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The effect of lubrication on density distributions of roller compacted ribbons

A.M. Miguélez-Morán[a,b], C.-Y. Wu[a,*], J.P.K. Seville[c]

[a] Department of Chemical Engineering, University of Birmingham, Birmingham, B15 2TT, UK
[b] Department of Pharmaceutical Technology and Biopharmacy, University of Heidelberg, Im Neuenheimer Feld 366, D69120, Heidelberg, Germany
[c] School of Engineering, University of Warwick, Coventry, CV4 7AL, UK

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ABSTRACT

Roller compaction is a continuous dry granulation process for producing free flowing granules in order to increase the bulk density and uniformity of pharmaceutical formulations. It is a complicated process due to the diversity of powder blends and processing parameters involved. The properties of the produced ribbon are dominated by a number of factors, such as the powder properties, friction, roll speed, roll gap, feeding mechanisms and feeding speed, which consequently determine the properties of the granules (size distribution, density and flow behaviour). It is hence important to understand the influence of these factors on the ribbon properties. In this study, an instrumented roller press developed at the University of Birmingham is used to investigate the effect of lubrication on the density distribution of the ribbons. Three different cases are considered: (1) no lubrication, (2) lubricated press, in which the side cheek plates of the roller press are lubricated, and (3) lubricated powder, for which a lubricant is mixed into the powder. In addition, how the powders are fed into the entry region of the roller press and its influence on ribbon properties are also investigated. It is found that the method of feeding the powder into the roller press plays a crucial role in determining the homogeneity of the ribbon density. For the roller press used in this study, a drag angle (i.e., the angle formed when the powder is dragged into the roller press) is introduced to characterise the powder flow pattern in the feeding hopper. It is shown that a sharper drag angle results in a more heterogeneous ribbon. In addition, the average ribbon density depends upon the peak pressure and nip angle. The higher the peak pressure and nip angle are, the higher the average ribbon density is. Furthermore, the densification behaviour of the powder during roller compaction is compared to that during die compaction. It has been shown that the densification behaviour during these two processes is similar if the ribbons and the tablets have the same thickness.

1. Introduction

Roller compaction is a dry granulation process in which powder blends are compressed between two counter-rotating rollers to form strips, flakes or briquettes, which are subsequently milled to obtain granules with desirable size and size distribution for making capsules or tablets (Guigon et al., 2007). Low demand for space, personnel, energy and time consumption makes roller compaction the most cost-effective agglomeration process. For formulations with drugs that are sensitive to heat, moisture or solvents, roller compaction is the most feasible granulation process because no moisture and additional heat are involved. In addition, compared to other dry granulation techniques, such as *slugging*, roller compaction is a continuous process with higher productivity but less energy consumption and can produce more homogeneous products. Furthermore, on-line control and automation of processing settings can be readily implemented in the roller compaction process so that batch-to-batch variations are minimised and the product quality is improved.

During roller compaction, the powder blends are fed into the compaction zone (the gap between two rollers). The compaction zone can be divided into three regions (Johanson, 1965, see also Fig. 1): (i) an entry (slip) region, (ii) a nip region and (iii) a release region. In the slip region, particle rearrangement, permeation of entrapped air and pre-agglomeration may occur. In the nip region, the powder blend is gripped and compressed between the two rollers as they continue to rotate. The velocity of the powder becomes close to the rotation speed and it is compacted as it is "nipped" between the two rollers. The compaction continues until the powder reaches the neutral angle at which the compression pressure is a maximum. Thereafter, the compressed powder moves to the release region in which relaxation (elastic recovery)

* Corresponding author. Tel.: +44 121 4145365; fax: +44 121 4145324.
E-mail addresses: c.y.wu@bham.ac.uk, miguelez@uni-hd.de (C.-Y. Wu).

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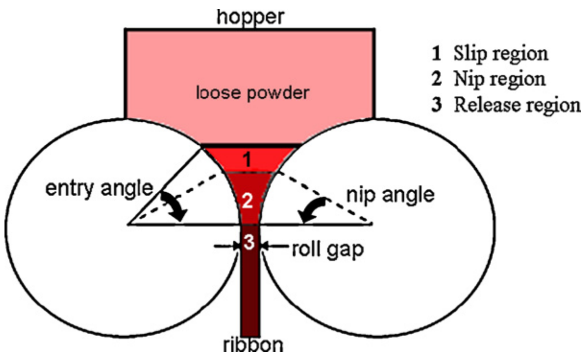


Fig. 1. Illustration of the main regions during roll compaction.

of the compressed powder may take place. The sizes of these three regions and the transition from one region to another depend on the material properties and the processing conditions. The densification behaviour of powders during roller compaction is governed by two key parameters: (1) the nip angle α and the maximum pressure (P_{max}). The nip angle defines the size of the nip region and the compression duration, while the maximum pressure (P_{max}) at the neutral angle indicates the maximum degree of densification. These two parameters are determined by both the inherent powder properties (internal friction, cohesion and the friction between the powder and the tooling) and processing conditions, such as roll speed and roll gap (Miller, 1997; Shlieout et al., 2002; Guigon and Simon, 2003; Simon and Guigon, 2003; Bindhumadhavan et al., 2005; Weyenberg et al., 2005; Mansa, 2004) in a very complicated manner. Due to the diversity of pharmaceutical powder blends and the large number of variables involved, roller compaction is still not well understood although it has attracted increasing attention over the last decade (Miller, 1997; Kleinebudde, 2004; Guigon et al., 2007).

Generally, the ribbons are subsequently milled into granules that are usually compressed into tablets. Wikberg and Alderborn (1991) studied the effect of shape and porosity of the granules on tablet properties and demonstrated that both shape and porosity affected the potential for granule deformation and hence the tablet properties. Nystrom and Alderborn (1993) showed that the main factors contributing to the strength of compacts were granule porosity and size, which were indeed determined by the properties of ribbons for a given milling condition. Sheskey and Hendren (1999) showed that the change in the ribbon strength varied with the grinding time at the mill. Thus, under the same milling condition, finer granules are produced with weaker ribbons (i.e., with lower tensile strength) than stronger ribbons, as demonstrated by Inghelbrecht and Remon (1998) and Von Eggelkraut-Gottanka (2002). Also Weyenberg et al. (2005) characterised the granules used to produce ocular mini-tablets of ciprofloxacin and found that stronger ribbons generated larger granules. Recent studies have revealed that the strength of compressed pharmaceutical compacts primarily depends on their relative densities, i.e., solid fraction (Tye et al., 2005; Wu et al., 2005, 2006). Hence, the properties of the granules will be predominantly determined by the density distributions of the ribbons.

Although ribbons with homogeneous density distribution are desirable in pharmaceutical processing, it is a challenge to produce such ribbons. Zinchuk et al. (2004) compared the ribbons produced using a lab-scale compactor with the tablets produced by uniaxial compression with a compactor simulator. They found that the ribbons presented much larger variations in tensile strength and solid fraction values than the tablets, which was due to the non-uniform stress distribution across the length and the width induced during the roller compaction process. Guigon and Simon (2000, 2003) examined the heterogeneity of the ribbons by mixing coal into a lactose monohydrate blend. They found that the number of fragmented coal particles was higher at those regions subjected to higher stresses. Consequently, those regions appeared darker in the photographic images and their lateral positions on the strip varied in a sinusoidal way. They also used an array of pressure transducers to obtain the stress profiles at the roller surface as the feeding screw rotated and observed a variation pattern whose periodicity corresponded to the screw rotation. They, hence, attributed the sinusoidal pattern to the period fluctuation of the powder feed as the feeding screw rotated. The density variation in roller compacted ribbons was also investigated by Perera (2005) and Busies (2006). Perera (2005) found a higher density in the central part of the ribbon than that at the edges using a gravity fed compactor with sealing plates at the compaction zone. Busies (2006) examined the density of ribbons produced with a screw fed compactor and showed that the fluctuation of solid fraction distribution along the ribbon width apparently depended on whether the compaction zone is sealed using rims that rotate with the roller at the same speed or sealing plates that are stationary.

Clearly, feeding which is non-uniform in time and/or space will result in ribbons with non-uniform density distributions. As in most powder flow problems, both internal and wall friction is implicated. The objective of the present study was to determine whether ribbons with more uniform density distributions can be produced with the aid of lubrication. Both internal (powder) lubrication and wall (boundary) lubrication has been investigated.

2. Materials and methods

A widely used pharmaceutical excipient, microcrystalline cellulose (MCC) of Avicel grade PH102 (FMC Biopolymer, USA), was used for all experiments reported here. Magnesium stearate (MgSt) (Liga MF-2-V, Saville Whittle, UK) was employed as the lubricant. The roller compaction experiments were performed using a laboratory scale instrumented roller compactor (see Fig. 2) developed at the University of Birmingham (Bindhumadhavan et al., 2005). The roll is 45 mm wide and 200 mm in diameter. The powders were fed into the compaction zone under gravity through a feeding hopper. For all

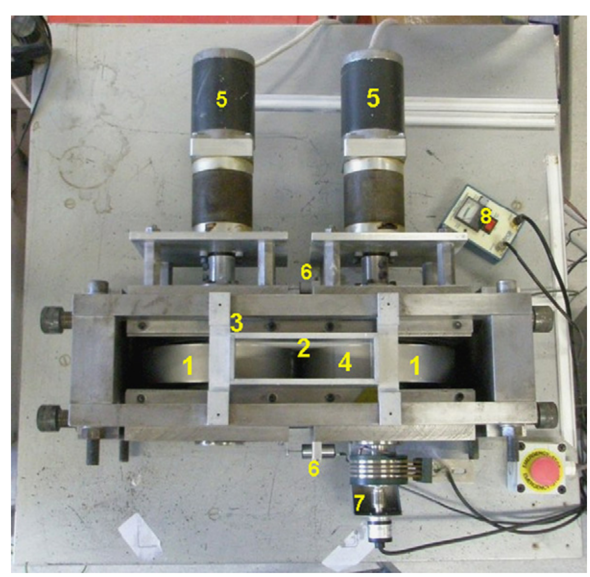


Fig. 2. The instrumented roller compacter used in this study. (1) Rollers, (2) cheek side plates, (3) hopper, (4) pressure transducer, (5) stepper motors, (6) displacement transducers, (7) encoder and (8) signal amplifier.

experiments reported here, the volumes of powders used were kept identical in such a way that the powder was filled into the feeding hopper manually until it formed a heap on the top of the hopper, which was then levelled off. Thereafter, the roller compaction was started and the compression pressure at the powder-roller interface was measured with a pressure sensor fitted in the middle of the roller on the right (see Fig. 2). In order to explore the influence of lubrication, three different cases were considered: (i) no lubrication, in which the as-received powder was roller compacted without lubricating either the tolling surface or the powder, (ii) lubricated press, in which the side cheek sealing plates were lubricated by dubbing a 0.5% (w/w) suspension of MgSt in ethanol onto the surfaces before the as-received powder was roller compacted, (iii) lubricated powder, in which the MCC powder was mixed with 0.5% (w/w) MgSt in a mixer (Lab-Mixer, Pascall, UK) at 45 rpm for 2 min. The true densities of the pure MCC powder and the lubricated powder were measured a helium pycnometer (AccuPyc 1330, Micromeritics, UK).

The powders were compacted through a roll gap of 1 mm at two roll speeds (3 and 5 rpm). Each test was run in triplicate. To ensure the ribbons considered were produced with the powder being fed into the compaction area in a similar manner, the ribbons produced at the beginning and the end of the roller compaction run with a given amount of powder were discarded and only those in between were chosen for further analysis. The compression pressure was collected every 0.39° of rotation. The data were processed using MATLAB to obtain the pressure profiles, from which the nip angle and the maximum compression pressure were determined using the same approach as reported by Bindhumadhavan et al. (2005) and Mansa et al. (2008), i.e., the value of maximum compression pressure is the highest value of pressure registered within one revolution and the nip angle is the value in degrees corresponding to the span of angular positions of the pressure profile around the peak.

In order to analyse the flow behaviour of the powder during the process of roller compaction, the powder profiles in the feeding hopper was recorded using a digital camera (Olympus FE-240) from the top. A scale was set on the top surface of the hopper wall to serve as a reference for the powder position. For each roller compaction run, seven pictures were taken when the interface between the powder and the roll surface was at a distance from the left sidewall of the hopper of 2–5 cm with an interval of 0.5 cm, i.e., with different levels of powder in the feeding hopper. For each picture, the projected angle of the powder boundary on the roll surface, which is referred to as the drag angle, was determined using the image-processing package, ImageJ (http://rsb.info.nih.gov/ij/). The drag angles on both rollers were determined, and there was no significant difference (<6%) in the drag angle measured with different levels of powder in the feeding hopper and the average value of the total 14 measurements was obtained and was regarded as the drag angle for a given process condition.

The selected ribbons were sectioned into rectangular blocks of approximately 10 mm × 10 mm (see Fig. 3) whose dimensions were measured using a slide calliper (Mitutoyo CD-6" CP) and the thickness of each block was measured with a micrometer (Mitutoyo Digimatic Series 293). The weight of each block was determined using a high precision balance (Sartorius 1702). Hence, the bulk density of each block was determined from its mass and volume. For each test, 20 blocks of the ribbon were used. The relative density was calculated as the ratio of the bulk density to the true density of the powder used. The width of the ribbon was also measured. Due to the irregular boundaries of the ribbon, the ribbon width was obtained by averaging the values measured from a 20 cm long segment at an interval of 2 cm using the slide calliper.

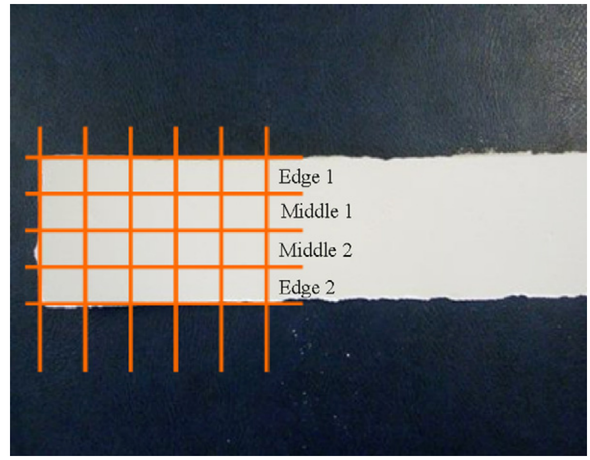


Fig. 3. Illustration of the method to section the ribbon for determining the ribbon density distribution.

3. Results and discussion

3.1. Powder flow behaviour in the feeding hopper

The powder flow behaviour in the feeding hopper during the roller compaction was recorded. The powder profiles at various instants for roller compaction of MCC (no lubrication) at a roll speed of 5 rpm are shown in Fig. 4. It can be seen that, although the initial powder bed has a flat top surface (Fig. 4a), the powder close to the middle of the roll width moves into the compaction zone at a higher rate than that at the edges as the two rolls rotate. This is due to the influence of friction between the powder and the side cheek sealing plates. Consequently, "v-shaped" patterns are obtained when the powder profiles are projected onto the roll surfaces (Fig. 4b–f). Close examination of the powder profiles reveals this "v-shaped" profile exists over the entire top surface of the powder as it flows into the compaction zone, i.e., there is a dip along the powder surface at the middle of the roll width. This v-shaped pattern is defined by a drag angle (see Fig. 4d.). The smaller the drag angle is, the larger is the difference between the flow of powder in the middle of the roll width and that at the edges. The drag angle depends on the powder properties, friction between powder and tooling surfaces, and the processing conditions.

Fig. 5 shows the powder patterns for the three cases considered in this study, pictured at the same degree of fill of the powder in the roll gap. Compared to the pattern for no lubrication (Fig. 5a), lubricating the tooling surface (lubricated press, Fig. 5b) slightly increases the drag angle, while the drag angle can be further increased if the powder is lubricated with MgSt (lubricated powder, Fig. 5c). In addition, for the lubricated powder, the powder surface is much smoother and no sharp angle can be identified, for which the drag angle is approximated as the angle formed by two straight lines drawn from the central point of the powder/roll interface to the intersecting points of this interface with the hopper walls. The measured drag angles for all cases considered are shown in Fig. 6. It is clear that roller compaction without lubricants (no lubrication) results in the smallest drag angle while the lubricated powder has the largest drag angle. The drag angle generally decreases as the roll speed increases. In addition, the difference between the drag angles at two roll speeds decreases when the lubricant is used and the drag angles for the lubricated powder at two roll speeds are very close. This indicates that when no lubrication is used, a higher speed increased the difference of displacement between the powder in the middle of the roll width and that close to the side plates. The lubrication at the side plates decreased the friction between powder and tooling, so the difference of particle displacement was smaller and the rate of powder fed into the roll gap increased. When MCC is blended with MgSt, the particle-particle friction is reduced and the powder flows much better than un-lubricated one. The powder flows into the compaction zone smoothly and no intermittent cascading (slumping) of powder was observed. The difference in the movement of powders at the different regions became smaller and consequently the powder forms a smooth surface with a larger drag angle.

3.2. Compaction pressure and nip angle

Using the pressure sensor fitted in the instrumented roller compactor, the pressure distributions for all three cases considered were obtained. Fig. 7 shows the pressure distribution at two different roll speeds (3 and 5 rpm). It is clear that the overall patterns for the roller compaction at 3 rpm (Fig. 7a) and 5 rpm (Fig. 7b) are similar. Among the three cases considered, the induced maximum pressure is the highest for the lubricated press. Although, at a low roll speed (say 3 rpm, Fig. 7a), the compaction pressure for no lubrication is close to that for the lubricated press, the difference between the maximum compaction pressures induced for these two cases increases as the roll speed increases (Fig. 7b). For the lubricated powder, the compaction pressure is much lower than the other two cases. For the lubricated press, the lubrication reduced the friction between powder and the side cheek plates so that more powder is fed into the nip region when compared to the no lubrication case. This results in an earlier start of the powder densification and a higher value of compaction pressure exerted on the powder. This effect becomes more significant for the roller compaction at a higher roll speed (see Fig. 7b). This is due to the fact that as the roll speed increases, more powder located close to the middle of roll width is dragged into the compaction zone at a higher speed, which hence increases the difference of the displacement between the particles close to the middle of the roll width and those at the boundaries, i.e., a sharp decrease in the drag angle (see Fig. 6). When the lubricated powder is used, compaction pressure decreases dramatically. This is attributed to the sharp increase in the flowability of the lubricated powder, which flows readily through the roll gap and leads to less compaction of the powder. Similar phenomena

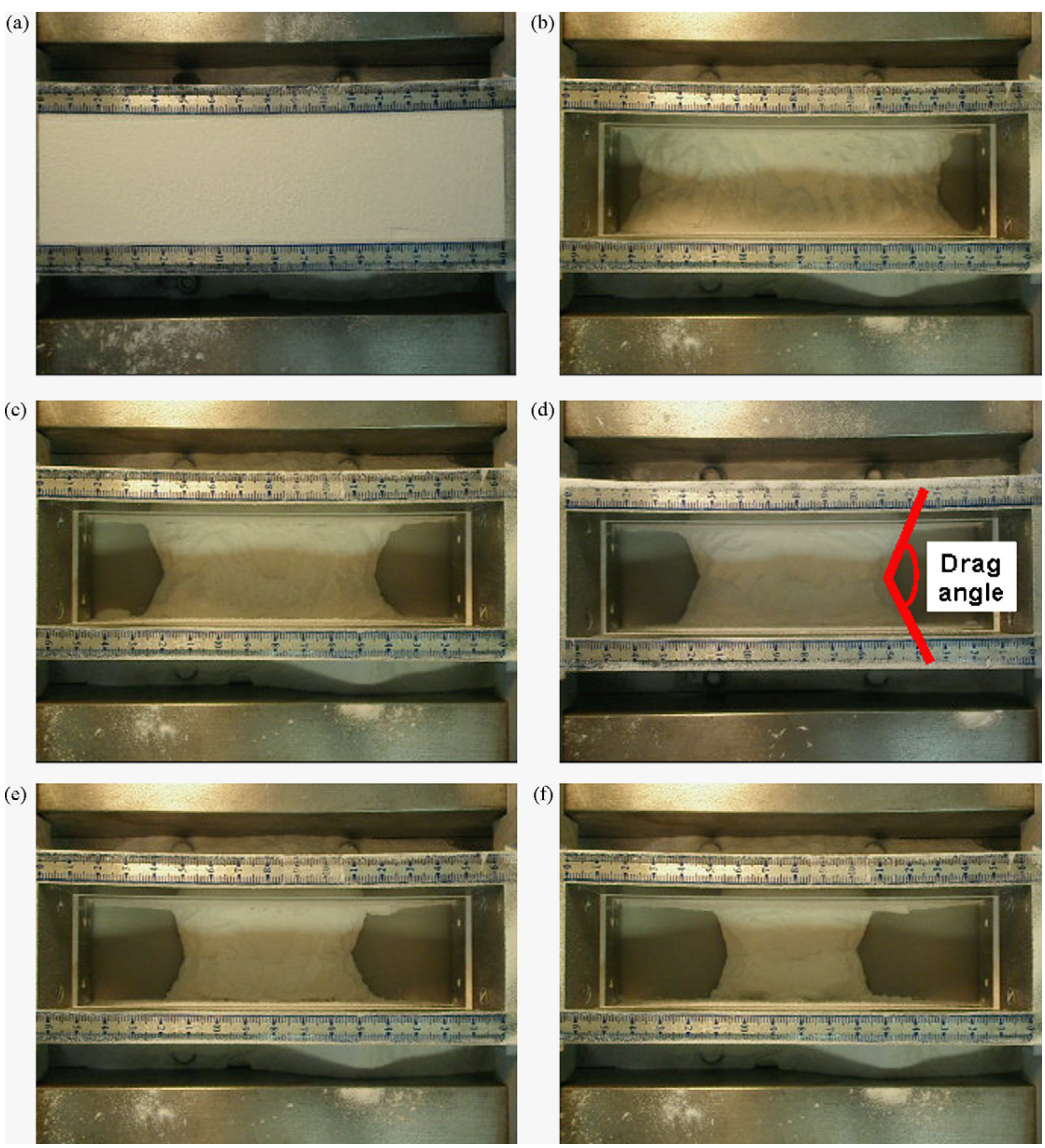
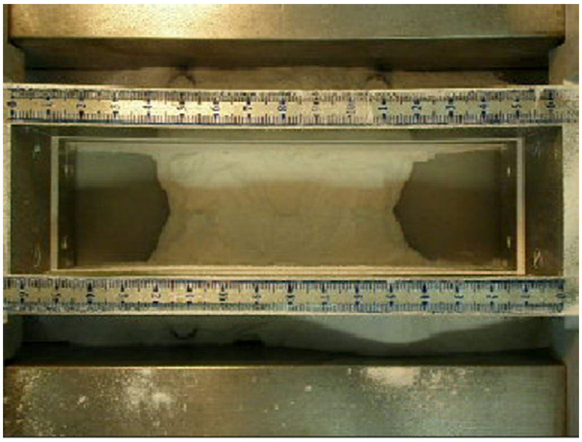
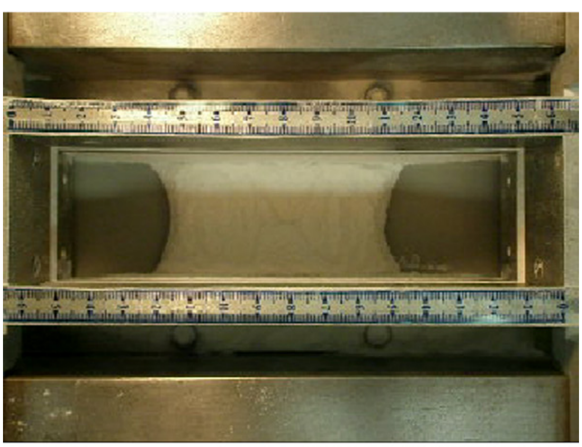


Fig. 4. Powder profiles at various instants during the roller compaction without lubricants at 5 rpm.



(a) No lubrication

(b) Lubricated press



(c) Lubricated powder

Fig. 5. Comparison of the powder profiles in the feeding hopper for all three cases considered during roller compaction at 5 rpm.

were also observed by Perera (2005), who reported a decrease in the nip angle due to the improvement of the powder flowability when MgSt was added to the investigated powders, and showed that, as the concentration of MgSt increased, the nip angle and the pressure applied on the powder decreased.

The nip angles obtained from the pressure profiles for all cases considered are shown in Fig. 8. It can be seen that the nip angle decreases as the roll speed increases, which is consistent with the observations of Bindhumadhavan et al. (2005) and Mansa et al.

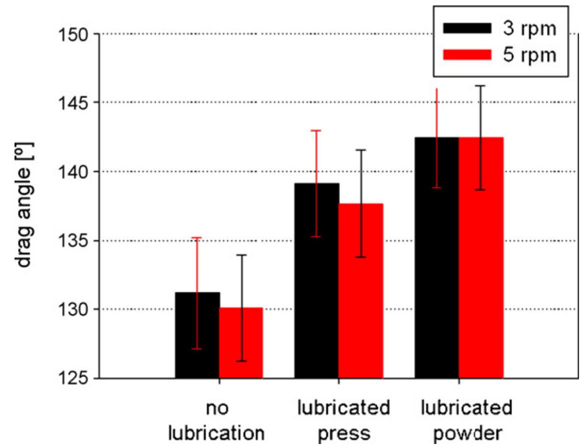
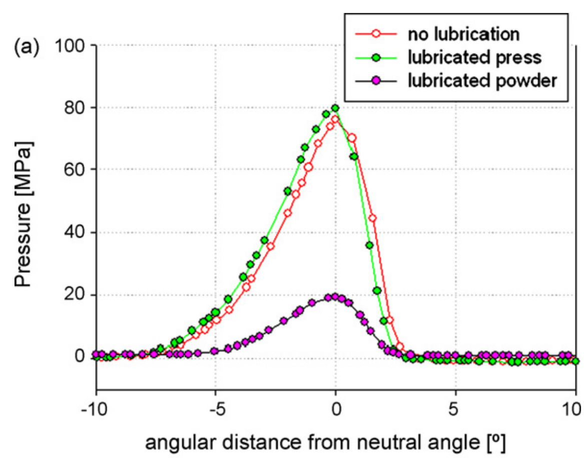


Fig. 6. The drag angle for all cases considered.

(2008). Compared to the case of no lubrication, the nip angle for the lubricated press is larger and a much smaller nip angle is obtained for the lubricated powder. The former is attributed to the reduced constraints from the side cheek plates as the lubricants are applied and the friction between powder and tooling surface is decreased, while the latter is due to the increase in the flowability of the powder. This indicates that the friction, the processing condition and powder flowability all play significant roles in the roller compaction process.



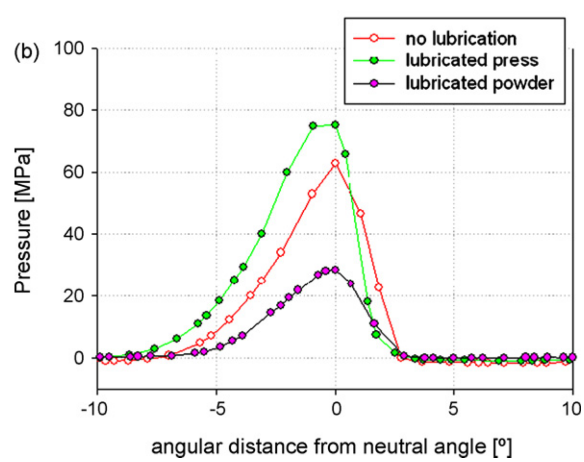


Fig. 7. Compression pressure profiles for the roller compaction at 3 and 5 rpm.

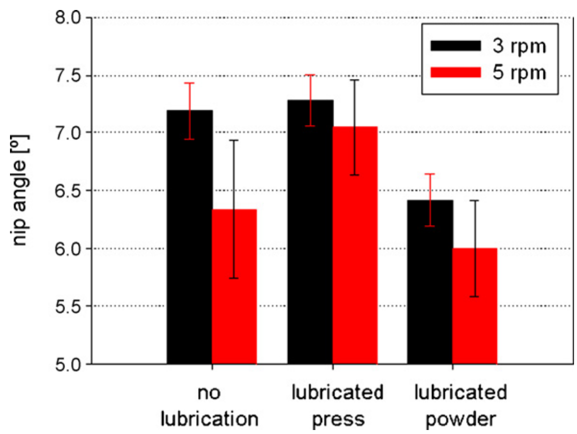


Fig. 8. The nip angle for all cases considered.

3.3. *Densification behaviour and ribbon properties*

As the friction between the powder and side cheek plates inhibits the flow in that region into the compaction zone (Figs. 4 and 5), the powder will be compacted non-uniformly as a result of different amounts of powder being compressed at different positions across the roll width. The powders close to the side cheek plates are less compacted so that either coherent compacts cannot be formed in these regions, or the compacted powders in these regions are relatively loose. These are partly responsible for the excess fines produced by milling roller compacted ribbons, which can also be induced by the leakage of powder at the edge of compressed strip (Michel, 1994). Consequently, the produced ribbons have a width which is less than the roll width (see Fig. 9). It is clear that the smaller the drag angle is (indicating more non-uniform powder feeding in the hopper), the narrower the width of the produced ribbon. Lubricating the side cheek plates (lubricated press) leads to a wider ribbon, as does increasing the roll speed. Furthermore, the produced ribbon has a non-uniform density distribution across its width, with lower densities at the edges and higher densities in the middle (see Fig. 10). Compared to un-lubricated powders (no lubrication and lubricated press), the lubricated powders can be compressed into more homogeneous ribbons, because the powder can be fed into the roll gap more uniformly with a larger drag angles (see Figs. 5 and 6). This can be further confirmed with an analysis of the density variation across the ribbon width, as shown in Fig. 11. In this figure, the relative deviation of density variation δ

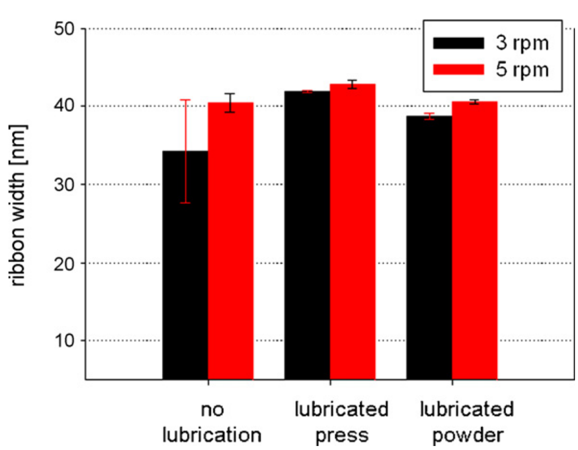


Fig. 9. The ribbon width for all cases considered.

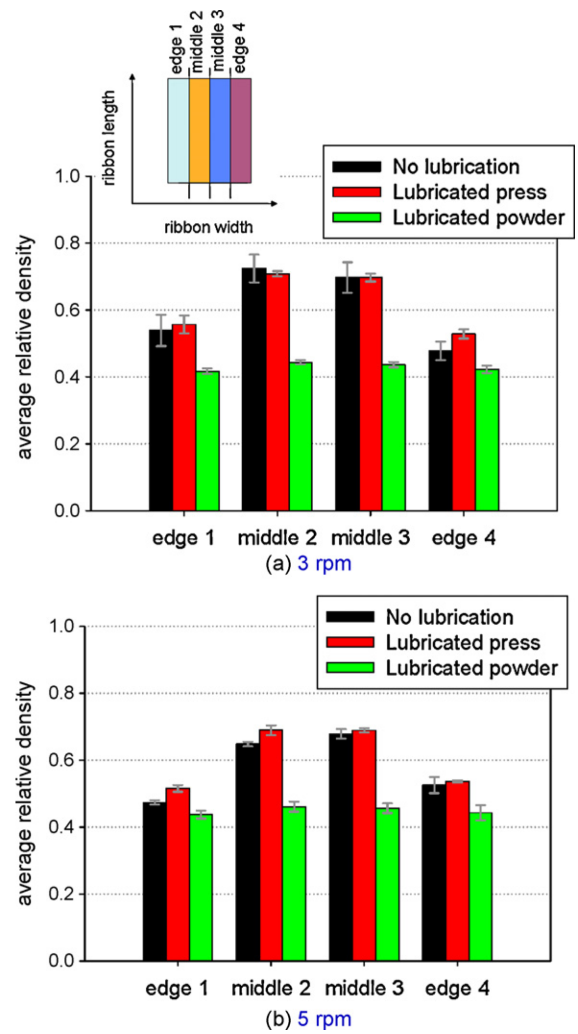


Fig. 10. The density variation along the ribbon width.

is defined as

$$\delta = \frac{\rho_{\max} - \rho_{\min}}{\bar{\rho}} \qquad (1)$$

where $\rho_{\max}$, $\rho_{\min}$ and $\bar{\rho}$ are the maximum, minimum and the average densities across the ribbon width, respectively. It can be seen

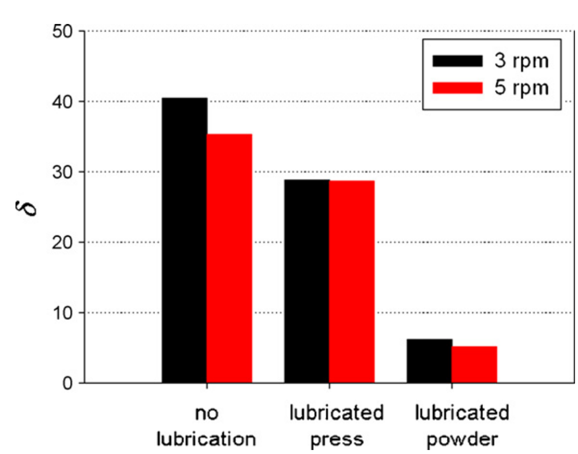


Fig. 11. The relative deviation in density distribution along the ribbon width for different cases considered.

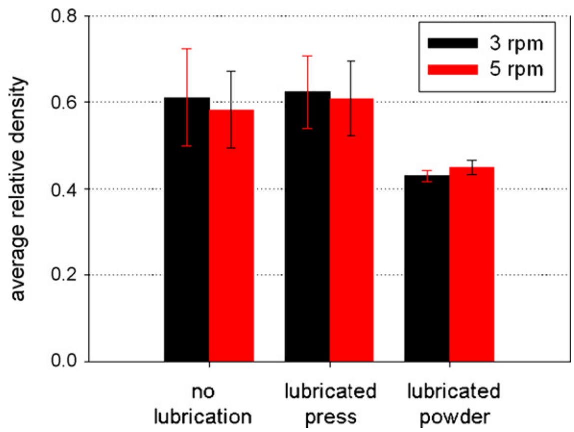


Fig. 12. The average relative density of ribbons produced under different roller compactions considered.

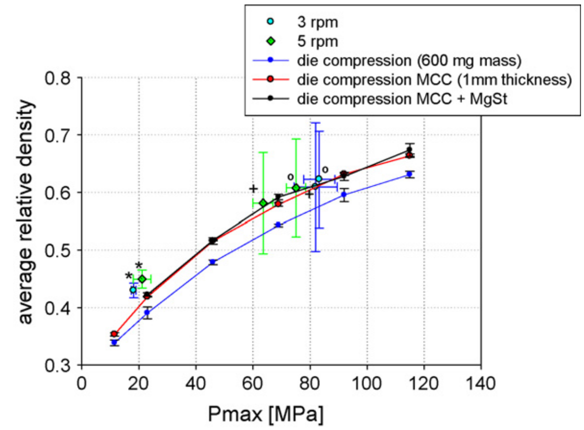


Fig. 14. The variation of average relative density of the compacts with the maximum compression pressure. (+) No lubrication, (○) lubricated press and (∗) lubricated powder.

from Fig. 11 that the relative deviation decreases once the tooling surfaces are lubricated (lubricated press). Furthermore, a much smaller deviation is obtained for the lubricated powder for which both powder and tooling surfaces are lubricated, demonstrating that a more uniform ribbon is produced. In addition, the increase in roll speed slightly reduces the relative deviation.

The average relative densities (solid fractions) of ribbons are shown in Fig. 12 for all cases considered. It is clear that, for unlubricated powders (no lubrication and lubricated press), the average relative density is around 0.6, while the average relative density of the lubricated powder is around 0.43. This is due to the change in the flowability of the powder and subsequently the sharp decrease in compression pressure (see Fig. 7). It should be noted that the average relative densities shown in Fig. 12 are for the coherent ribbons and the un-compacted powders close to the side cheek plates are excluded. This is why the cases of no lubrication and lubricated press yield similar average relative densities, although no lubrication produces narrower ribbons (Fig. 9).

The variation of the average value of the maximum pressure P_{max} with nip angle is shown in Fig. 13. It is clear that P_{max} increases as the nip angle increases. This is due to the fact that more powder is nipped into the roller gap and is compacted as the nip angle increases, and, consequently, a higher compression pressure is induced when the roll gap is fixed. Fig. 14 shows the variation of average relative density with the maximum compression pressure P_{max}. In this figure, results for uniaxial compression of the same

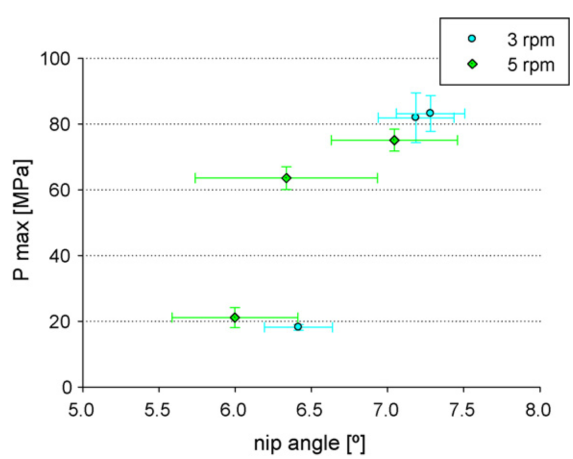


Fig. 13. II The relationship between the maximum compression pressure and the nip angle.

powders (lubricated and unlubricated MCC) at difference maximum pressures are also superimposed. For the die compaction, a die of 13 mm in diameter was used and two sets of experiments were performed: (1) with a constant powder mass of 600 mg resulting in different tablet thickness at different pressures and (2) with a final thickness of approximately 1 mm, which is the thickness of the ribbons, by using different amounts of powders. It can be seen that the average relative density increases with the maximum compression pressure. The results for two different roll speeds coalesce to form a master curve and there is no significant difference between the densification behaviour between two different powders (lubricated and unlubricated MCC). This is due to a very small amount of MgSt (0.5%, w/w) used in the MCC/MgSt mixture, which causes insignificant change in the inter-particle and particle-wall frictions as demonstrated by Bindhumadhavan et al. (2005). It is also interesting to find that the variation of ribbon density with the maximum pressure for roller compaction follows the same relationships as that for die compaction of tablets with the same thickness (ca. 1 mm). This is in excellent agreement with the observations of Michel (1994), who compared the densification behaviour of aluminium powders during uniaxial die compaction with that during roller compaction and found that the same density could be reached at the same maximum compression pressure if the tablet and the ribbon had the same thickness. This indicates that the same relative density can be obtained at the same maximum compression pressure for roller compaction and die compaction if the final products (ribbon and tablet) have the same thickness. Die compaction with a constant amount of powder of 600 mg led to thicker tablets and the relative densities of those tablets were smaller than the ribbons and tablets of 1 mm thickness, because of the well-known effects of wall friction in tabletting, which reduces the average compression stress as the tablet thickness increases.

4. Conclusions

In this study the effect of lubrication on the roller compaction behaviour of MCC powders was investigated using an instrumented roller compactor. A new concept, the drag angle, was introduced to characterise the powder flow behaviour into a roll press. It has been found that the homogeneity of ribbon density is determined by how the powder is fed into the compaction zone and a sharper (smaller) drag angle results in a ribbon with a greater variation in density across its width. In general, nip angle, peak stress in the nip region and variation in density across the ribbon width increase with increase in friction and therefore decrease if the powder is lubricated. It has also been found that similar densification behaviour can be obtained during roller compaction and in uniaxial die compaction if the ribbon and the tablet have the same thickness. Uniaxial compaction can therefore be used as a means of pre-screening formulations before roll pressing trials are carried out. The primary implications of this work are hence two-fold: (1) lubrication of the side walls (cheek plates) in roll compaction is relatively ineffective and (2) lubrication of the powder reduces feed rate into the nip region, so reducing the nip angle and the peak pressure, but also reducing the variation of density across the ribbon.

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