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SOME FACTORS INFLUENCING PELLET CHARACTERISTICS MADE BY AN EXTRUSION/SPHERONISATION PROCESS

PART I. : EFFECTS ON SIZE CHARACTERISTICS AND MOISTURE CONTENT DECREASE OF PELLETS

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ABSTRACT

The effect of five process parameters - speed of extrusion, speed of spheronisation, time of spheronisation, load of the spheronizer, moisture content of the wet granulated mass - were investigated on size distribution parameters /e.g main sieve fraction, sieve fraction <0.40 mm, sieve fraction >1.60 mm and the calculated mean diameter / of the pellets obtained by an extrusion / spheronisation process and on the moisture content decrease during manufacturing from the beginning of extrusion to the end of spheronisation. The significant factors and interactions were determined and characterised by multilinear regression. The study have revealed that the spheronizer speed, the time of spheronisation, the moisture content of the wet powder mass and the first order interactions of them have the most significant effect on the tested dependent variables.

INTRODUCTION

The production of pellets was first described by Conine and Hadley[1] and Reynolds[2]. The pellet characteristics have already been studied by several authors[3-9] some of them applying statistical methods[4-6,8-9].

The present work is a further contribution to their results revealing some similarities and dissimilarities particularly in the scope of the secondary aim of this study to characterise the Pharmex 35T/Spheromat250T instrumented laboratory extruder/ spheronizer /Wysstec Ag, Switzerland/.

Five process parameters were chosen as main factors for establishing a set of experiments according to a complete 2^5 factorial design. Selecting the factors, our aim was to choose those factors, wich are the most important ones from the point of view of manufacturing. Therefore, the speed of extrusion, the time of spheronisation, the load of the spheronizer, the moisture content of the wet granulated mass have been chosen. During the manufacturing process, the other process parameters were held constant.

MATERIALS AND METHODS

Materials

Placebo pellets were used for the experiments. The manufacturing composition consisted of one part of lactose and one part of microcrystalline cellulose /type PH 101/. The formulation was first dry mixed and then granulated with different amount of water determined by the experimental design. The moistended mass was, then, placed into the extruder/spheronizer and pellets were made applying a 1.0 mm screen under the conditions determined by the experimental design. The diameter of the friction plate of the spheronizer was 250 mm. The size characterisation was made by applying a set of sieves using a shaking sieve apparatus after drying the pellets at room temperature up to 3-3.5 % residual moisture content.

Test Methods

1. The particle size characterisation was performed by applying a shaking sieve with a set of sieves consisting of sieves with 0.4, 0.63, 0.80, 1.00, 1.25 and 1.6 mm apertures. The obtained results were evaluated according to the following four groups :

1. < 0.4 mm sieve fraction representing the dust formation,

2. 0.8 - 1.25 mm sieve fraction representing the main sieve fraction, the yield of the process,

3. > 1.60 mm sieve fraction representing the tendency of the extrudates or pellets to agglomerate during the spheronisation porocess.

4. Mean pellet diameter calculated from the results of the sieve analysis by applying the following formula :

$$\bar{d} = \frac{\Sigma x_i d_i}{100} \qquad /1/$$

where x_i is the mean of the upper and lower limits of sieve fraction and d_i is the percentage of the i fraction.

2. Moisture content decrease was determined as follows. Three samples were taken from the wet powder mass prior extrusion and three samples were taken after finishing the spheronisation process. The loss on drying was determined for each sample using a Sartorius Thermo Control infrared thermobalance /YTC 01 L/ at 105 ^{o}C. The means were calculated and the differences were determined and used for the further analyses.

Experiments

The Table 1. shows the two levels of each factors applied in the trials and the range of variation.

TABLE. 1.

EXPERIMENTAL DESIGN

Factors		**Low level**	**High level**	**Range of variation**
Extruder speed	/A/	40 rpm	60 rpm	10 rpm
Spheronizer speed	/B/	800 rpm	1200 rpm	200 rpm
Spheronisation time	/C/	2 min	4 min	1 min
Spheronizer load	/D/	600 g	800 g	100 g
Moisture content	/E/	33.33 %	36.51 %	1.69 %

The Table 2. shows the experimental matrix according to the experiments were performed.

The lower case letters in the table denote that the factor indicated this way is at the high level while the other factors are at the low level. In the first experiment, for example, the **de** denotes that the **d** and **e** factors are at the high level while the other factors are at the low level. The number 1 denotes that all the factors are at the low level. The order of the experiments was randomized.

Statistical method

The results were evaluated by applying a multilinear regression study for each dependent variables following the analysis of correlation of the data in order to select the highly correlated ones for the regression study. The resulting

TABLE 2.

EXPERIMENTAL MATRIX

Exp. No.	Factors	Exp. No.	Factors	Exp. No.	Factors	Exp. No.	Factors
1	de	9	c	17	bce	25	ae
2	cde	10	1	18	e	26	bde
3	bcde	11	ab	19	a	27	abce
4	bcd	12	bd	20	cd	28	acde
5	abd	13	ce	21	ac	29	abe
6	bc	14	ade	22	b	30	be
7	abcd	15	abcde	23	abc	31	abde
8	ad	16	ace	24	acd	32	d

models were used for the analysis of the significant factors and interactions.

Interpretation of main factors was carried out according to Adler et al.[10]. This principle says if a factor has a negative sign, the value of the dependent variable will increase if the value of the factor decreases and if increases, the dependent variable will decrease. On the other side, if a factor has a pozitive sign, the dependent variable will increase if the value of the factor increases and will decrease if the factor level decreases.

Interpretation of the first order interactions was also carried out according to the principle described in /10/ . This principle says if a first order interaction has a positive sign, the value of the dependent variable will increase if the both factors simultaneously decrease or increase depending on their sign and will decrease if the factors simultaneously change in the opposite direction.

If a first order interaction has a negative sign, the value of the dependent variable will increase if the factors change oppositely at the same time and will decrease if the factors change the same direction simultaneously.

RESULTS AND DISCUSSION

Determination of the factor levels

In order to determine the factor levels some pre-experiments were performed. The moisture content of the wet powder mass was selected so that the two levels represent nearly the possible limits of the operation.

The levels of spheronizer speed was selected by performing a set of experiments. During these experimental runs the other process parameters were held at a constant level /extruder speed was 60 rpm, spheronizer load was 600 g, the time of spheronisation was 3 min and the cooling water temperature was 20 ^{o}C/. The runs were performed at six levels of spheronizer speed /400, 600, 900, 1000, 1100 and 1500 rpm/ and the results were evaluated from the point of view of the main sieve fraction, the sieve fraction <0.40

mm representing the dust formation, the sieve fraction > 1.25 mm, the main sieve fraction / 0.80-1.25 mm / and the mean diameter of pellets.

Figure 1. shows the effect of spheronizer speed on dust formation. The curve implies that a minimum exist in the generation of dust somewhere between 600 and 1000 rpm. From 1000 rpm , however , the generation of dust begins to increase dramatically.

Figure 2. shows the effect of spheronizer speed on the bigger particles. This curve clearly describes the exponentially decreasing effect of spheronizer speed on sieve fraction >1.25 mm. This effect is very strong from 400 to 1000 rpm. From 1100 rpm, however the increasing spheronizer speed has hardly any influence on this size fraction.

Figure 3. outlines the effect of spheronizer speed on the main sieve fraction.This figure shows a peak in the yield of the process somewhere between 800-1000 rpm.

Figure 4. presents the effect of the spheronizer speed on the calculated mean diameter of pellets. This sigmoidal curve implies that increasing the speed of spheronisation a plateou can be achieved between 900-1000 rpm.

Summarizing the results of this pre-experiment, the 1000 rpm was chosen for the speed of spheronisation as a base level and 200 rpm as the range of variation.

The other process parameters were selected arbitrarily based on the experience of the prior runs.

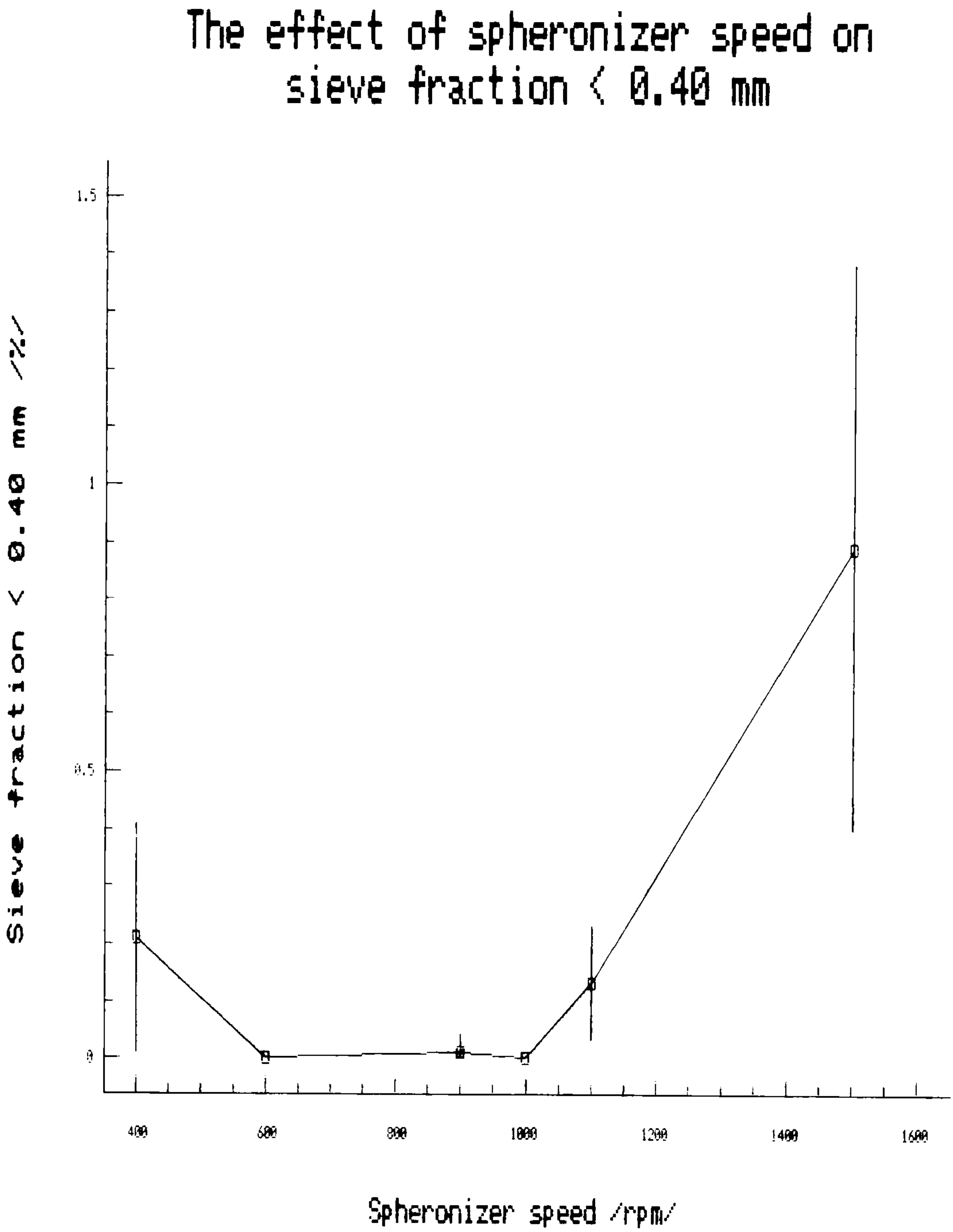

FIGURE 1.
The effect of spheronizer speed on sieve fraction < 0.40 mm representing the dust formation

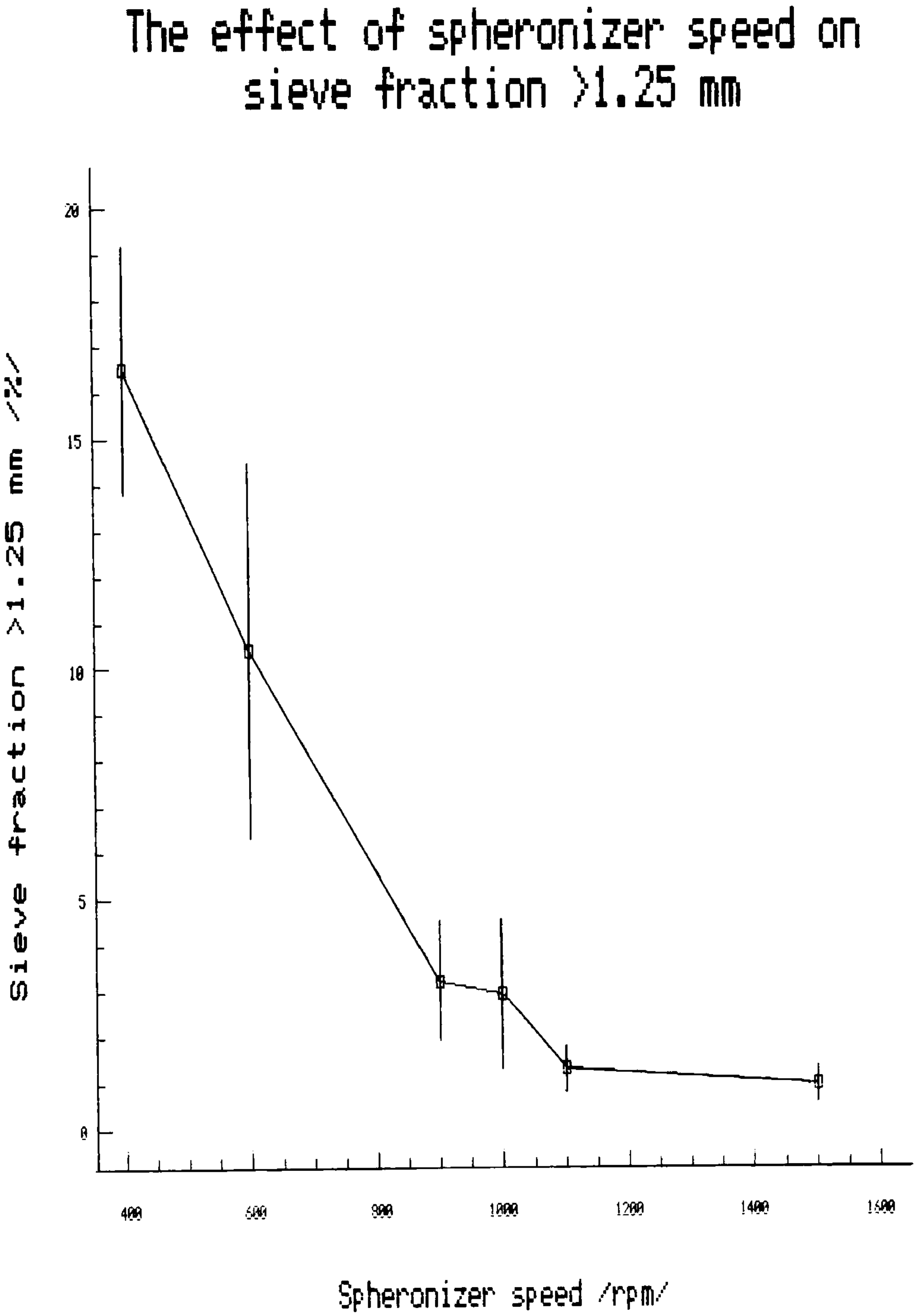

FIGURE 2.
The effect of spheronizer speed on sieve fraction > 1.25 mm.

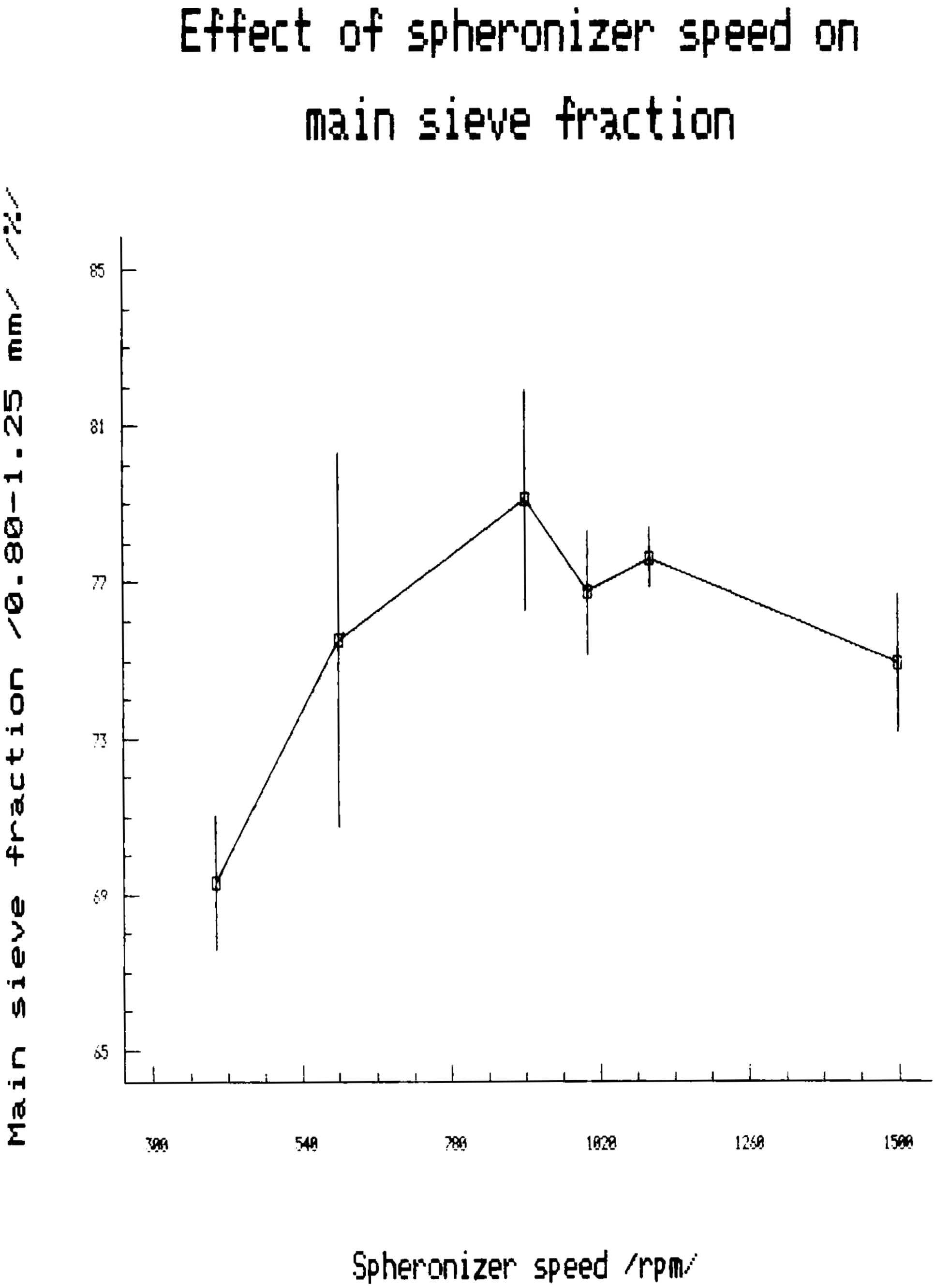

FIGURE 3.
The effect of spheronizer speed on main sieve fraction / 0.80-1.25 mm /

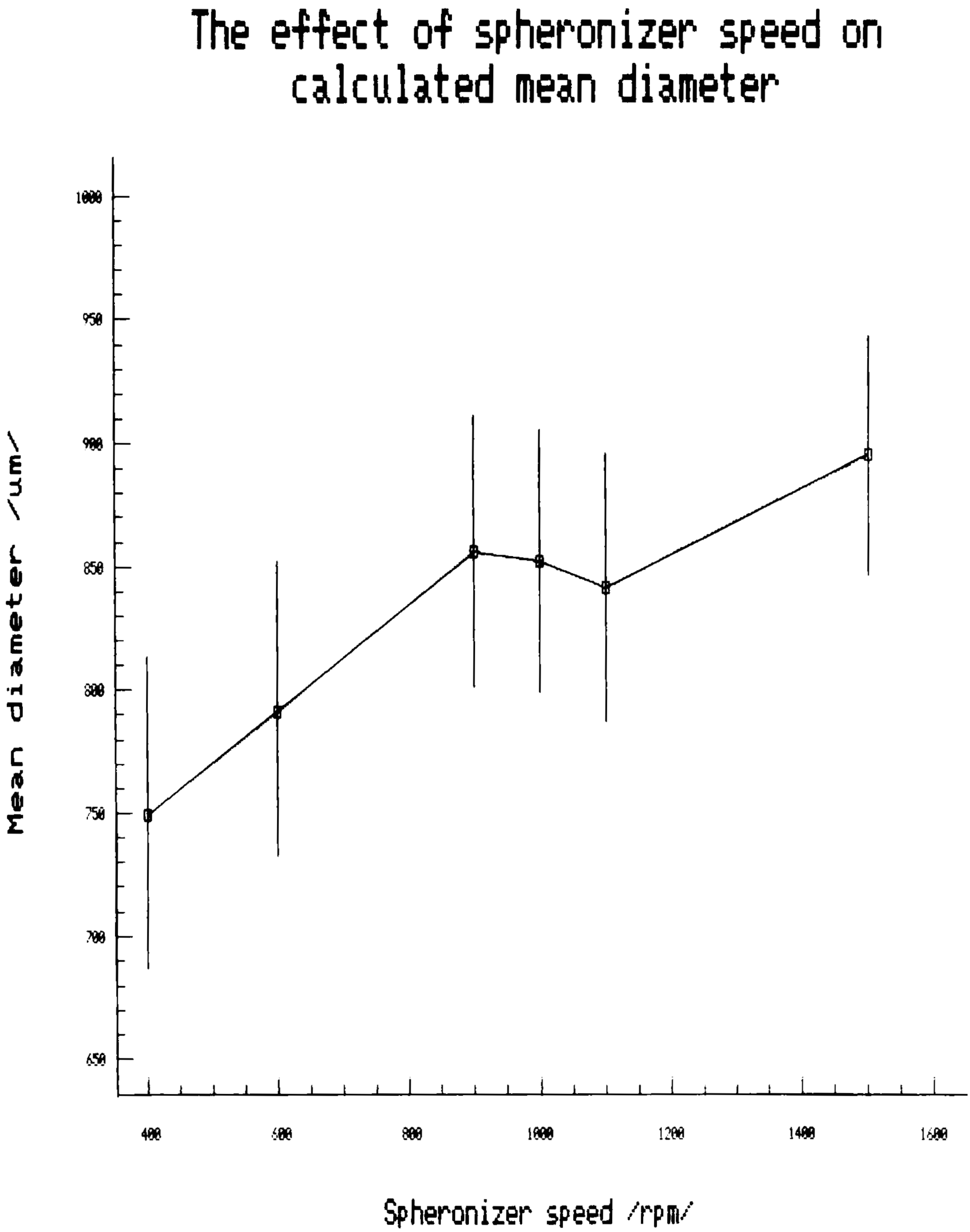

FIGURE 4.
The effect of spheronizer speed on calculated mean diameter /μm/

Results

Table 3. describes the results achieved by performing the sieve analysis. The results in this table show that the fractions with the highest percentage values fall always into the 0.8-1.25 mm category with the changing probability eighter in the 0.8-1.0 or in the 1.0-1.25 mm fraction.

Table 4. shows the first model including the significant factors and interactions influencing the dust formation during manufacturing.

This table reveals that the moisture content /E/, the spheronizer speed /B/ and spheronisation time /C/ has significant / $p<0.001$ / effect on dust formation.

Since all of the coefficients of these factors have a negative sign, the amount of dust produced during the process reduces if the level of these factors increase.

Beside the three significant main factors, the combination of them - the BE, BC and CE interactions - are also significant / $p<0.001$ / . Accomplishing the interpretation described under the paragraph of "Interpretation of the First Order Interaction", it can be established that since the both composing factors have the same negative sign for all the three cases and the interactions themselves have positive signs, the dust formation reduces if the factors change oppositely at the same time. Practically, if one intends to reduce the dust formation, one can eighter increase the moisture content /E/, the spheronizer

TABLE 3.

RESULTS OF SIEVE ANALYSES

Exp. No.	<0.4	0.4-0.63	0.63-0.8	0.8-1.0	1.0-1.25	1.25-1.6	1.6<mm
1	0.66	0.56	27.30	50.50	20.03	1.04	0
2	0.12	0.20	17.90	37.61	39.32	4.86	0
3	0.01	0.02	1.38	9.27	38.24	26.07	25.03
4	0.40	3.62	16.28	22.19	56.10	1.64	0
5	1.33	5.33	20.50	29.81	42.67	0.35	0
6	0.83	2.85	16.68	21.98	55.42	2.26	0
7	0.29	2.94	16.05	21.00	56.25	3.38	0.10
8	7.94	4.85	26.41	55.36	5.29	0.08	0.09
9	1.28	3.72	17.85	32.92	43.97	0.27	0
10	4.45	4.69	23.15	58.19	9.39	0.13	0.02
11	1.27	4.03	23.81	25.12	45.64	0.14	0
12	0.81	2.88	13.83	22.23	59.16	1.05	0.05
13	0.14	1.14	16.86	41.42	39.69	0.69	0.08
14	0.95	2.97	26.82	52.57	16.36	0.34	0
15	0	0.38	14.34	25.97	53.93	5.01	0.38
16	0.84	3.09	25.16	55.27	15.50	0.15	0
17	0.44	2.57	19.10	25.87	50.92	1.02	0.1
18	0.70	3.38	28.52	61.15	6.26	0	0
19	2.09	2.35	9.68	45.76	39.8	10.13	0.2
20	3.33	2.3	7.78	28.38	55.8	21.03	1.37
21	1.77	2.81	8.46	21.63	63.72	0.49	1.14
22	0.90	2.93	7.34	15.78	72.18	0.89	0
23	0.99	2.76	7.39	20.59	62.96	5.32	0
24	4.04	4.09	8.82	30.43	52.58	0.05	0
25	0.16	0.53	10.74	46.23	41.18	0.98	0.21
26	0.14	2.48	8.52	27.71	50.83	7.24	3.10
27	0	0	1.0	55.82	44.57	19.98	28.59
28	0.05	1.46	11.69	48.27	37.23	1.26	0.05
29	0.05	1.43	11.34	26.32	58.75	0.84	1.28
30	0.10	2.73	16.33	33.97	45.96	0.44	0.49
31	0.05	1.71	12.97	18.38	65.29	1.51	0.10
32	4.08	4.42	9.87	45.41	35.30	0.93	0

TABLE 4.

SIEVE FRACTION : < 0.4 mm

Variables	Coefficients	t-values	Level of significance
E	-1.163	15.728	***
B	-0.927	12.525	***
BE	0.787	10.633	***
C	-0.448	6.054	***
ABCD	0.385	5.209	***
ACD	-0.382	5.167	***
ACDE	0.347	4.693	***
BC	0.34	4.626	***
CE	0.337	4.55	***
AD	0.312	4.212	**
ABD	-0.29	3.984	**
ABCDE	-0.292	3.941	**
ABDE	0.278	3.764	**
ABC	-0.270	3.646	**
ADE	-0.247	3.333	**
ABCE	0.233	3.156	**
BCE	-0.217	2.936	*
ACE	-0.200	2.708	*
AC	0.198	2.674	*
Intercept	1.402		

R = 0.9925

F = 41.7197 > $F_{(19, 12)}$=2.56

Level of significance

p<0.001 = 4.318 ***

p<0.01 = 3.055 **

p<0.05 = 2.179 *

speed /B/ or the time of spheronisation /C/ one at a time separately or one can increase, for example, the moisture content /E/ and reduce the speed of spheronisation /B/ or the time of spheronisation /C/ at the same time /consider BE and CE interactions/.

Considering these changes in the process, the best way is to choose the most significant factor to decide the direction of the change /e.g. increase the moisture content /E/ / and then adjust to this the change of the second factor /e.g. decrease the speed of spheronisation /B/ /. The same applies to BE interaction.

The interpretation of BC interaction has a very strong implication to manufacturers. Considering the meaning of this interaction, it should be realized that this interaction represents the total number of the rotation of the friction plate of the spheronizer e.g. :

Spheronizer speed / rotation/min / x spheronization time /min/ =
Total number of rotation

Therefore, the proper number of friction plate rotation should be achieved in order to obtain a minimized dust generation.

The BC interaction involves this phenomenon since if one increases the spheronizer speed, one should decrease the spheronization time at the same time in order to reduce the dust formation during manufacturing.

Table 5. shows the significant factors and interactions on sieve fractions > 1.60 mm representing the agglomeration tendency.

TABLE 5.

SIEVE FRACTION : >1.60 mm

Variables	Coefficients	t-values	Level of significance
BE	1.842	14.589	***
E	1.841	14.584	***
B	1.827	14.470	***
ADE	-1.784	14.134	***
AD	-1.782	14.114	***
ABDE	-1.777	14.079	***
ABD	-1.773	14.050	***
ABCDE	-1.556	12.326	***
BC	1.550	12.282	***
ABCD	-1.547	12.257	***
CE	1.545	12.237	***
ACDE	-1.538	12.183	***
ACD	-1.528	12.104	***
C	1.523	12.069	***
BCE	1.523	12.064	***
Intercept	1.875		

R = 0.9970

F = $174.5618 > F_{(15,16)} = 2.35$

Level of significance

$p<0.001 = 4.015$ ***

The first thing to be realized at the first glance is that the significant factors on agglomeration are the same as were previously on dust formation. The signs of these factors, however, are just the opposit, therefore, their effects act on the contrary as well. In order to reduce the increase of the amount of sieve fraction >1.60 mm, the moisture content /E/, the spheronizer speed /B/ or the time of spheronisation /C/ should decrease.

When someone changes the level of the moisture content /E/, the spheronizer speed /B/ or the time of spheronisation /C/ in eighter direction, this will cause opposit changes paralell in <0.4 mm and >1.6 mm fraction.

The first order interactions of B, C and E factors, the BC, CE and BE interactions, have the same signs as the main factors have. This suggests that the two factors composing each interaction should be changed oppositely at the same time in order to reduce the agglomeration. For example, reducing the moisture content /E/, the spheronizer speed /B/ should increase in order to reduce the agglomeration.

As described under the effects on the sieve fraction < 0.40 mm, the same refers here to the BC interaction with a little modification. Since the most significant factor is involved in this interaction, the B, has a positive sign it makes necessary to decrease the speed of spheronisation and paralell increase the time of spheronisation.

Table 6. shows the significant factors an interactions on the main sieve fraction /0.80-1.25 mm/ wich represents the yield of

TABLE 6.

SIEVE FRACTION : 0.80 - 1.25 mm

Variables	Coefficients	t-values	Level of significance
BC	-4.247	11.323	***
ABD	3.831	10.214	***
BCE	-2.845	7.585	***
AE	2.498	6.660	***
ACDE	2.480	6.612	***
ACD	2.427	6.470	***
ADE	2.286	6.094	***
ABCDE	2.163	5.766	***
CE	-1.937	5.165	***
B	-1.761	4.696	***
ACE	-1.751	4.669	***
E	-1.734	4.624	***
D	-1.511	4.029	**
CD	1.358	3.621	**
AC	1.255	3.345	**
BE	-1.220	3.254	**
BCD	-1.204	3.211	**
AB	-0.879	2.342	*
BCDE	0.806	2.149	*
BD	0.710	1.893	
Intercept	77.4411		

R = 0.9926

F = 31.895 > $F_{(18,13)}$=2.48

Level of significance

p<0.001 = 4.221 ***

p<0.01 = 3.012 **

p<0.05 = 2.160 *

the process and ranges from 47.51 - 87.96 % /See Table 7/. From the main factors, the speed of spheronisation/B/, the moisture content of the wet powder mass /E/ and the load of the spheronizer /D/ has a significant effect. Since all the three factors have a negative sign, their decrease increases the yield of the main fraction.

The BC interaction has in this model the most significant effect. Since the spheronizer speed /B/ the only significant component in the interaction, the percentage of the main fraction increases if one decreases the spheronizer speed /B/ and simultaneously increases the time of spheronisation /C/.

The next significant first order interaction is the AE. This interaction means if one intends to increase the amount of the main sieve fraction, one should simultaneously decrease the speed of extrusion and the moisture content.

The first order interaction of spheronisation time and the moisture content, the CE, is also significant at $p<0.001$. If one intends to increase the amount of the main sieve fraction, one should decrease the moisture content /E/ and increase the time of spheronisation /C/.

There is an other interaction, the BE, which proved to be more significant in the previous both cases /$p<0.001$/ then here /$p<0.01$/. Since the signs of the composing factors are the same and their coefficients and t-values are nearly the same, the percentage of the main fraction may increase whether one decreases the spheronizer speed /B/ and simultaneously

TABLE 7.

RESULTS

Exp No.	Main sieve fraction / % /	Calculated mean diameter / mm /	Moisture content decrease / % /
1	70.53	0.89	1.75
2	76.93	0.98	2.08
3	47.51	1.35	2.01
4	78.29	0.99	2.82
5	72.48	0.93	3.75
6	77.40	0.99	3.54
7	77.25	1.00	3.23
8	60.65	0.79	0.29
9	76.89	0.94	1.89
10	67.58	0.83	1.41
11	70.76	0.94	1.76
12	81.39	1.00	1.26
13	81.11	0.96	2.71
14	68.93	0.87	1.42
15	79.90	1.02	2.39
16	70.77	0.87	2.24
17	76.79	0.97	3.21
18	67.41	0.84	1.55
19	85.57	0.95	0.29
20	84.20	1.00	0.63
21	85.35	1.02	1.01
22	87.96	1.04	0.13
23	83.55	1.04	2.08
24	83.01	0.96	0.37
25	87.41	0.98	2.36
26	78.54	1.05	2.04
27	53.39	1.36	3.53
28	85.50	0.96	1.84
29	85.07	1.02	2.51
30	79.93	0.97	2.88
31	83.67	1.02	2.10
32	88.71	0.92	1.16

increases the moisture content /E/ or increases the spheronizer speed /B/ and decreases the moisture content /E/.

Table 8. shows the significant main factors and interactions on the calculated mean diameter of the produced pellets /see Table 7./.

The table reveales that the spheronizer speed /B/, the time of spheronisation /C/ and the moisture content of the wet powder mas /E/ have significant effects. Since each of them have a positive sign, the mean diameter increases if the level of these factors increase.

The BE interaction has a significant effect here. This implies if someone wants to increase the mean diameter, one should increase both the spheronizer speed /B/ and the moisture content /E/. On the other side if one intends to decrease the mean diameter, one should decrease the speed of spheronisation and increase the moisture content simultaneously.

Table 9. shows the significant factors and interactions on the moisture content decrease during extrusion and spheronisation /see Table 7./. According to the main factors, the moisture content decrease may reduce if one decreases the speed of spheronisation /B/, the moisture content /E/ and the time of spheronisation /C/ and increases the load of the spheronizer /D/.

Evaluating the first order interactions, it could be established, if one intends to reduce the moisture content decrease it is better not to change one factor alone but change the two factors paralell. For example, if one decreases the two most significant factors, the speed of spheronisation /B/ and the

TABLE 8.

CALCULATED MEAN DIAMETER

Variables	Coefficients	t-values	Level of significance
B	0.060	9.774	***
C	0.043	6.938	***
AD	-0.040	6.432	***
ABDE	-0.033	5.419	***
ABCD	-0.033	5.419	***
BE	0.028	4.507	***
E	0.024	3.900	**
BCE	0.024	3.900	**
ABCDE	0.021	3.393	**
ADE	-0.016	2.583	*
ACE	-0.015	2.380	*
ACDE	-0.015	2.380	*
ABC	0.014	2.279	*
Intercept	0.9830		

R = 0.9740

F = 25.324 > $F_{(13, 18)}$ = 2.31

Level of significance

p<0.001 = 3.922 ***

P<0.01 = 2.878 **

P<0.05 = 2.101 *

TABLE 9.
MOISTURE CONTENT DECREASE

Variables	Coefficients	t-values	Level of significance
B	0.507	19.123	***
E	0.344	12.962	***
C	0.279	10.501	***
ABCE	0.257	9.688	***
BDE	-0.235	8.863	***
AB	0.213	8.027	***
BE	-0.212	8.004	***
DE	-0.211	7.968	***
CD	-0.179	6.731	***
ABE	-0.174	6.567	***
AC	-0.141	5.306	**
BCE	-0.131	4.941	**
ACE	0.130	4.882	**
ADE	-0.126	4.741	**
D	-0.124	4.658	**
BD	0.121	4.576	**
BC	0.120	4.517	**
ABC	-0.120	4.505	**
AB	0.102	3.846	**
AD	0.100	3.751	**
CDE	0.092	3.481	*
ABCDE	-0.075	2.809	*
ACD	0.074	2.809	*
CE	-0.066	2.491	*
Intercept	1.9448		

R = 0.9974
F = 55.9159 > $F_{(24,7)}$ = 3.41

Level of significance
p<0.001 = 5.408 ***
p<0.01 = 3.499 **
p<0.05 = 2.365 *

moisture content /E/, this will cause a greater reduction in the moisture content decrease since the BE interaction contribute itself to the results significantly.

The moisture content may reduce if one reduces the spheronizer speed /B/ and the speed of extrusion /A/.

The DE interaction implies if once a decreased moisture content occured, the best way to reduce the moisture content decrease is to reduce the load of the spheronizer.

The interpretation of CD interaction suggests that the moisture content decreases if one decreases the time of spheronisation /C/ and increases the load of the spheronizer /D/.

If one decreases the time of spheronisation /C/, the extruder speed /A/ should also decrease according to the CA first order interaction in order to reduce the moisture content decrease during the process.

The moisture content decreases if one decreases the spheronisation speed /B/ and paralell increase eighter the load of the spheronizer /D/ or the time of spheronisation /C/ /see the BD and BC interactions/.

SUMMARY

Summarizing the effects of the main factors on the selected dependent variables, see Table 10. showing what happens when the level of a factor increase. This summarizing table reveales that the extruder speed /A/ has no significant effect

TABLE 10.
EFFECTS OF FACTOR INCREASING ON THE TESTED DEPENDENT VARIABLES

Dependent Variables	Factors				
	A	B	C	D	E
	Extruder speed	Spheronizer speed	Spheronizer load	Spheronizer time	Moisture content
Sieve analysis 0.8-1.25 mm	-	D	-	D	D
<0.4 mm	-	D	D	-	D
>1.60 mm	-	I	I	-	I
Mean diameter	-	I	I	-	I
Moisture cont. decrease	-	I	I	D	I

I = Increases
D = Decreases

TABLE 11.

SUMMARY OF SIGNIFICANTFIRST ORDER INTERACTIONS

Dependent Variables	Interactions									
	AB	AC	AD	AE	BC	BD	BE	CD	CE	DE
Main sieve fraction	*	**	-	***	***	-	**	***	***	-
< 0.4 mm	-	*	***	-	***	-	***	-	***	-
> 1.6 mm	-	-	***	-	***	-	***	-	***	-
Mean diameter	-	-	***	-	-	-	***	-	-	-
Moisture cont. decrease	***	***	**	-	***	***	***	***	*	***

eighter on size and size distribution characteristics /9./ nor the moisture content decrease charactersitics of the produced pellets. This implies to the manufacturer that within the studied range of operation /40-60 rpm/ it is no use to take into consideration the extruder speed /A/. Considering the rate of the process and the moisture content decrease during the process, however, it is better to choose the highest possible speed of extrusion.

The spheronizer load /D/ has significant effects only in two cases both resulting in a decrease.

The time of spheronisation /C/ and mainly the speed of spheronisation /B/ and the moisture content of the wet powder mass /E/ have the strongest impact on the evaluated dependent variables. It is worth to consider that the speed of spheronisation /B/ and the moisture content of the wet powder mass /E/ affect the dependent variables always in the same direction.

The Table 11. shows the effects of the first order interactions on the dependent variables. The table reveales that not only the main factors like the spheronisation speed /B/, the spheronisation time /C/ and the moisture content of the wet powder mass /E/ have significant effects on the dependent variables but the first order interaction of them - the BC, BE and CE - have significant effects in all cases as well.

Considering the BC interaction, a general conclusion can be established which is based on the findings of this study that in order to optimize a particular dependent variable, the composing factors in the BC interaction had to change in all cases paralell in the opposite direction. This fact supports our outlined assumption that the total number of the friction plate revolution plays the key role in determining the size and size distribution characteristics of the pellets.

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