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European Journal of Pharmaceutics and Biopharmaceutics 54 (2002) 59–64

European Journal of Pharmaceutics and Biopharmaceutics

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Research paper

Multiple compaction of microcrystalline cellulose in a roller compactor

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Received 24 August 2001; accepted in revised form 17 April 2002

Abstract

The effect of multiple roller compaction was investigated using microcrystalline cellulose as a model substance. Granules were prepared, examined and recompacted in a Gerteis 3 W-Polygran roller compactor up to ten times. Examinations were carried out for granule size distribution, density and flow properties. Ribbons were investigated for quality, and adhesion of ribbons to the rolls was traced. Finally tablets were produced from the granule samples and examined for their compression behaviour. Multicompression reduces the amount of fines, increases mean granule size and flow properties and also improves size distribution. Although roll adhesion diminishes with increasing cycles, this decrease is not sufficient enough to result in a visibly reduced gap variability. By multicompaction, bulk density increases which indicates that the porosity of granules decreased during the multiple compaction cycles. However, the ability of MCC to form bondings with neighbouring particles is diminished during various cycles which results in decreasing crushing forces of the subsequently prepared tablets.

Keywords: Roller compaction; Dry granulation; Multiple compaction; Granule size distribution; Flowability; Roll adhesion; Gap variability

1. Introduction

Dry granulation with roller compactors is a quick and efficient way of producing granules for development as well production purposes [1,2]. Moreover roller compaction equipment is rather small compared to conventional wet granulation installations for the same 8 h throughput. Since dry granulation does not require the use of granulation liquid, it is also a well-suited process for water or solvent sensible ingredients.

Two different types of roller compactors are commercially available: fixed gap systems and those which allow variable gap size due to moveable rolls.

Fixed-gap roller compactors always produce ribbons of the same geometrical dimensions but ribbon porosity might be changing. This effect can be explained as follows: the powders which are fed to the roller compactors usually are non-free-flowing, otherwise they would be subject to direct compression rather than to roller compaction. Those powders must be conveyed from the filling hopper to the so-called nip area (the area right in front of the gap) until it is drawn into the gap by the rolls themselves. When non-flowing powders are conveyed, for example, by augers, the actual local apparent density of the powder might change due to powder bridges and holes. If such an inhomogeneous powder is fed between two rolls, which are mounted at fixed positions, the porosity of the produced ribbon has to change and one will see variations in compaction pressure if ever recorded. This finally leads to unwanted changes in product quality.

The used Gerteis 3 W-Polygran compactor does not show this variability in product quality due to the innovative variable gap assembly: machines of this type are equipped with a movable slave roll which allows variable gap size. At given compaction pressure, actual gap size mainly results from auger speed, roll speed and density of the fed powder. Thus transportation of non-free-flowing powder and resulting changes in powder density may only lead to gap size variations which causes non-uniform ribbon thickness, but the effects on porosity are almost negligable since compaction pressure is constant.

In order to keep even ribbon thickness at a predefined level, an intelligent mechanism can be activated that controls auger speed in a way that the gap size is kept constant. This contributes to ribbons of uniform thickness and porosity which are prerequisites for reproducible product quality. This makes gap uniformity a watchpoint for current and following investigations.

Furthermore the movable gap system offers the possibi-

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PII: S0939-6411(02)00047-4

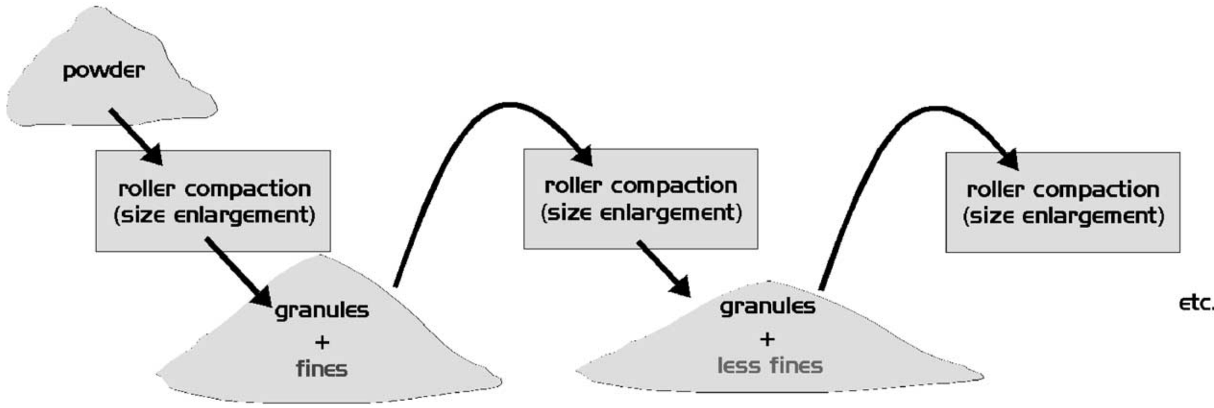

Fig. 1. Rationale for multiple compaction: roller compaction as a way of converting fine powder to coarse granules.

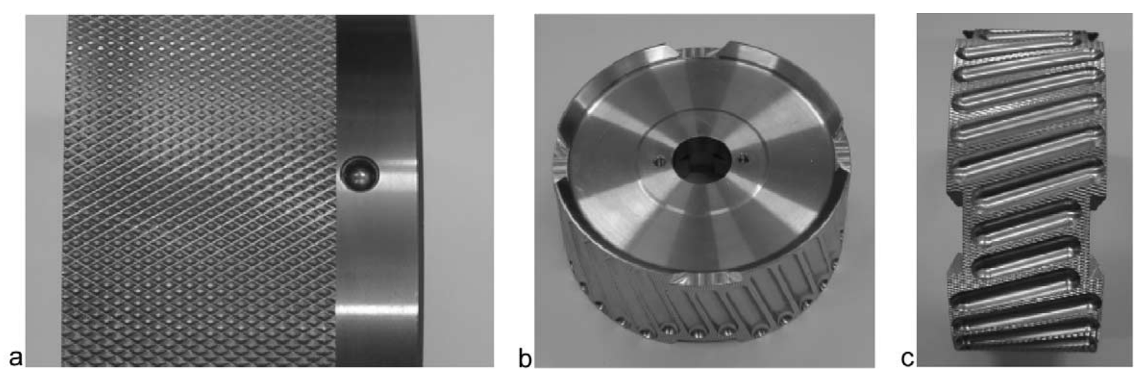

Fig. 2. Surface structure of compaction roll and granulator. (a) Grooved (knurled) surface of a compaction roll, (b) front and (c) side view of pocket mould grooved granulator.

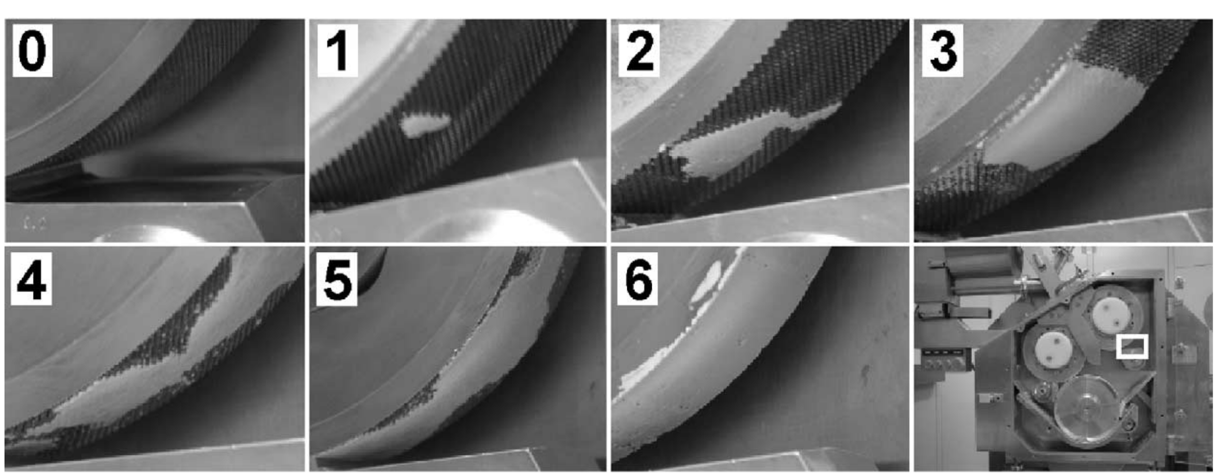

Fig. 3. Illustration of roll adhesion scaling (0..6).

Table 1
Semi-quantitative scaling of roll adhesion and ribbon quality (best values in italics)

Scaling	Adhesion	Ribbon quality
0	*No adhesion*	No ribbon: powder leaves the gap
1	Up to five adhesive plaques of ca. 1 cm^2. Spots are mainly removed by stripper	Weak ribbon that breaks ca. 4 cm after leaving the gap and disintegrates to powder when in contact with granulator
2	Up to 20 plaques of ca. 3 cm^2. Spots are mainly not removed by stripper	Weak ribbon that breaks ca. 7 cm after leaving the gap and disintegrates to small parts or powder when in contact with granulator
3	Extended adhesion: up to five adhering regions reaching from side to side of roll	Ribbon with fringed sides, breaks into small parts when in contact with granulator
4	Adhesion areas at least 5 cm in length, reaching from side to side	Ribbon with fringed sides, breaks into large parts when in contact with granulator
5	Large adhesion areas: the roll is almost completely covered	Ribbon with fringed sides, breaks when pressed pulled against parts of machine
6	Roll is completely covered	*6a: Solid ribbon showing distinct sharp sides, breaks when pressed against parts of machine* 6b: Like 6a but splits in the middle

lity to reduce product loss during the startup-section to a minimum (for more details on the roller compaction process, see Refs. [1–3]).

However, the solvent-free dry granulation process has one minor disadvantage: due to the lack of water or other granulation fluid, capillary forces, that could contribute to particle bondings, are missed, too. Thus, the amount of fines might be somewhat increased compared to conventional granulation, especially if process conditions are not adjusted properly.

When understanding the roller compaction process as a way of converting fine powder to coarse granules, one might think of diminishing the amount of fines in the product by simply recompacting the product (Fig. 1). The question that arises is whether the product properties (flowability, tabletting properties, densities etc.) are affected.

2. Materials and methods

2.1. Compaction

Microcrystalline cellulose (MCC, Avicel PH® 101, Lehmann and Voss and Co, D-Hamburg) is granulated and recompacted in a Gerteis 3 W-Polygran® roller compactor (GMP Gerteis Maschinen + Processengineering AG, CH-Jona; explained in detail in Ref. [3]) under standardized conditions (roll speed: 2 rpm, preselected gap size: 3 mm, compaction pressure: 7 kN/cm, way of powder addition: along feeding and tamping auger, production mode: Startmode ‘A’ and Stopmode ‘A’, roll type: grooved (see Fig. 2a), gap sealing: conventional heart plate assembly, granulator type: pocket mould grooved (see Fig. 2b,c), granulator speed and moving angle: 50 rpm right, 300°, 50 rpm left, 270°, distance between granulator and sieve: Position ‘2’, mesh-size of sieve: 1000 μm).

2.2. Granule properties

The granules were investigated after runs 1,2,3,5 and 10. Granule size distribution was determined using standard sieves (vibratory sieve shaker ‘analysette 3’, Fritsch, D-Idar-Oberstein) and expressed as d' and n according to RRSB distribution with d' being the characteristic diameter and n representing the width of distributions. The amount of fines is expressed as mass proportion of particles smaller than 100 μm. Bulk density was obtained by using the method described in PhEur, 3rd edition. Angle of repose was investigated according to DIN ISO 4324. For examination of flow rate, the time for flowout of 50 g granules out of the funnel used for angle of repose experiments was recorded.

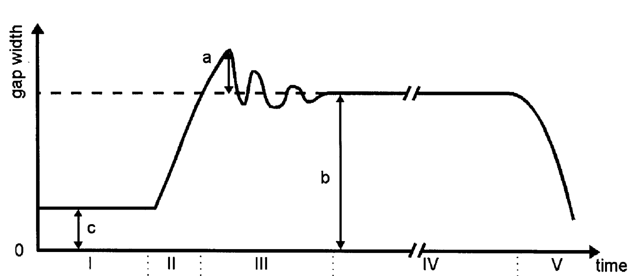

Fig. 4. Various sections of the roll compaction process. The controlled section (IV) is evaluated for gap variability. (I) Filling section, (II) gap opening, (III) adjustment section, (IV) controlled steady state section, (V) ending section due to lack of powder.

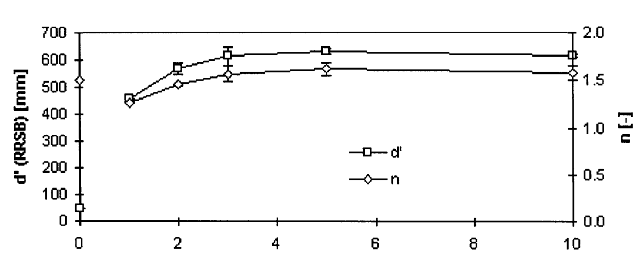

Fig. 5. Effect of multicompaction on granule size distribution (zero compression cycles: uncompacted MCC powder).

Table 2
Size distribution, fines, flow and bulk density data: mean (standard deviation)

Compaction cycle	d' (μm)	n	Fines (%)	Flow rate (g/s)	Repose angle (°)	Bulk density (g/ml)
Uncompacted MCC powder	50	1.50	80.0	No flow	No flow	0.326
1	457 (2)	1.26 (0.00)	19.8 (0.3)	5.2 (0.8)	36.9 (0.2)	0.439 (0.021)
2	570 (21)	1.46 (0.01)	11.1 (0.7)	6.1 (0.1)	34.6 (0.1)	0.505 (0.006)
3	615 (35)	1.57 (0.08)	8.0 (0.4)	6.6 (0.0)	33.2 (1.1)	0.531 (0.006)
5	631 (11)	1.62 (0.07)	7.0 (0.4)	6.7 (0.1)	31.6 (1.8)	0.563 (0.009)
10	617 (4)	1.58 (0.07)	7.2 (07)	7.4 (0.1)	30.0 (0.6)	0.592 (0.004)

2.3. Ribbon properties

After each run, the ribbons were examined in terms of ribbon quality and roll adhesion (both semi-quantitative visual evaluation; see Table 1 and Fig. 3).

2.4. Process

Since nearly constant gap size during the roller compaction process is a prerequisite for high quality products [2], special attention was drawn to gap variability. Variable gap systems offer the advantage of minimized product loss during the startup process: during the filling section, powder is quickly advanced to the empty nip area. In this stage, the amount of powder in the gap is too low to produce a ribbon, so compaction rolls stay in their nearest possible position (c in Section I in Fig. 4) and turn at reduced speed. As more and more powder is promoted to the nip area, a ribbon can be formed and gap opening starts (II in Fig. 4; initial overshooting a might occur). If nominal gap size is reached, roll speed is raised from reduced speed to production speed and from now on gap size is subject to gap control algorithm. After several seconds of adjustment (III in Fig. 4), this control provides a constant gap (IV in Fig. 4) until the process runs out of powder and comes to end (V in Fig. 4).

The variability of the gap during the compaction process was observed and expressed as relative standard deviation of gap size (b in Section IV in Fig. 4) during the controlled section of the process.

2.5. Tabletting properties

Tabletting properties (compression and crushing strength-values) were calculated according to Eqs. (1) and (2) [4] from the results of tabletting the granules without lubricant addition at seven to 15 different pressures in an instrumented custom built pneumatic press.

For convenient visualization, the tablet crushing force was recalculated afterwards from these values for 8 mm ∅, 200 mg tablets at a compression force of 5 kN:

Eq. (1): Compression values $\rho_{r_{max}}$, ρ_{r_0} and k_D explain relative density ρ_r in dependence of applied pressure P

$$\rho_r = (\rho_{r_{max}} - \rho_{r_0})\cdot(1 - e^{-k_D \cdot P}) + \rho_{r_0} \qquad (1)$$

Eq. (2): Crushing strength values a and b explain relative crushing strength B (N/mm^2) in dependence of relative density ρ_r

$$\log_{10} B = a + b \times \rho_r \qquad (2)$$

3. Results

As expected, the MCC granules compared to the MCC powder exhibit superior properties – especially size (Fig. 5 and Table 2) and flow (Fig. 6 and Table 2) – for further tabletting procedure, but changes in the granule properties due to multiple compaction are also visible.

By increasing the number of compression cycles, granule size still increases from 457 μm at initial compression to 631 μm at five cycles and remains greater than 600 μm for the subsequent cycles. Also the uniformity of distributions improves clearly from 1.26 to about 1.6 (Fig. 5 and Table 2)

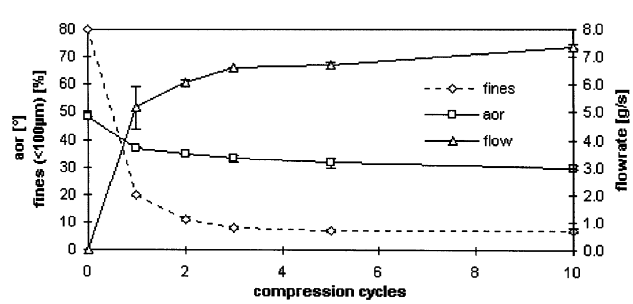

Fig. 6. Effect of multicompaction on granule flow (expressed as angle of repose and flow rate) and the amount of fines (zero compression cycles: uncompacted MCC powder).

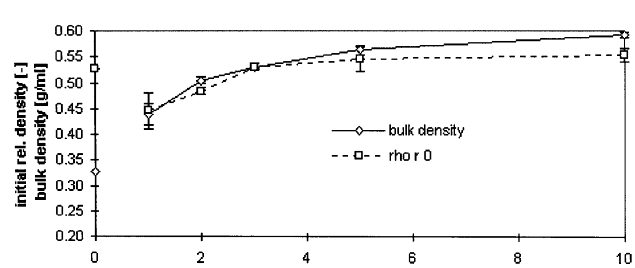

Fig. 7. Effect of multicompaction on initial relative tablet density and bulk densities of the granules (zero compression cycles: uncompacted MCC powder).

Table 3
Compression and crushing strength values plus recalculated crushing force (tablets: 8 mm ∅, flat, 200 mg, 5 kN compression force) data: mean (standard deviation)

Compaction cycle	ρ_{r_0}	$\rho_{r_{max}}$	k_D	a	b	CF (N)
Uncompacted MCC powder	0.424 (0.050)	0.949 (0.006)	0.0181 (0.0018)	−1.43 (0.08)	2.93 (0.07)	301
1	0.446 (0.034)	0.937 (0.004)	0.0168 (0.0022)	−2.32 (0.10)	3.71 (0.01)	175
2	0.484 (0.006)	0.940 (0.004)	0.0154 (0.0010)	−2.85 (0.15)	4.23 (0.04)	138
3	0.529 (0.002)	0.947 (0.002)	0.0146 (0.0010)	−2.84 (0.03)	4.15 (0.08)	125
5	0.547 (0.023)	0.954 (0.012)	0.0129 (0.0001)	−2.90 (0.06)	4.18 (0.04)	112
10	0.553 (0.013)	0.950 (0.005)	0.0143 (0.0032)	−3.28 (0.06)	4.56 (0.13)	110

since the amount of fines is drastically reduced from almost 20% at initial compaction down to about 7% at more than five cycles (Fig. 6, Table 2). This results in better flowing properties: the angle of repose and the flow rate are improved (38–32°, and 5.2–7.4 g/s, respectively). Although the amount of fines diminishes and percolation theory would lead to expecting lower bulk densities, there is a remarkable increase in bulk density from 0.439 to 0.592 g/ml as well as

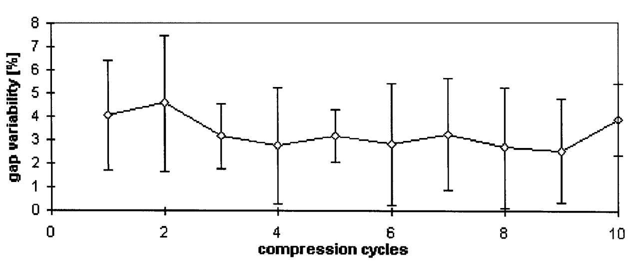

Fig. 8. Effect of multicompaction on tablet crushing force (no lubricant added to granules).

initial relative tablet density from 0.446 to 0.553 (Tables 2 and 3 and Fig. 7) which can be explained by the counteracting and overcompensating densification of the granules (lower intraparticular porosity). This increased densification is also reflected in the change of crushing strength values a, b and recalculated crushing force that result in weaker

Table 4
Ribbon quality, adhesion and gap variability data: mean (standard deviation)

Compaction cycle	Ribbon quality [6..0]	Adhesion [0..6]	Gap variability (%)
1	6.0 (0.0)	1.8 (0.8)	4.1 (2.3)
2	6.0 (0.0)	1.5 (0.9)	4.6 (2.9)
3	6.0 (0.0)	1.3 (1.2)	3.2 (1.4)
4	6.0 (0.0)	1.3 (0.8)	2.7 (2.5)
5	6.0 (0.0)	1.2 (0.8)	3.2 (1.1)
6	5.5 (0.7)	0.8 (0.3)	2.8 (2.6)
7	5.5 (0.7)	0.5 (0.5)	3.3 (2.4)
8	5.5 (0.7)	0.5 (0.5)	2.7 (2.6)
9	5.5 (0.7)	0.5 (0.5)	2.6 (2.2)
10	5.5 (0.7)	0.5 (0.5)	3.9 (1.5)

tablets at high compression cycles (175 N at initial compaction down to 110 N at 10 cycles; see Table 3 and Fig. 8).

Roll adhesion decreases with increasing number of compaction steps but still remains at widely varying values which is the cause for gap variability in the range of 1–7% (Table 4, Figs. 9 and 10). This effect might be improved by adding a lubricant for example.

4. Conclusion

By multiple compaction of pure MCC, the amount of fines can be reduced. This results in improved size distribution and granule flow. On the other hand, compressibility decreases through the first two compression cycles. MCC which is not only used as a filler but more as an excellent dry binder due to its plastic deformability, loses a lot of its dry binding potential by each recompaction step.

In the dry granulation processes compared to wet granulation, one significant additional binding principle (capillary forces caused by the wetting agent) is missing, which makes dry binding activities so important for roller compaction. One can assume that a limited binding potential exists for MCC and unfortunately each compression step irreversibly uses up a relevant portion of this potential. This loss in the ability to create bindings subsequently affects other granule properties to a significant extent as described above. On the other hand, MCC not only loses its ability to form powder–powder bindings but it also loses its ability to form bindings between powder and metal parts, which is reflected in the slight decrease of roll adhesion.

If multicompaction is considered for product optimization, one or a maximum of two recompaction steps are

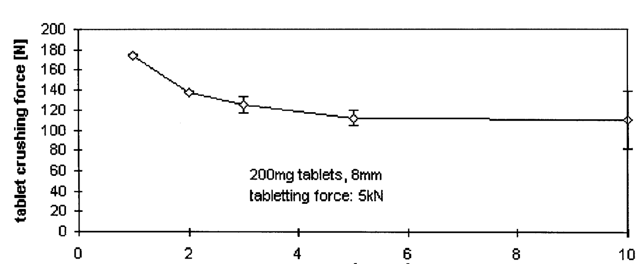

Fig. 9. Effect of multicompaction on roll adhesion.

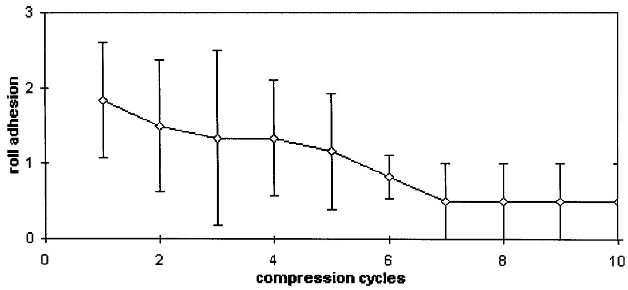

Fig. 10. Effect of multicompaction on gap variability.

suggested in order to reduce fines. A higher number of recompression cycles should not be taken into consideration since the loss in binding potential would affect tablet crushing strength too much and additionally would prolong total processing time, so one of the advantages of roller compaction would get lost.

The changes in gap size might be due to poor flow properties of the microcrystalline cellulose. This may be improved by adding a glidant which could also be the cause for a desired decrease in roll adhesion. Other communications show the remarkable effect of magnesium stearate as glidant on the roller compaction process and product quality [5].

Acknowledgements

This study was kindly supported by GMP Gerteis Maschinen + Process engineering AG, CH-Jona and Lehmann and Voss and Co, D-Hamburg.

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