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THE GRANULATION OF LACTOSE AND STARCH IN A RECORDING HIGH-SPEED MIXER, DIOSNA P25

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ABSTRACT

Lactose 100 mesh was granulated faster than the 350 mesh quality.

Corn starch required large volumes of granulating solution. When agglomerating pure corn starch, its loss on drying influenced the process.

Suitable limits for the end-point determination when granulating a mixture of 2/3 of lactose 100 mesh and 1/3 of corn starch, with povidone as binder, were determined for the liquid addition under controlled conditions.

In a $\frac{1}{2} \cdot 2^6$ factorial experiment, the influence of the process variables on the response variables was studied. The former are the main impeller and chopper speed; the method of fluid addition; the way of adding the binder; the volume of granulating liquid added, and the wet massing time. The response variables concerned are the fraction <0.150 or >2.00 mm; the granule median diameter; the change in the rotation rate of the impeller shaft; and heat production in the mass. The

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impeller and chopper speed, the way of adding the binder, and the volume of granulating solution that was added, influenced all the response variables significantly. However, the dominating variables were the volume of solution and the impeller rate. Besides, the granule median diameter was influenced by the method of fluid addition. Also, the heat production during granulation was influenced by the method of fluid addition as well as by the wet massing time.

INTRODUCTION

Recently, a report has been submitted concerning the effects of process variables during liquid addition with regard to the granulation of lactose in high speed mixers[1]. The possibility of determining the end-point of the granulation of lactose on the basis of rotation-rate changes affecting the main impeller shaft during the addition of the granulating liquid has lately been reported, too[2].

The granulation of a combination of lactose and corn starch, with povidone as binder, will be studied. This means that the effect of impeller and chopper speed, the method of fluid addition, the dry mixing or dissolution of the binder, the amount of binder solution, and the wet massing will be examined. An instrumental method, based on measuring the rotation rate of the impeller motor shaft[3], will be tested in the course of attempts to determine the end-point. A sieve analysis of the dried mass, and the measurement of the heat production in the wet mass, will also be used in evaluating the process conditions.

EXPERIMENTAL

Materials

Lactose 100 mesh[4], corn starch[5] and povidone[6] according to Table 1.

TABLE 1
Powder characteristics

Characteristics	Lactose	Corn starch	Povidone
Geometric mean diameter by weight, µm	101	-	62
Geometric standard deviation	1.6	-	1.6
Volume-surface mean diameter[7], µm	-	14.6	-
Apparent density[8], kg/m^3	780	500	400
Tap density[9], kg/m^3	890	730	490

When PVP was dry-mixed, water was used as a granulating fluid. Otherwise, PVP solutions of 17.2, 20.0 or 23.7 %w/w were used as binder solutions at 20-22^{o}C. In this temperature range, the density of the solution was 1038, 1044 or 1052 kg/m^3.

The loss on drying[10] of the starch was 8.2 - 9.4% except in some experiments when the material was dried to 2.4% or humidified to 12.6%.

Granulation

All experiments were performed at a degree of filling of the bowl corresponding to approximately 36% calculated on basis of the tap density.

The powder mixture according to Table 2 was granulated with water in a recording Diosna P25, equipped with a peristaltic pump and a nozzle of the two-fluid type[3] at different combinations of main impeller and chopper speed. The rotation rate of the main impeller motor shaft, which was approximately 1500 and 3000 rpm respectively during no-load operation, was reduced in the gear box. Thus, the idling speed of the impeller was 180 and 360 rpm respectively. The mixture without

TABLE 2
Granule composition

Component	kg
Lactose	5.44
Corn starch	2.56
Povidone	0.25

PVP was granulated with PVP solutions, but the amount of PVP in the granulation was the same in all experiments. Samples for sieve analysis were frequently withdrawn.

When atomized, the droplet size of the binder solution or water was mainly 20-60 µm at a fluid-addition rate of 250 ml/min, and mainly 20-100 µm at a liquid flow rate of 350 ml/min. A slide with a layer of viscous oil[11] was passed across the spray cone at a distance corresponding to the distance between the nozzle opening and the powder bed. The droplet size was immediately determined in a microscope.

7.0 kilogrammes of corn starch were granulated with a 20 %w/w PVP solution which was added at a flow rate of 500 ml/min. Samples for sieve analysis were frequently withdrawn.

A $\frac{1}{2} \cdot 2^6$ factorial experiment was designed; see Table 3A and B. The granulating liquid was added during 4 mins. which meant that the liquid flow rate was 250 or 350 ml/min. Thus, the differences with regard to process times during the liquid addition were avoided. Sampling times were immediately after the addition of the liquid, i.e. wet massing time 0, and during the kneading 2.5 and 5 mins. after the addition of the liquid.

TABLE 3 A

Design and results of a ½ · 2^6 factorial experiment

Factors						Response variables				
						%			difference in	
A	B	C	D	E	F	<0.150 mm	>2.00 mm	$d_{50\%}$, mm	rate of impeller shaft, rpm	mass temp., °C
L	L	L	L	L	L	18.1	9.8	0.22	13	5.1
L	L	L	L	H	H	2.2	20.7	0.87	22	10.5
L	L	L	H	L	H	21.9	2.2	0.205	12	7.3
L	L	L	H	H	L	9.5	23.4	0.38	16	3.4
L	L	H	L	L	H	15.1	1.9	0.215	15	8.7
L	L	H	L	H	L	4.6	31.2	0.70	23	4.1
L	L	H	H	L	L	18.1	3.5	0.215	11	2.8
L	L	H	H	H	H	7.4	3.1	0.325	19	7.9
L	H	L	L	L	H	9.7	10.9	0.265	18	18.6
L	H	L	L	H	L	2.4	38.8	1.05	24	10.8
L	H	L	H	L	L	17.1	7.7	0.225	12	8.2
L	H	L	H	H	H	3.3	28.4	0.60	22	18.6
L	H	H	L	L	L	12.7	14.2	0.245	15	9.8
L	H	H	L	H	H	1.4	37.2	1.18	24	19.8
L	H	H	H	L	H	18.8	4.7	0.205	13	16.9
L	H	H	H	H	L	6.1	24.2	0.43	22	7.7
H	L	L	L	L	H	9.7	17.7	0.34	96	18.8
H	L	L	L	H	L	1.3	42.6	1.50	124	9.0
H	L	L	H	L	L	13.9	21.7	0.39	83	7.1
H	L	L	H	H	H	4.8	13.2	0.50	113	19.5
H	L	H	L	L	L	7.9	31.0	0.44	93	6.6
H	L	H	L	H	H	1.1	48.7	1.92	131	21.7
H	L	H	H	L	H	13.4	17.6	0.265	97	17.1
H	L	H	H	H	L	5.4	31.3	0.62	112	6.0
H	H	L	L	L	L	7.6	34.0	0.50	112	14.2
H	H	L	L	H	H	0.7	61.3	3.00	157	32.9
H	H	L	H	L	H	9.9	26.1	0.36	104	27.4
H	H	L	H	H	L	3.3	41.5	1.32	128	11.7
H	H	H	L	L	H	5.7	45.4	1.50	107	28.0
H	H	H	L	H	L	0.9	53.0	2.34	138	13.5
H	H	H	H	L	L	10.9	31.9	0.45	95	15.5
H	H	H	H	H	H	1.8	54.7	2.83	130	27.4

TABLE 3B

Factors and factor levels

	Factor	Factor levels	
		L	H
A	Impeller speed, rpm	180	360
B	Chopper speed, rpm	2000	4200
C	Method of fluid addition	not atomized	atomized
D	Way of adding the binder	dry	dissolved
E	Volume of granulating liquid added, l	1.0	1.4
F	Wet massing time, mins	0	5

By means of a scoop, samples of approximately 0.1 kg were withdrawn from the granule stream in the vicinity of the chopper. The samples were immediately dried in a hot-air oven at 50°C. Sieve analyses of the dried samples were performed through sieves measuring 2.00, 1.50, 1.00, 0.750, 0.500, 0.250 and 0.150 mm[12]. The duration of the sieving process was 2 mins.

The temperature of the mass during granulation was measured by means of dipping a thermoelement[13] into the circulating mass at predetermined intervals.

Yates's method of computing factorial effect totals[14] was used after logarithmic[15] transformation of the data. The residual variance was calculated after pooling the results from 10 trials of factor combination LLLHLH and 10 trials of type HHHLHL in Table 3A and B.

RESULTS AND DISCUSSION

The granulation of lactose

As was seen from Fig.1, there was initially a larger reduction of the rotation rate of the main

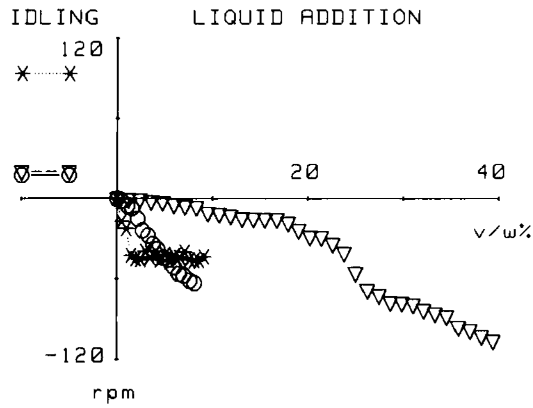

FIGURE 1

Changes in the rotation rate of the impeller shaft in comparison to dry mixing during idling and liquid addition. The added amounts of liquid expressed as volume per mass (%v/w).

✱ lactose 100 mesh
○ lactose 350 mesh
▽ corn starch

impeller shaft in respect to lactose 100 mesh as compared to lactose 350 mesh, or to corn starch at a similar degree of filling.

Lactose 100 mesh was more quickly granulated than the 350 mesh quality or starch. After adding about 3 %v/w of solution, granules were formed from lactose 100 mesh, while the 350 mesh quality required about 7 %v/w and starch approximately 30 %v/w. Low impeller speed required larger volumes of solution than the high speed.

With regard to lactose 100 mesh, the fast agglomeration very soon led to a plateau on the curve showing the impeller rate versus the added volume of granulating solution.

The granulation of corn starch

A higher starch humidity caused earlier changes in the impeller rate, changes indicating earlier granule formation and growth; see Fig. 2.

During the addition of the granulating liquid, the production of heat was higher when using starch with a high loss on drying. During kneading, too, the heat production was higher with the humidified quality. However, the gelatinization temperature of corn starch[16], 62-72°C, was never attained.

During wet massing, the total amount of water in the mass determined whether there was to be an increase or decrease in the granule median diameter. When the loss on drying on the part of the starch was normal or low, a decreasing impeller speed entailed an almost linear increase in temperature.

The granulation of lactose and starch

The powder mixture according to Table 2 was granulated with water added at a flow rate of 250 ml/min, without atomization and with a high chopper speed, and a low or high impeller speed, but without wet massing. The influence of a change in the impeller rate on the fraction <0.150 mm, fines, and >2.00 mm, lumps, as well as on the median diameter, d50%, is seen in Fig. 3A and B, at low and high impeller speeds.

In Table 4, the change in the rotation rate of the main impeller shaft is stated at different stages during granulation. This means that suitable granules are obtained at a rotation rate change amounting to 15-25 rpm at a low impeller speed, and to 80-110 rpm at a high impeller speed. These limits can be used for determining the end-point during the addition of water under controlled conditions.

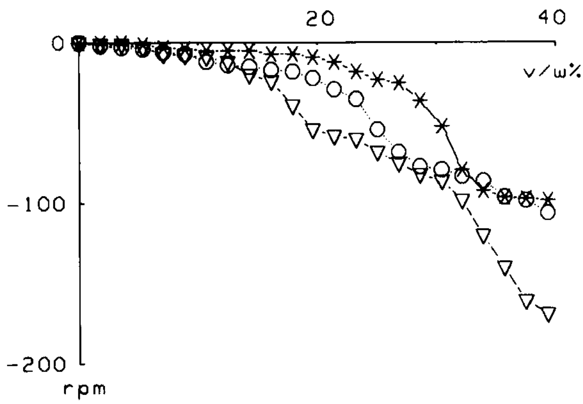

FIGURE 2

Changes in the rotation rate of the impeller shaft versus volume of added granulating liquid during the liquid addition.

✳	LOD of starch 2.4%
○	LOD of starch 9.1%
▽	LOD of starch 12.6%

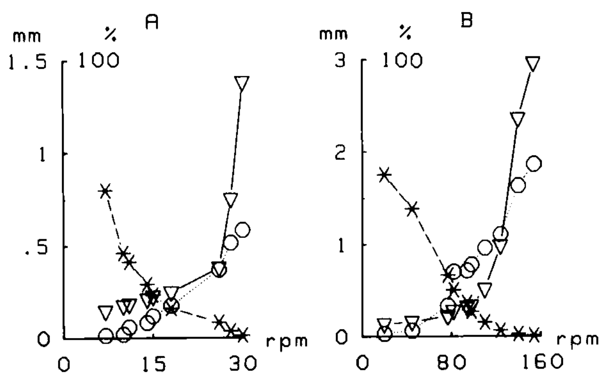

FIGURE 3

Percentage of fines and lumps or granule median diameter as a function of the rotation-rate change of the impeller shaft at low (A) and high (B) impeller speed.

✳	<0.150 mm, %
○	>2.00 mm, %
▽	$d_{50\%}$, mm

TABLE 4

Rotation-rate change of the main impeller shaft at different stages during granulation

Stage	Change of rate, rpm	
	Impeller speed: Low	High
Granule formation	<12	<70
Granule growth	15 - 25	80 - 110
Overwetting	>26	>120

The fine granule fractions were formed earlier than the coarse fractions, as the former reached their maximal proportions at lower volumes of water; see Table 5. The coarse fractions are formed from the fine fractions.

As the fine and medium fractions were formed after the addition of smaller volumes of water at a high impeller speed, agitation during the addition increased the granule size; see Table 5.

Similar results were obtained with PVP solution and liquid atomization.

$\frac{1}{2} \cdot 2^6$ factorial experiment

As a central measure of granule size, the median diameter was used. Fines and lumps were suitable indicators of the granule growth[17]. The change of rotation on the part of the impeller shaft during the liquid addition[2] was used for the purpose of end-point determination when granulating lactose with gelatin solution. Therefore, this response variable was selected. Heat was produced during the process. Therefore, the temperature of the mass was also selected as a response variable.

TABLE 5

Added amount of water required for the occurrence of maximal proportions on the part of different size fractions.

Granule fraction, mm	Water added, %v/w	
	Impeller speed: Low	High
<0.150	<4.5	<4.5
0.150-0.250	7.6	6.1
0.250-0.500	15.2	13.6
0.500-0.750	18.2	15.2
0.750-1.00	18.2	16.7
1.00-1.50	18.2	18.2
1.50-2.00	18.2	18.2
>2.00	18.2	18.2

The residual variance, based on log data for %<0.150 mm, %>2.00 mm, d50%, difference in the impeller-shaft rate, and mass temperature respectively, was 0.00844, 0.0312, 0.000783, 0.00154 and 0.000285 respectively.

The results of 0 or 5 mins. wet massing in combination with the other process variables with regard to the response variables are supplied in Table 3A. In Table 6 A and B, the results of the analysis of variance are given; 5 mins. wet massing time.

The results obtained without wet massing were calculated as a 2^5 factorial experiment; 0 min wet massing time. Besides, the results of 2.5 mins. kneading time were calculated as a $\frac{1}{2} \cdot 2^6$ factorial experiment. These results are also stated in Table 6A and B. Data from time 0 min are included in the $\frac{1}{2} \cdot 2^6$ experiments.

TABLE 6 A

Analysis of variance in factorial experiments, 2^5 (0 min) and $\frac{1}{2} \cdot 2^6$ (2.5 and 5 mins.)

Factor	Response variables														
	% <0.150 mm					% >2.00 mm					Granule median diameter				
	Wet massing time: mins.					Wet massing time: mins.					Wet massing time: mins.				
	0	2.5	5			0	2.5	5			0	2.5	5		
	Sign	Sign	Effect (mean)	F	Sign	Sign	Sign	Effect (mean)	F	Sign	Sign	Sign	Effect (mean)	F	Sign
Total	-	-	0.759	2183.0	-	-	-	1.275	1.667.6	-	-	-	-0.256	2670.7	-
A	***	***	-0.272	70.0	***	***	***	0.479	58.8	***	***	***	0.342	1192.8	***
B	***	***	-0.184	32.0	***	***	***	0.290	21.6	***	***	***	0.197	395.8	***
C	-	-	-0.008	0.06	-	***	-	-0.034	0.3	-	-	-	0.039	15.4	***
D	***	***	0.326	100.6	***	***	***	-0.223	12.8	**	***	***	-0.226	523.5	***
E	***	***	-0.665	418.6	***	***	***	0.383	37.7	***	***	***	0.480	2354.8	***
F	-	-	-0.099	9.4	**	-	*	-0.167	7.2	*	-	*	0.046	21.7	***
AB													0.099	99.3	***
AC						***						*	0.079	63.6	***
AD						**					**	*	-0.032	10.6	**
AE						***	***	-0.212	11.5	**			0.032	10.4	**
BC						**							0.040	16.1	***
BD															
BE											***	***	0.065	43.5	***
BF												***	0.080	65.2	***
CF												*	0.067	45.7	***
DE	***	***	0.156	23.0	***						***	***	-0.101	103.6	***
DF												***	-0.048	23.1	***
EF													0.038	14.9	**

Sign means significance: * $P<0.05$
** $P<0.01$
*** $P<0.001$

TABLE 6 B

Analysis of variance in factorial experiments, 2^5 (0 min) and $\frac{1}{2} \cdot 2^6$ (2.5 and 5 mins.)

	Response variables									
	Difference in impeller speed					Difference in temperature				
	Wet massing time: mins.					Wet massing time: mins.				
	0	2.5	5			0	2.5	5		
Factor	Sign	Sign	Effect (mean)	F	Sign	Sign	Sign	Effect (mean)	F	Sign
Total	-	-	1.640	55860.7	-	-	-	1.057	125467.9	-
A	***	***	0.821	3499.6	***	***	***	0.251	1762.0	***
B	***	***	0.058	17.7	***	***	***	0.295	2434.6	***
C	-	-	0.002	0.0	-	**	***	-0.030	25.6	***
D	***	***	-0.066	22.6	***	***	***	-0.074	152.6	***
E	***	***	0.159	130.6	***	-	-	0.019	9.6	**
F	-	-	0.007	4.3	-	-	***	0.356	3550.6	***
AB						***	***	-0.064	114.9	***
AD							***	0.031	26.3	***
AE	***	**	-0.041	8.8	•					
AF								0.023	14.8	**
BC							***	0.023	15.4	***
BD							***	0.023	14.8	**
BE								-0.017	8.4	**
BF							***	-0.038	41.6	***
DE							**	-0.019	10.3	**
DF								0.018	9.2	**
EF							**	0.028	22.4	***

Sign means significance : * P<0.05
** P<0.01
*** P<0.001

The relative order of the F-values pertaining to the process variables A-E was similar for all the response variables after 0, 2.5 and 5 mins. kneading.

Factors E and A, i.e. volume of solution and impeller speed, were predominant as compared to the other significant factors in respect to fines, lumps, d50% and the difference in the impeller-shaft rate. Where the production of heat in the mass is concerned, however, factors B and F - i.e. chopper speed and wet massing time - dominated over the other significant factors.

With regard to the fines, increasing impeller and chopper speed, the use of a dry-mixed binder, and an increasing amount of granulating liquid, reduced the magnitude both during liquid addition and wet massing. However, increased kneading time also reduced the fines after 5 mins. The interaction DE was not unexpected. The method of fluid addition made no difference.

Increasing impeller and chopper speed, the use of a dry-mixed binder, and an increasing volume of granulating liquid, increased the coarse-fraction percentage. The effect of the method of fluid addition, factor C, at 0 min kneading time was confusing. However, kneading reduced the lumps produced when the granulating liquid was added without atomization.

When the results of the interjacent fractions were calculated as 2^5 or $\frac{1}{2} \cdot 2^6$ factorial experiments, the volume of liquid added proved to be the dominating main effect with regard to the 0.150 - 0.250 mm up to the 1.00 - 1.50 mm fraction. Where the 1.50 - 2.00 mm fraction was concerned, the impeller speed and the volume of added solution were the dominating main effects. This indicates the importance of the impeller speed for the growth of the larger granules.

The median diameter was not significantly influenced until after 5 mins. of kneading. The dominating factors were the granulating liquid volume and the impeller speed. Increasing volume or speed increased the diameter. Increased chopper speed, a dry-mixed binder, and kneading also increased the granule diameter. The many interactions were not unexpected.

The granule growth of lactose was primarily controlled by the amount of binder solution and the impeller speed[1]. This was in accordance with our results.

The main effects and interactions pertaining to differences in the rotation rate of the impeller shaft were similar for 0, 2.5 and 5 mins. of kneading time. Increasing impeller and chopper speed, a dry-mixed binder, and an increasing volume of granulating liquid increased the difference in the rate of the impeller shaft.

The main effects and interactions with regard to heat production during the agglomeration varied with the length of the kneading time. With longer wet massing times, the influence of this variable and of the granulating-solution volume increased. Increasing impeller and chopper speed, the use of a non-atomized granulating solution, a dry-mixed binder, an increasing volume of liquid, and longer kneading time all increased the influence of the heat production in the process.

CONCLUSION

Because of the many significant main effects of the process variables on the granule size, it is necessary to control these variables during the agglomeration process, especially the amount of granulating liquid added and the impeller speed. These two process variables - the amount of liquid that was added, and the impeller rate - were the most important ones with regard to the other response variables, too, with the exception of the heat production. The way in which the binder was added - whether it was dry-mixed or dissolved - also had a significant influence on the granule size.

The heat production in the mass was especially patently affected by the kneading time and the chopper speed.

Under controlled granulation conditions, the end-point for liquid addition can be determined by measurements of the changes in the rotation rate of the main impeller shaft.

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