contact with the wall.

This result is of major importance for the processing of low-binder or weak

granulates, as it is known that the destruction of the granulate is partially due to the shear force of the mixer arm on the granulate during drying. In order to avoid this effect of the mixer arm, the frequency of use of the mixer arm can be reduced, but when we work with a static bowl, this leads to an increase in drying time (5).

The swinging bowl now offers a solution to this problem: the frequency of use of the mixer arm can be drastically reduced without increasing the drying time, on the contrary, even reducing it.

As the use of the swinging bowl during drying reduces drying time, as well as the need for use of the mixer arm, it can be expected that it also has a positive effect on the granulate quality and more specifically on the particle size distribution.

Influence on granulate properties

Particle size distribution. A comparison of the particle distribution of the reference batch and the batches dried with and without use of the swinging bowl is presented in Figure 3 and Table III

(average of 3 measurements for each batch and all batches dried with the same method).

From this comparison can be seen that vacuum drying without use of the swinging bowl almost completely destroys the weak granulate leaving an enormous amount of fines (43.1 % smaller than 75 µm). The use of the swinging bowl reduces the amount of fines to 15.5%.

It can also be seen that the particle distribution of the batches dried with use of the swinging bowl comes closer to that of the reference batch, which is an almost ideal particle size distribution and represents the particle size distribution obtained after granulation (as no mechanical action was exerted on the granulate).

As explained above, the 2 main reasons for the beneficial effect of the use of the swinging bowl on particle size are the facts that the drying time is shorter and the mixer arm is only used sporadically.



Single pot dryer

Flowability testing (Table IV). When measuring the flow rate of the granulate before it was mixed with magnesium stearate, it was observed that all batches dried under vacuum without the use of the swinging bowl formed bridges in the hopper. Therefore it was not possible to determine the flow rate. When the hopper was submitted to vibration, the granulate flowed freely through it.

By contrast, all batches dried under vacuum using the swinging bowl presented a very good flow rate. On average, a sample of 100 g flowed through the hopper in 3.27

Table III: Particle size distributions

Sieve size (µm)	Reference batch (%)	Vacuum drying without swinging (%)	Vacuum drying with swinging (%)
>1000	8.4	3.0	4.9
>850	2.8	1.2	1.1
>500	9.2	5.8	6.1
>250	45.4	20.0	26.8
>150	19.6	9.2	9.5
>75	11.1	17.7	36.0
>38	3.1	36.0	14.5
<38	0.4	7.1	1.0

Table IV: Results on flowability and bulk density testing

	Before addition of magnesium stearate		After addition of magnesium stearate	
	Vacuum drying without swinging	Vacuum drying with swinging	Vacuum drying without swinging	Vacuum drying with swinging
Flow rate (for 100 g of granulate)	N/A	3.27 seconds	6.66 seconds	3.60 seconds
Poured bulk density	0.71 g/cm ³ (0.006)*	0.65 g/cm ³ (0.005)*	0.86 g/cm ³ (0.016)*	0.77 g/cm ³ (0.007)*
Tapped bulk density	0.84 g/cm ³ (0.008)*	0.77 g/cm ³ (0.005)*	0.95 g/cm ³ (0.011)*	0.86 g/cm ³ (0.004)*
Carr's Index	15.68	15.81	9.32	10.59
Hausner ratio	1.19	1.19	1.10	1.12

* standard deviation (SD)

seconds without having to apply vibration to the hopper.

The test on flow rate was repeated after mixing the granulate with 0.5 % magnesium stearate.

The magnesium stearate had no significant effect on the flow rate of the batches dried using the swinging bowl. The average time it took a sample of 100 g to flow through the hopper was 3.60 seconds, which is very comparable to the results obtained with the granulate before addition of magnesium stearate.

However, addition of magnesium stearate to the granulate had an enormous effect on the flowability of the batches dried without use of the swinging bowl. Although in 1/3 of the tests there was still a problem with bridging, in the other 2/3 of the tests, the granulate flowed freely through the hopper and it took 100 g of granulate on average 6.66 seconds.

The null hypothesis that the average flow times for the batches dried with and without use of the swinging bowl are not different can be rejected at a significance level of 1% (p=0.006), meaning that the flow rates are significantly different, which might have an effect on the tableting properties.

Bulk density testing (Table IV). Before addition of magnesium stearate, the batches dried without use of the swinging bowl have an average poured bulk density of 0.71 g/cm³ (SD = 0.006) and tapped bulk density of 0.84 g/cm³ (SD = 0.008). Under the same conditions, the batches dried with use of the swinging bowl have a poured bulk density of 0.65 g/cm³ (SD = 0.005) and a tapped bulk density of 0.77 g/cm³ (SD = 0.005).

There is no difference in the Hausner ratio with a result of 1.19 for both drying methods, nor is there a major difference in the Carr's Index: 15.68 for the batches

dried without swinging bowl and 15.81 for the batches dried with swinging bowl. The poured and tapped bulk density of the granules was also tested after addition of 0.5% magnesium stearate and the results are seen in Table IV.

These results indicate that in both cases excellent flow properties with low inter-particle friction are obtained. The reason bridges are formed in batches dried *without* swinging, whilst the batches dried *with* swinging do not, can be found in the results for the particle size distribution. The first have a larger amount of fines that cause these bridges.

It can be expected that the granules of both drying methods can be tableted on a rotary press after addition of a lubricating agent such as magnesium stearate. However, the batches dried without use of the swinging bowl will probably present more problems on high-speed presses than the batches dried with use of the

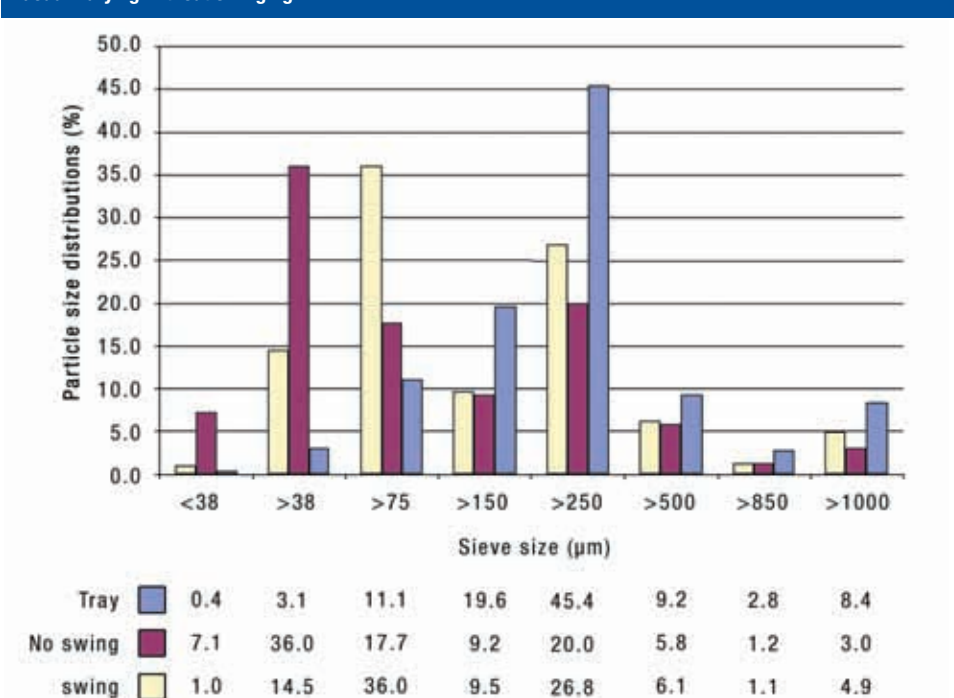
swinging bowl, due to the difference in flow rate and the tendency of the granulate dried without swinging to form powder bridges. In most modern tablet presses however, vibration is applied to the feeding hopper, and as is mentioned above, no flow problems occurred for any batch when vibration was applied to the hopper.

Conclusion

The results of this study clearly show that use of the swinging bowl during vacuum drying has a positive influence on the drying times and granule properties of low-binder formulations.

Drying times in a laboratory scale machine, when using the swinging bowl, are about 15 percent shorter than drying methods without the use of the swinging bowl. Also the particle size distribution improves with less resulting fines and a distribution that comes closer to the ideal

Figure 3: Particle size distributions produced by tray drying, vacuum drying with swinging and vacuum drying without swinging



of the reference, tray dried batch. This results in much better flow properties for the granulate dried with use of the swinging bowl compared to that dried without use of the swinging bowl.

Little difference, however, was found in the Carr's Index and the Hausner ratio, suggesting that both drying methods can produce granulates suitable for tableting. As a conclusion, the results of this study show that the use of the swinging bowl might present a solution to process old, weak and low-binder formulations in a completely contained process without destroying the granulate.

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