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The roller compaction of different types of lactose

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Abstract

The influence of the roller compaction process on the granule quality of four different types of lactose showing different particle size, bulk density, crystallinity and morphology was compared by modeling. For each type of lactose the influence of the parameter settings on the friability was modeled by a second order polynomial having different average relative deviation values. Pressure, roll speed, vertical and horizontal screw speed were important parameters for all types of lactose but pressure was the most important parameter followed by the roll speed and the horizontal screw speed. Type, particle size and density had an influence on the usable roller compactor parameter settings. The best quality was obtained if at a high pressure a low horizontal screw speed was chosen for each roll speed. Roller compaction of spray-dried lactose was difficult. A gradual decrease of granule quality was seen for α-lactose monohydrate 200M, anhydrous β-lactose, α-lactose monohydrate 90M and spray-dried α-lactose, respectively. The roller compaction process using the different types of lactose was reproducible. © 1998 Elsevier Science B.V. All rights reserved.

Keywords: Roller compaction; Lactose; Dry granulation; Granule; Friability

1. Introduction

In a previous study (Inghelbrecht et al., 1997) the roller compaction process parameters for drum-dried waxy maize starch (DDWM), a plastic deforming material were optimized and evaluated using the particle size distribution and friability data. A neural network (a non-linear model) successfully described the behaviour of the friability of the DDWM granules. This paper reports the optimization of the granule quality by

Abbreviations: ARD%, average relative deviation (%); CV%, coefficient of variation (%); F, granule friability (%); HS, horizontal screw speed (rpm); P_{air}, air pressure (kPa); P_{oil}, hydraulic pressure, oil pressure (MPa); RS, roll speed (rpm); SF, sieve fraction 250–1000 μm (%); VS, vertical screw speed (rpm).

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modeling using lactose, a mainly fragmenting material to determine the influence of different material behaviour. The roller compaction behaviour and the granule quality of three different types of lactose (anhydrous β-lactose, spray-dried α-lactose and sieved α-lactose monohydrate 90M) showing an almost similar mean particle size and particle size distribution were compared. The three lactose types differed in crystallinity and particle morphology. The influence of the particle size distribution of the raw material on the granule quality was examined by comparing α-lactose monohydrate 200M and sieved α-lactose monohydrate 90M.

2. Materials and methods

2.1. Description and instrumentation of the roller compactor

The Fitzpatrick L83 Chilsonator (The Fitzpatrick Company, Elmhurst, USA) consisted of two counter rotating rolls, having smooth surfaces. One of the rolls could move horizontally and was connected to two hydraulic jacks. An air-hydraulic booster system converted an air pressure (P_{air}) into a 25 times higher hydraulic pressure (P_{oil}) between the rolls. A vertical screw, having a de-aerating and a predensification function transported the powder to the nip of the rolls. This vertical screw was fed by a horizontal screw fixed in the powder reservoir. The adjustable parameters of the compactor were: air pressure (P_{air}, kPa), roll speed (RS, rpm), horizontal screw speed (HS, rpm) and vertical screw speed (VS, rpm). Roll speed ranged from 3 to 13 rpm, HS from 0 to 60 rpm and VS from 100 to 1000 rpm. The P_{air} could be adjusted from 100 to 700 kPa, resulting in a maximum hydraulic pressure (P_{oil}) and a compaction force of 2.5 MPa and 17.5 MPa, respectively. The compactor was instrumented with a piëzo-electric pressure sensor (Greisinger Electronic GmbH, Regenstauf, Germany) to measure the instantaneous force between the compacting rolls, and with a displacement transducer (LVDT, Solartron Metrology, Mulheim, Germany) to determine the instantaneous gap between the rolls (Inghelbrecht et al., 1997). When the torque on the vertical screw exceeded its maximum value due to an excess of powder, the motor of the horizontal screw stopped automatically until overfeeding had disappeared. Then the motor restarted automatically. This situation of overfeeding was avoided during the experiments.

2.2. Roller compaction and granulation process

The materials used were anhydrous β-lactose (Pharmatose® DCL21), spray-dried α-lactose (Pharmatose® DCL11), sieved α-lactose monohydrate 90M (Pharmatose® 90M) and α-lactose monohydrate 200M (Pharmatose® 200M). All lactose products were supplied by De Melkindustrie Veghel (Veghel, The Netherlands). The influence of lactose morphology and crystallinity (granular/non-granular, crystalline/amorphous) on granule quality was investigated comparing three materials with an almost similar mean particle size and particle size distribution. Anhydrous β-lactose (Pharmatose® DCL21) is a granular crystalline material with a mean particle size of 140 μm. Spray-dried lactose (Pharmatose® DCL11) consists of α-lactose monohydrate crystals glued with amorphous lactose and had a mean particle size of 120 μm. Sieved α-lactose monohydrate 90M (Pharmatose® 90M) (160 μm) is a non-granular crystalline product. The bulk and tap densities (g/l) were 630/790, 620/740 and 760/910 for Pharmatose® DCL21, DCL11 and 90M, respectively. Differences in particle size were evaluated by comparing the behaviour of Pharmatose® 90M (160 μm) and 200M (40 μm). The bulk and tap densities were 550/850 and 760/910 g/l for the 200M and the 90M sizes respectively. The particle size distribution was determined by laser diffraction (Helo Particle Size Analyser, Sympatec GmbH, Etten-Leur, Netherlands). The lactoses were compacted using different combinations of the four compactor parameter settings: P_{air}, RS, VS and HS. Minimal and maximal values of P_{air}, RS, VS and HS for each RS were determined. After roller compaction, the compact was milled during 6 min using a Frewitt granulator MG624 (Frewitt, Fribourg, Switzerland) equipped with a

1-mm square sieve and operating at a rotor speed of 130 rpm. The distance between rotor and sieve was kept minimal. The quality of the obtained granules was evaluated by sieve analysis and by friability (Inghelbrecht et al., 1997). The reproducibility of the dry granulation process during 6 consecutive days was examined by compacting α-lactose monohydrate 200M at two different parameter setting combinations resulting in a good and a poor compact quality. The good quality granules were obtained by using $P_{air} = 300$ kPa, $P_{oil} = 6.9$ MPa, VS = 1000 rpm, RS = 7 rpm and HS = 9 rpm (combination 1) while with the combination $P_{air} = 100$ kPa, $P_{oil} = 2.3$ MPa, VS = 1000 rpm, RS = 7 rpm and HS = 9 rpm the poor granule quality was obtained (combination 2). The milling process and the analyses were performed following the procedure described above.

2.3. Statistical analysis

The initial friability set was divided into a larger model set and a smaller test set. For a representative selection, the algorithm of Kennard and Stone (Kennard and Stone, 1969) was used. A polynomial regression was used to describe the roller compaction behaviour of the lactoses.

3. Results

The between-day reproducibility of the whole process was evaluated using the friability values of the granules and the sieve fraction yield 250–1000 μm. For the parameter setting combination 1, the friability was 37.2% with an S.D. of 1.33% and a CV% of 3.58, and the sieve yield was 73.0% with an S.D. of 2.79% and a CV% of 3.82. For the parameter setting combination 2 the friability was 71.2% with an S.D. of 2.50% and a CV% of 3.51 and the sieve yield was 59.7% with an S.D. of 0.56% and a CV% of 0.94.

Tables 1–4 show the parameter settings used with the corresponding friability value and sieve yield for the different types of lactose. Using the algorithm of Kennard and Stone, the data set was divided into a model set and a test set as shown in the tables to create an appropriate model.

Fig. 1 shows a good correlation between the sieve fraction and the friability for the four types of lactose. Hence only the influence of the roller compactor parameters on the friability data were further used and modeled by a second order polynomial. For every case the average relative deviation (ARD%) between the experimental and the predicted values was calculated. The ARD% was 11.9%, 7.7%, 4.5% and 7.1% for α-lactose monohydrate 200M, α-lactose monohydrate 90M, anhydrous β-lactose and spray-dried lactose, respectively.

4. Discussion

The dry granulation process of α-lactose monohydrate 200M can be considered as reproducible. Previously, a between-day reproducibility of the process for the plastic deforming drum-dried waxy maize starch (DDWM) was already shown (Inghelbrecht et al., 1997). A linear relationship was found between the friability and the sieve fraction 250–1000 μm for all lactoses tested and this was in accordance with the data found for DDWM (Inghelbrecht et al., 1997) using the same parameters.

The models of the friability were evaluated by their ARD% value, the average relative deviation between the predicted and the experimental data. For all the lactoses pressure, RS, VS, and HS were important parameters in each model. The equations of the models showed that the pressure was the most important parameter. For the friability (F) models the coefficients of P_{air} were negative indicating that an increased air pressure resulted in a decrease in the value of F which involved an improvement of the granule quality. The importance of the pressure exerted on the rolls by the hydraulic system for the granule quality could be explained by the behaviour of lactose when pressure was applied. Alderborn et al. (1985), De Boer et al. (1986), Duberg and Nyström (1982) and Roberts and Rowe (1986) showed that fragmentation was the predominant mechanism of consolidation for all types of crystalline lactose. During roller compaction the P_{air} converted in the hydraulic system to a 25 times

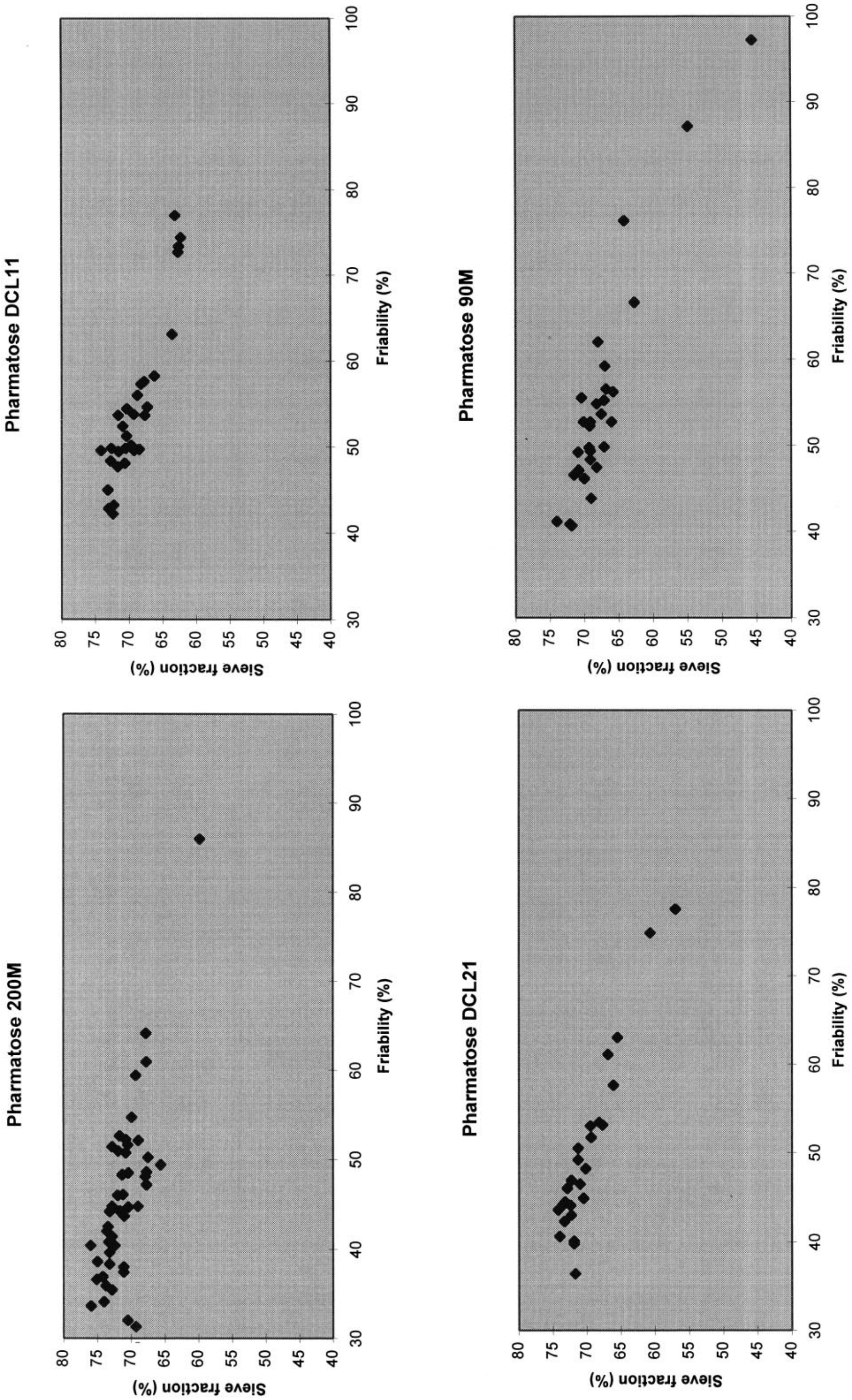

Fig. 1. Relationship between sieve fraction (%) and friability (%) for Pharmatose® 200M, Pharmatose® DCL11, Pharmatose® DCL21 and Pharmatose® 90M.

Table 1
Roller compactor parameter combinations with their corresponding friability (%) and sieve fraction 250–1000 μm (%) values for Pharmatose® 200M

P_{air} (kPa)	RS (rpm)	VS (rpm)	HS (rpm)	Friability (%)	Fraction (%)
300	3	100	5	40.4	72.4
300[a]	3	250	5	42.0	73.6
300	3	500	5	38.6	75.0
300	3	750	5	36.9	74.2
300[a]	3	1000	5	35.9	73.7
300	3	100	10	48.6	67.7
300	3	250	10	49.4	65.6
300	3	500	10	47.2	67.7
300	3	750	10	50.2	67.5
300	3	1000	10	48.1	67.9
300	13	250	24	52.2	70.8
300	13	500	24	42.5	73.4
300	13	750	24	44.2	73.2
300	13	1000	24	39.6	73.2
300	13	250	34	50.7	70.8
300	13	500	34	52.6	71.7
300	13	750	34	52.1	68.9
200[a]	3	1000	5	48.5	70.4
300	3	1000	5	38.3	73.2
400[a]	3	1000	5	34.1	74.0
200[a]	3	1000	9	64.1	67.8
300[a]	3	1000	9	44.7	70.4
400	3	1000	9	36.6	75.1
100	7	1000	11	85.9	59.8
200	7	1000	11	60.9	67.7
250	7	1000	11	48.3	71.3
300	7	1000	11	46.0	72.0
350	7	1000	11	46.1	71.2
400	7	1000	11	41.4	72.8
200	13	1000	24	51.6	70.5
400	13	1000	24	33.6	75.9
200	13	1000	34	59.4	69.3
300	13	1000	34	43.7	71.0
400	13	1000	34	35.4	72.8
300[a]	5	1000	5	32.0	70.5
300	7	1000	5	31.3	69.3
300	5	1000	10	40.8	73.3
300	7	1000	10	37.4	71.1
300	9	1000	10	38.0	71.1
300[a]	7	1000	20	54.7	69.9
300[a]	10	1000	20	44.8	72.8
300[a]	12	1000	20	51.4	72.8
300	3	1000	4	50.9	71.9
300	3	1000	6	44.3	71.7
300	3	1000	8	44.8	69.0
300	13	1000	28	40.4	76.0

[a] Data of the test set (algorithm of Kennard and Stone, 1969).

Table 2
Roller compactor parameter combinations with their corresponding friability (%) and sieve fraction 250–1000 μm (%) values for Pharmatose® DCL11

P_{air} (kPa)	RS (rpm)	VS (rpm)	HS (rpm)	Friability (%)	Fraction (%)
200	6	250	6	57.4	68.2
200	6	750	6	49.7	68.5
200[a]	6	1000	6	51.2	70.3
200[a]	6	250	7	63.1	63.6
200[a]	6	750	7	54.6	67.3
200[a]	6	1000	7	57.6	67.8
200	11	250	12	49.8	72.6
200	11	500	12	43.2	72.3
200	11	750	12	42.2	72.4
200	11	1000	12	42.8	73.0
200	11	250	21	54.4	70.3
200	11	500	21	56.0	68.8
200	11	750	21	53.7	71.6
200[a]	11	1000	21	49.4	71.6
100	6	1000	4	74.4	62.3
200	6	1000	4	58.2	66.2
250	6	1000	4	53.6	67.7
100[a]	6	1000	7	76.9	63.2
250[a]	6	1000	7	50.2	69.7
100	11	1000	12	73.3	62.6
250	11	1000	12	48.1	70.6
100	11	1000	21	72.6	62.7
250	11	1000	21	49.6	69.3
200	6	1000	12	47.7	71.7
200	9	1000	12	48.3	72.7
200	7.5	1000	18	45.0	73.1
200[a]	9	1000	18	49.5	74.1
200	10	1000	18	49.8	70.5
200	11	1000	15	53.8	69.3
200	11	1000	18	52.4	70.9

[a] Data of the test set (algorithm of Kennard and Stone, 1969).

higher P_{oil}, acting on the movable roll, influences the degree of fragmentation. The RS and the HS values were also important parameters to a smaller extent than the pressure. The HS controls the amount of material between the rolls and influences the material force which counteracts the hydraulic pressure. A decrease of the HS resulted in an improved granule friability. The smaller influence of the HS for the spray-dried lactose could be due to the problems during compaction including the lack of residence of the powder in the compactor, due to a continuous flow of the material through the rolls. A higher RS value resulted in an improved F. The RS determines the dwell time of the material between the rolls. The dwell time dependence of the lactose was due to its partially plastic deforming behaviour (Vromans et al., 1985). VS was the least important parameter for all lactoses. A higher VS value resulted in better granule quality. The influence of the VS has to be seen in its predensification and de-aeration function.

The influence of lactose morphology and crystallinity (granular/non-granular, crystalline/amorphous) on granule quality using a roller compactor was investigated comparing anhydrous β-lactose (Pharmatose® DCL21), spray-dried lactose (Pharmatose® DCL11) and sieved α-lactose monohydrate 90M (Pharmatose® 90M), which have an almost similar mean particle size and

Table 3
Roller compactor parameter combinations with their corresponding friability (%) and sieve fraction 250–1000 μm (%) values for Pharmatose® DCL21

P_{air} (kPa)	RS (rpm)	VS (rpm)	HS (rpm)	Friability (%)	Fraction (%)
300	12	250	17	46.9	72.3
300	12	500	17	44.2	73.5
300	12	750	17	44.5	73.2
300[a]	12	1000	17	44.1	72.4
300	12	250	26	51.7	69.4
300	12	500	26	53.0	69.5
300	12	750	26	53.1	67.7
300[a]	12	1000	26	50.5	71.3
100	3	1000	5	63.0	65.5
200	3	1000	5	53.4	68.2
300[a]	3	1000	5	40.6	74.0
100	12	1000	17	74.8	60.7
200	12	1000	17	57.6	66.1
100	12	1000	26	77.5	57.0
200	12	1000	26	61.1	66.9
350	12	1000	26	42.3	73.3
300	5	1000	9	43.6	74.2
300[a]	7	1000	9	44.9	70.5
300	10	1000	9	39.8	71.9
300	10	1000	20	49.2	71.3
300[a]	12	1000	20	43.0	72.3
300	13	1000	20	46.0	72.9
300	3	1000	4	40.1	71.9
300	7	1000	6	36.4	71.7
300	7	1000	14	46.5	71.0
300[a]	12	1000	26	48.2	70.2

[a] Data of the test set (algorithm of Kennard and Stone, 1969).

particle size distribution. Roller compaction of Pharmatose® DCL11 caused some problems. Due to its excellent flow, a continuous powder flow from the reservoir through the screws and rolls occurred, even if the compactor was not operating. For this lactose type, only a small HS range from 6 to 11 rpm and a hydraulic pressure range between 2.3 MPa and 4.6 MPa was usable. For the other lactoses the value of RS could be varied between 3 and 12 rpm and the P_{oil} between 2.3 MPa and 6.9 MPa. The range over which the value of HS could be varied was very similar. Anhydrous lactose showed the highest maximal and minimal HS value. Above the maximal hydraulic pressures (6.9 and 4.6 MPa, respectively), the noise produced by the roll compactor (roll scatter) became an enormous problem and in order to prevent equipment damage, this and higher pressures were avoided. The roll scatter was due to the stickiness of the material to the rolls. The friability of Pharmatose® DCL21 granules was lower than the friability of Pharmatose® 90M granules. For both products an acceptable friability (below 50%) was obtained if at the maximal hydraulic pressure (6.9 MPa) a low HS was chosen for each RS. A high HS resulted in an increased displacement of the movable roll and in a high friability. The maximal usable hydraulic pressure for the Pharmatose® DCL11 was 4.6 MPa. Only at this pressure and at a high RS and a low HS value, was friability acceptable. The sieve yield of Pharmatose® DCL21 and Pharmatose® 90M granules was similar. Only for Pharmatose® DCL11 granules were lower values obtained. This was influenced by the lower maximal pressure. The highest sieve yield was obtained

Table 4
Roller compactor parameter combinations with their corresponding friability (%) and sieve fraction 250–1000 μm (%) values for Pharmatose® 90M

P_{air} (kPa)	RS (rpm)	VS (rpm)	HS (rpm)	Friability (%)	Fraction (%)
300[a]	12	100	16	46.1	70.0
300	12	300	16	49.8	67.1
300	12	700	16	49.7	69.3
300	12	100	22	55.2	67.1
300[a]	12	300	22	56.5	66.8
300	12	700	22	56.2	65.8
300[a]	12	1000	22	59.2	67.0
300	3	100	6	49.3	69.1
300	3	300	6	48.3	69.1
300	3	700	6	43.8	69.0
300[a]	3	1000	6	52.7	66.0
100	12	1000	16	87.1	54.9
200	12	1000	16	66.6	62.7
350	12	1000	16	40.8	72.1
100	12	1000	22	97.2	45.6
200	12	1000	22	76.1	64.2
350	12	1000	22	52.7	70.1
200	3	1000	3.5	47.1	70.8
300[a]	3	1000	3.5	40.6	71.8
350	3	1000	3.5	41.1	74.0
300	4	1000	9	53.6	67.5
300[a]	7	1000	9	47.4	68.2
300	9	1000	20	62.0	68.0
300[a]	11	1000	20	55.5	70.4
300[a]	3	1000	6	52.7	69.1
300	7	1000	8	46.5	71.5
300[a]	7	1000	11	49.2	70.9
300	7	1000	14	54.8	68.2
300	12	1000	19	52.2	69.2

[a] Data of the test set (algorithm of Kennard and Stone, 1969).

if, at a high P_{air}, a low HS was chosen. Vromans et al. (1985) described that the presence of water of crystallization, the α/β ratio and the degree of crystallinity had no influence on the type of binding mechanism for crystalline lactoses. They also found a relationship between particle texture and compatibility (Vromans et al., 1987). The granular forms (anhydrous lactose, spray-dried lactose) showed better binding capacities than the non-granular ones (α-lactose monohydrate). The reason was that anhydrous crystals were weaker, softer, less elastic and underwent brittle fracture more easily and at lower stresses than the monohydrate crystals. This was the result of the removal of the water of crystallization resulting in a partial disruption of the crystalline order. A similar behaviour was shown during roller compaction as the friability was lower and sieve yield higher for anhydrous lactose than for sieved lactose monohydrate 90M. The lower bulk density of the anhydrous lactose could also contribute to a better compatibility (Zuurman et al., 1994). But in general differences between both products were rather small. Spray-dried lactose contained 80–85% α-lactose monohydrate and 15–20% amorphous lactose. The consolidation of spray-dried lactose was determined by the fragmentation of the crystalline α-lactose monohydrate, whereas the binding was largely determined by the amorphous lactose fraction (Bolhuis and Chowhan, 1996). In this study it was difficult to show the better binding capacity of the spray-dried lactose because no identical maximal hydraulic pressure as with the other lactose types could be used. The lower maximal hydraulic pressure for the spray-dried lactose resulted in a lower granule quality. Roller compaction of pure spray-dried lactose was difficult due to a continuous powder flow.

The influence of particle size, particle size distribution and bulk density on the granule quality during roller compaction was evaluated by comparing α-lactose monohydrate 200M (Pharmatose® 200M) and sieved α-lactose monohydrate 90M (Pharmatose® 90M). The 200M size was known to have a poor flowability and fair binding properties while the sieved 90M size showed poor binding properties but an excellent flowability. Some differences in parameter setting combinations were observed. The range in which the value HS could be varied for a certain RS value was larger for the 200M size than for the 90M size. For the 90M size, the maximal RS, the minimal HS and the maximal HS values were lower. At hydraulic pressures above 6.9 MPa an enormous noise produced by the compactor was observed due to sticking of the lactose on the rolls. Falzone (1990) showed by IR detection that no loss of water of hydration was involved in sticking problems. The granule quality was acceptable if the RS:HS ratio was higher than 0.5 at high pressure. The friability was lower for the 200M than for the 90M granules. An acceptable friability ($<50\%$) was obtained for both products at the high oil pressure (6.9 MPa) using a low HS for each RS while smaller differences between both products were seen for the sieve fraction yield. The improved granule quality obtained with a decreasing particle size was in agreement with the results of De Boer et al. (1986) and McKenna and McCafferty (1982) who observed an increase in the compatibility with a decreasing particle size. This phenomenon was explained by the higher surface area available for bonding if a finer particle size was used. Also the lower bulk density of Pharmatose® 200M powder resulted in a better compatibility which was in agreement with the findings of Zuurman et al. (1994).

The roller compaction behaviour of the mainly fragmenting α-lactose monohydrate 200M was totally different than the behaviour of the plastic deforming drum-dried waxy maize starch (Inghelbrecht et al., 1997). Lactose needed a low HS for each RS (high RS:HS ratio) while DDWM needed a high HS for each RS (low RS:HS ratio) to obtain optimal granule quality. Higher hydraulic pressures could be used for DDWM. For an identical parameter setting combination, a higher friability was obtained for lactose 200M than for DDWM. Besides, DDWM was less sticky to the rolls than the lactose.

5. Conclusion

The roller compaction behaviour of different types of lactose evaluated by the granule friability could be described by a linear quadratic model which was in contrast with the non-linear modeling of the granule friability for the plastic deforming DDWM. The linear quadratic equations showed that pressure, roll speed, vertical and horizontal screw speed were found to be important during compaction of the lactose types investigated. Pressure was the most important parameter, followed by the HS and RS, and by the VS. A high hydraulic pressure and a low HS for a high RS resulted in the best granule quality. An influence of particle size and particle morphology was seen.

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