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A comparative study of roll compaction of free-flowing and cohesive pharmaceutical powders

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ABSTRACT

Roll compaction is widely adopted as a dry granulation method in the pharmaceutical industry. The roll compaction behaviour of feed powders is primarily governed by two parameters: the maximum pressure and the nip angle. Although the maximum pressure can be measured directly using pressure sensors fitted in the rolls, it is not a trivial task to determine the nip angle, which is a measure of the size of the compaction zone and hence the degree of compression. Thus a robust approach based upon the calculation of the pressure gradient, which can be obtained directly from experiments using an instrumented roll compactor, was developed. It has been shown that the resulting nip angles are comparable to those obtained using the methods reported in literature. Nevertheless, the proposed approach has distinctive advantages including (1) it is based on the intrinsic features of slip and no-slip interactions between the powder and roll surface and (2) it is not necessary to carry out wall friction measurements that involve plates that may not be representative of the roll compactor in terms of the surface topography and surface energy. The method was evaluated by investigating the effect of roll speed for two pharmaceutical excipients with distinctive material properties: microcrystalline cellulose (MCC) and di-calcium phosphate dihydrate (DCPD). It was found that the maximum pressure and nip angle for DCPD, which is a cohesive powder, decrease sharply with increasing roll speed whereas they are essentially independent of roll speed for MCC, which is an easy flowing powder. The roll compaction behaviour of MCC–DCPD mixtures with various compositions was also investigated in order to evaluate the effect of flowability. It was found that the nip angle and maximum pressure generally increased with improved flowability of the feed powders.

1. Introduction

Roll compaction is a continuous agglomeration process first developed in the late 19th century to produce coal briquettes (Simon and Guigon, 2003). It has been adopted as a dry granulation process in the pharmaceutical industry for more than 50 years (Kleinebudde, 2004). The technique produces ribbons or flakes that are then milled to form granules (Bennett and Cole, 2003). The purpose of this process is mainly to increase bulk density, flowability and uniformity of formulation blends for producing high quality tablets with low dosage and weight variations.

During roll compaction, powders are fed, gripped in the decreasing gap between the counter-rotating rolls and compressed. Johanson (1965) proposed that there are three distinctive regions, i.e. *slip*, *nip* and *release* regions (Fig. 1). In the slip region, particles slip at the roll surfaces and are rearranged, so that there is a small degree of densification and small compression pressures are developed. In the nip region, the velocity of the powder adjacent to the rolls is equal to that of the roll surfaces, and the powder undergoes traction induced compaction due to the decreasing roll gap and the friction along the surfaces of the rolls. The compacted powder finally enters the release region after passing through the minimum roll gap. A nip angle that defines the angular location of the onset of the nip region was introduced to specify the transition from slip to no-slip wall boundary conditions. The maximum compression pressure and nip angle are two important parameters since they govern the extent of powder densification.

Roll compaction is a complex process that depends on a number of factors, such as the system layout, processing conditions and feed powder properties (Guigon et al., 2007; Miller, 1997). The system layout includes the feeding method (Guigon and Simon, 2003; Inghelbrecht and Remon, 1998b), sealing systems (Funakoshi et al., 1977; Miguélez-Morán et al., 2009) and powder de-aeration method (Spinov and Vinogradov, 1967). Inghelbrecht and Remon

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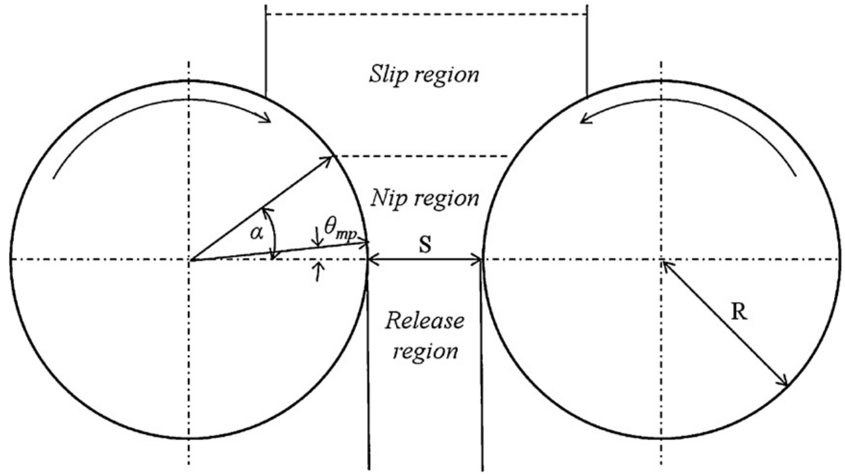


Fig. 1. Scheme diagram of roll compaction showing the slip, nip and release region as defined by Johanson's theory (Johanson, 1965), R is the roll radius, S is the minimum roll gap, and α and θ_{mp} are the nip angle and angular position where the maximum pressure occurs.

(1998b) investigated the roll compaction of lactose with two smooth-surface rolls (L83 Chilsonator, Fitzpartrick, USA) instrumented with a screw-feeding system consisting of a vertical screw and horizontal screw. The powders were pre-densified and transported to the nip of the rolls by a vertical screw having a horizontal screw feed. The speeds for both screws were adjustable. The compacted ribbons were milled using a granulator (MG624, Frewitt, Switzerland) in order to evaluate their quality by sieve analysis and friability testing (Inghelbrecht et al., 1997) of the corresponding granules. It was found that the speeds of the horizontal and vertical screw feeders have a significant influence on the product quality. They argued that the horizontal screw speed controlled the amount of feeding powder. The effects of the vertical screw speed were mainly on the pre-densification and de-aeration of the feed powder. Guigon and Simon (2003) carried out experiments with lactose monohydrate, alumina and sodium chloride using a laboratory roll compactor (B100QC, K.R. Komarek, USA) having a vertical roll configuration and a horizontal screw feeding system. They concluded that the speed of the screw feeder is the only dominating factor for the throughput in the case of screw feeding. They also found that the roll compression stress applied to the ribbons exhibited periodic fluctuation with frequency that were similar to that of the rotation of the single screw feeding system. Spinov and Vinogradov (1967) examined the roll compaction of a copper powder at a constant roll speed and investigated the effect of air entrainment. They pointed out that aeration resulted in discontinuities of the density across the entire width of the ribbon, formation of large voids on the ribbon surface and a decrease in the width of the ribbons. They introduced a vacuum deaeration facility and showed that it was able to minimise the pores and enhance the uniformity and quality of the products. Powder leakage during roll compaction is a problem leading to insufficient compression. In order to solve this problem, sealing systems such as cheek plates (Miguélez-Morán et al., 2009) or a rim on one of the rolls (Funakoshi et al., 1977) are used. Miguélez-Morán et al. (2009) characterised the density of MCC ribbons produced using a laboratory scale roll compactor with cheek plates sealing. They found that non-uniform powder feeding was caused by the friction between the feeding powders and the cheek plates, which resulted in a non-uniform density distribution across the ribbon width. Funakoshi et al. (1977) designed a concavo-convex pair of rolls to prevent leakage of powders and thus improve the uniformity of the pressure across the width of the roll surfaces. The uniformity index, $P_{\max}/P_{\min}$, which is the ratio of the maximum and minimum pressures across the roller surface width, was combined with the amount of leaked powder to evaluate the efficiency of the sealing system. They examined the uniformity index and the amount of leaked powder at various rim wall slope angles, and found that 65° was the optimal concavity.

The performance of the feed powders in roll compaction can also be affected by the process parameters, such as roll pressure (Inghelbrecht and Remon, 1998b; Parrot, 1981), roll speed (Petit-Renaud et al., 1998; Yusof et al., 2004) and roll gap (Bindhumadhavan et al., 2005). Inghelbrecht and Remon (1998b) stated that the hydraulic pressure is the most important parameter that affects the size distribution and friability of the resulting granules. Large hydraulic pressures resulted in sufficient compression and hence strong granules that had a high fraction in the required size range. Petit-Renaud et al. (1998) found that an increase in roll speed of an instrumented compactor (model B-100QC, K.R. Komarek, USA) resulted in a linear increase of the mass throughput but a decrease of the normal pressure and nip angle at a constant roll gap. Yusof et al. (2004) showed that the throughput increased linearly with increasing in roll speed for maize as a feed powder. Bindhumadhavan et al. (2005) roll compacted MCC powders (Avicel PH 102) using a laboratory scale instrumented roll compactor with gaps in a range of 0.9–2 mm. They reported that the compression pressure decreased with increasing roll gap, and the values of the pressure were consistent with the predictions obtained using Johanson theory (Johanson, 1965). Parrot (1981) examined various pharmaceutical powders such as acetaminophen, precipitated calcium carbonate, DCPD and lactose at five different compression pressures using a concave–convex roll compactor. Their results showed that the bulk densities of the produced ribbons were linearly proportional to the logarithm of the pressure applied for all the samples.

In order to increase the efficiency and robustness of roll compaction, it is necessary to improve the current understanding of the influence of the system design and process conditions on particular feed powders and also develop a knowledge base of the influence of the properties of the feed formulations on those of the resulting granules. This has attracted increasing interest (Bacher et al., 2007; Chang et al., 2008; Endale et al., 2008; Inghelbrecht and Remon, 1998a; Kleinebudde, 2005; von Eggelkraut-Gottanka et al., 2002). In particular, the properties of the ribbons and granules made from various raw materials, and the tablets made from the granules have been investigated intensively. It has been shown that the tensile strength of the ribbons and tablets, the bulk density of the ribbons and granules, and the flow properties of the granules strongly depend on the formulation, particle size, moisture content, morphology and friction coefficient of the feed powders

(Bacher et al., 2007; Chang et al., 2008; Grulke et al., 2004; Gupta et al., 2005; Herting et al., 2007). Herting et al. (2007) measured the tensile strength and dissolution properties of the tablets made from granules, which were obtained from roll compaction, in order to evaluate the performance of four different dry binders based on binary mixtures and dicalcium phosphate (DCP). It was shown that the dissolution behaviour of the tablets containing copovidones of different particle sizes was comparable, but the tensile strength of the tablets with a binder of smaller particle size was greater. Chang et al. (2008) examined the roll compaction of mixtures of a ductile API and excipients (*i.e.* mannitol and lactose) and the particle size of the corresponding granules. It was found that the granules containing lactose were generally smaller than those with mannitol due to the brittleness of lactose. Grulke et al. (2004) investigated the roll compaction of MCC (Avicel PH 101), lactose monohydrate (LM Granulac 200) and DCPD (Emcompress) and 1:1 mixtures of these powders at two specific 'compaction rates' of 2 and 7 kN/cm. They showed that the bulk and tapped densities of the granules had a similar trend to the values for the raw materials, implying that the densities of the feed powders play an important role in roll compaction. Gupta et al. (2005) explored the influence of ambient moisture on the roll compaction behaviour of MCC powder (Avicel PH 200), and showed that the presence of moisture resulted in a decrease in the strength of the ribbons. They also introduced a critical density of powders at which the densification from particle arrangement reaches a maximum value before the onset of particle deformation and found that the critical density was independent of the moisture content of the feed powder. Bacher et al. (2007) investigated the roll compaction behaviour of calcium carbonate powders with various morphological forms and sorbitols of different particle sizes. The ribbons were ground into granules. The improvement of the flowability, compactibility (Jørn, 2006) and compressibility characterised by the Walker coefficient (Walker, 1923) were calculated in order to evaluate the quality of the products. It was shown that particle morphology and particle size were the most influential factors in determining the properties of the compacts. A relationship between wall friction angle and maximum compression pressure was obtained by Bindhumadhavan et al. (2005), who investigated the roll compaction of lubricated MCC (Avicel PH 102) with a roll gap of 1.2 mm at a roll speed of 2 rpm. They found that the maximum pressure increased with increasing wall friction between the powders and stainless steel roll surfaces.

The flowability of the feed powder is an important factor in the performance of roll compaction since it affects the compression behaviour (Mansa, 2006) and the cohesion of the granules (Chang et al., 2008). von Eggelkraut-Gottanka et al. (2002) argued that the poor flowability of feed powders with a small particle size might result in the fluctuation of the powder filling even when a screw feeder was used. This phenomenon might cause aeration during roll compaction, which could facilitate the formation of large voids in compacted ribbons and therefore limited densification as shown by Spinov and Vinogradov (1967). How powder flowability affects on the feeding and subsequent compression behaviour was explored by Miguélez-Morán et al. (2008), who examined the effect of lubrication using magnesium stearate (MgSt) on the roll compaction of MCC (Avicel PH 102). The results showed that the compaction pressure and homogeneity of the ribbon density was dominated by the way that the powders were fed into the compaction zone, which was determined by the flowability of the feed powders. Mansa (2006) examined the roll compaction of MCC (Comprecel M101), DCPA (Anhydrous Emcompress) and mixtures of these two powders with various ratios and found that an increase in the cohesion of the feed powder resulted in an increase of the nip angle. Chang et al. (2008) found that the granules with lactose as a feed powder were less cohesive than those with mannitol, which was consistent with the better flow behaviour of lactose.

Although roll compaction has been investigated intensively in the last few decades, it is still not well understood primarily due to the diversity in the controlling factors and material properties. For example, although previous studies highlighted that the materials properties of the feed powders, particularly the flow properties, play an important role in roll compaction, it is still unclear how the dominating compression parameters (*i.e.* compaction pressure and nip angle) depends upon the properties of the feed powder. This was the objective of the current work, especially the influence of the flow properties and roll speed. For this purpose two pharmaceutical excipients MCC and DCPD with distinctive mechanical and flow properties were used. A detailed analysis of the mechanical response of these two powders was performed, for which a robust method for determining the nip angle was established and the advantage of this method will also be discussed. In addition, the affect of roll speed on the maximum pressure and nip angle for these powders will be explored.

2. Materials and methods

2.1. Materials

Two commonly used pharmaceutical excipients were selected: microcrystalline cellulose (MCC) of Avicel grade PH 102 (FMC Biopolymer, USA) and dibasic calcium phosphate dihydrate (DCPD) of Calipharm D grade (Rhodia, France). MCC is a crystalline powder (crystallinity > 78%) with needle-shaped particles (see Fig. 2a). DCPD (Calipharm D) is also a crystalline powder but with shale-like particles (Fig. 2b).

Binary mixtures of MCC and DCPD of various compositions, i.e. with 25%, 50%, 75% and 90% MCC (w/w), were prepared using a laboratory scale double cone blender, in order to evaluate the effects of changes in flowability on roll compaction behaviour.

2.2. Powder characterisation

The true densities of the powders were measured using a helium pycnometer (AccuPycII 1340, Micromeritics, USA). A laser particle size analyser with a HELOS sensor (SympaTec, Germany) was used to measure the particle size distributions. The frictional properties were measured using a RST-XS ring shear cell tester (Dietmar Schulze, Germany) with an applied normal stress in the range 4–10 kPa, from which the effective angle of friction, flow function and the angle of wall friction with a smooth stainless steel plate were determined.

2.3. Uniaxial compression

The powders were compressed uniaxially in a stainless steel die with an diameter of 13.0 mm (Specac, UK) using a universal material testing machine (Z030, Zwick Roell, Germany). The compression speed was 0.5 mm/s, which is comparable to the speeds to be considered in roll compaction, and the maximum compression forces were in the range of 8–16 kN.

2.4. Roll compaction

The powders were roll compacted using a laboratory scale instrumented device developed at the University of Birmingham (Fig. 3) (Bindhumadhavan et al., 2005; Miguélez-Morán et al., 2008; Patel et al., 2010). The stainless steel roll is 46 mm in width and 100 mm in radius. A constant volume of powders was fed using a hopper with a rectangular cross-section that was filled manually, and the excess was levelled off gently. As the rolls start to

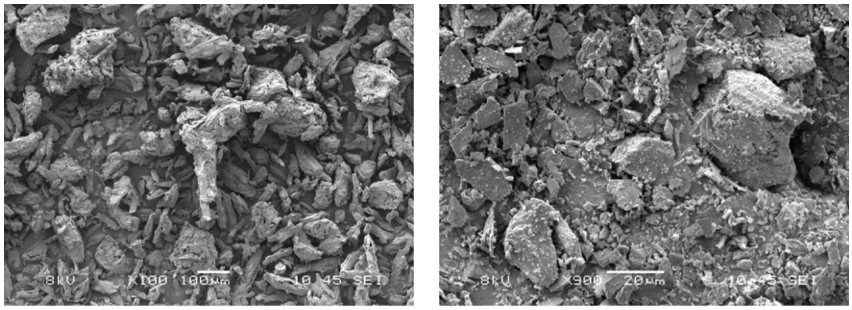


Fig. 2. SEM images of MCC (Avicel PH 102) and DCPD (Calipharm D).

counter-rotate, the powders were fed between the rolls under gravity and compacted. In this study, the minimum roll gap, S, was fixed at 1.0 mm and the roll speed, u, was varied between 0.5 and 5 rpm. The angular position, θ, which is measured from the minimum roll gap, and the corresponding radial roll pressure, p, were both recorded with a piezo-electric pressure sensor (PCB 105C33, Techni-Measure, Studley, UK), from which compaction pressure distributions were obtained.

3. Results

3.1. Characterisation of powders

The material properties of the feed powders are summarised in Table 1. The mean particle size (D_{50} = 8.12 μm) of DCPD, which has a higher true density, is more than an order magnitude less than that of MCC (D_{50} = 90.65 μm). The values of the flow function, ff_c, which represents the flowability, indicate that DCPD is a cohesive powder (i.e. $2 < ff_c < 4$) while MCC is an easy-flowing powder (i.e. $4 < ff_c < 10$). Although the effective angles of internal friction ϕ_e of DCPD and MCC are similar, the angle of wall friction ϕ_w for DCPD is much greater than that for MCC. Thus MCC has a better flowability and a smaller wall friction than DCPD. The flowability of the binary mixtures generally increases with increasing mass fraction of MCC (see Table 1), as expected, but it reaches a maximum at 75% (w/w) MCC. This is believed to be due to the fact that at this mass fraction, there are sufficient fine DCPD particles to form a monolayer surrounding the relatively large MCC particles. This would result in a decrease in the frictional forces and adhesion between the MCC particles and therefore an apparent optimum flowability of the mixture i.e. the DCPD is acting as a flow aid.

3.2. Determination of compressibility factor

The compressibility of a powder is defined as the variation of the relative density with the applied pressure (Jenike and Shield, 1959). Johanson (1965) introduced a compressibility factor κ and proposed the following pressure–density relationship:

$$\frac{\sigma}{\sigma_\alpha} = \left(\frac{\rho}{\rho_\alpha}\right)^\kappa \quad (1)$$

where σ and ρ are current normal stress and density of the powder, σ_α was defined as the nip pressure by Johanson (1965), but it is actually a fitting parameter defining the lower limit for which this relationship describes the data (Patel et al., 2010) and ρ_α is the corresponding density. The uniaxial compaction data were fitted to Eq. (1) and the values of κ are given in Table 1. The compressibility factor κ of DCPD is more than a factor of two greater than that of MCC and thus MCC has a greater compressibility than DCPD.

3.3. Pressure profiles for MCC and DCPD

The pressure distribution for DCPD at the same roll gap (1.0 mm) and roll speed (1.0 rpm) is presented in Fig. 4 for comparison. It can be seen that a considerably greater pressure and a larger compaction zone were induced for MCC, compared to DCPD. It is also interesting to note that the maximum pressure does not occur at the minimum roll gap (i.e. $\theta = 0$), instead it shifts into the compaction zone (nip region). For DCPD, the maximum pressure occurs further away from the minimum gap compared to that for MCC. For both

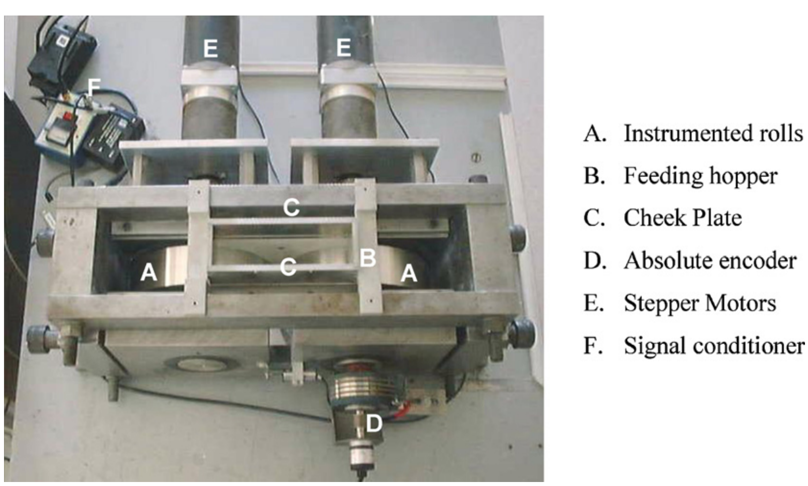


Fig. 3. Laboratory scale instrumented roll compactor developed at University of Birmingham.

Table 1
Materials properties of MCC and DCPD.

Powder	True density ρ_t (kg/m^3)	Mean particle size D_{50} (μm)	Flow function ff_c	Effective friction angle ϕ_e (°)	Wall friction angle ϕ_w (°)	Compressibility factor κ
DCPD	2582	8	3.2 ± 0.49	45 ± 0.96	17.0 ± 0.62	7.74 ± 0.45
MCC	1569	91	7.6 ± 0.30	41 ± 0.58	9.8 ± 0.21	3.24 ± 0.11
DCPD/MCC (25% MCC)	–	–	4.1 ± 0.53	44 ± 0.72	15.2 ± 0.83	5.84 ± 0.53
DCPD/MCC (50% MCC)	–	–	6.8 ± 0.37	43 ± 0.33	13.6 ± 0.42	4.52 ± 0.72
DCPD/MCC (75% MCC)	–	–	11.2 ± 0.88	41 ± 0.61	12.4 ± 0.88	3.76 ± 0.26
DCPD/MCC (90% MCC)	–	–	8.6 ± 0.42	41 ± 0.54	11.2 ± 0.64	3.66 ± 0.32

DCPD and MCC, the release region is much smaller than the nip region, as expected.

3.4. Determination of nip angle

The angular location at which the pressure starts to increase (Fig. 4) can be treated as a first order approximation to the value of the nip angle. It is clear that the nip angle for MCC is larger than that for DCPD, which corresponds to a larger compaction region. There is a significant uncertainty in estimating the nip angle using this method and various alternative approaches have been proposed.

Johanson (1965) adopted the Jenike–Shield yield criterion and derived the equations for the pressure gradient under kinematic wall boundary conditions, with or without slip along smooth roll surfaces, as follows:

$$\frac{d\sigma}{\sigma dx} = \frac{4(\pi/2-\theta-\nu)\tan\phi_e}{(D/2)[1+S/D-\cos\theta][\cot(A-\mu)-\cot(A+\mu)]} \quad (2)$$

$$\frac{d\sigma}{\sigma dx} = \frac{\kappa(2\cos\theta-1-S/D)\tan\theta}{(D/2)[(1+S/D-\cos\theta)\cos\theta]} \quad (3)$$

where the x coordinate corresponds to the centre of the gap between the rolls with an origin at the minimum roll gap such that positive values are against the direction of powder flow and D is the diameter of the roll. The parameters ν and A are functions of the effective internal friction angle, ϕ_e, and the wall friction angle, ϕ_w, defined as:

$$\nu = \frac{1}{2}\left(\pi - \arcsin\frac{\sin\phi_w}{\sin\phi_e} - \phi_w\right) \quad (4)$$

$$A = \frac{\theta+\nu+(\pi/2)}{2} \quad (5)$$

σ is the pressure applied in an orthogonal direction to the roll surfaces at an angular position, θ, such that $\theta = 0$ at the minimum roll gap S. The angle that corresponds to the intersection of Eqs. (2) and (3) was considered to be the nip angle since it represents the demarcation between slip and stick at the powder–wall interface. In order to use Johanson model to predict the nip angle, the effective friction angle ϕ_e, the wall friction angle, ϕ_w, and compressibility factor, κ, need to be determined accurately.

In order to obtain the nip angle directly from the pressure distribution using an instrumented roll compactor, an alternative method was developed by Bindhumadhavan et al. (2005). The nip angle was defined as the difference between two angular positions with a pre-defined pressure threshold in the nip and release regions of the measured circumferential roll pressure distributions. These positions were identified with a threshold pressure that is relatively small compared to the maximum pressure. The value of nip angles determined using this method depends on the specified threshold pressure.

A more robust approach is proposed here for determining the nip angle directly from measured pressure profiles. It is based on an analysis of the pressure gradient calculated using the measured pressure profiles as follows. Using experimental pressure-angular position data, the pressure change, $\Delta\sigma$, and corresponding pressure gradient, $\partial\sigma/\partial x$, as a function of angular location were obtained numerically. A typical plot of $\partial\sigma/\sigma\partial x$ with angular position, θ, for MCC and DCPD is shown in Fig. 5. It can be seen that the value of $\partial\sigma/\sigma\partial x$ initially increases as the angle increases until it reaches a maximum, thereafter it decreases as the angle increase further. Since the trend shown in Fig. 5 is similar to that predicted from Johanson's theory (Johanson, 1965), the data corresponding to angles less than the maximum value of $\partial\sigma/\sigma\partial x$ were fitted to Eq. (2) and those at greater angles were fitted to Eq. (3). This involved multivariate fitting with κ, ϕ_e and ϕ_w being the free fitting parameter. The nip angles for MCC and DCPD obtained from Fig. 5 using this method are 8.8° and 3.4°, respectively, which correspond well to the angular locations at which the pressure starts to increase (Fig. 4). The compressibility factors, κ, obtained using this method are 7.99 for DCPD and 3.36 for MCC. These are in good agreement with those obtained from uniaxial compression (see Table 1). The values of ϕ_e obtained from the fitting to Eq. (2) are generally greater than those measured, while ϕ_w is underestimated. This might be

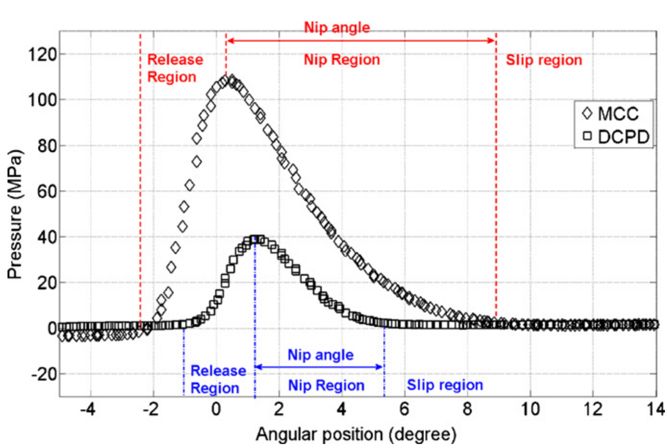


Fig. 4. Pressure distributions for MCC and DCPD (S = 1.0 mm, u = 1.0 rpm).

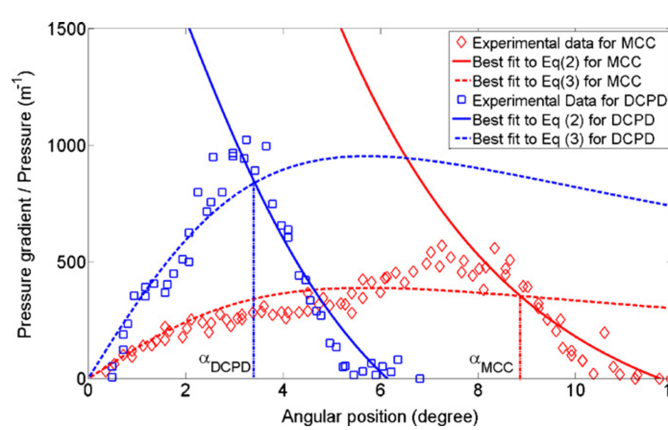


Fig. 5. The determination of nip angle from pressure gradient data (S = 1.0 mm, u = 1.0 rpm).

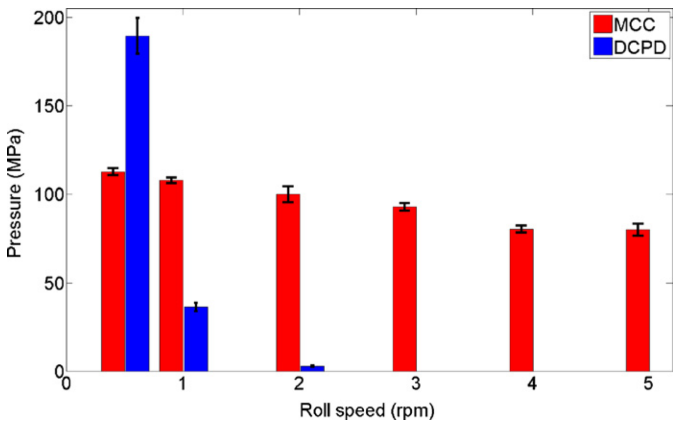


Fig. 6. Maximum pressure for MCC and DCPD at various roll speeds.

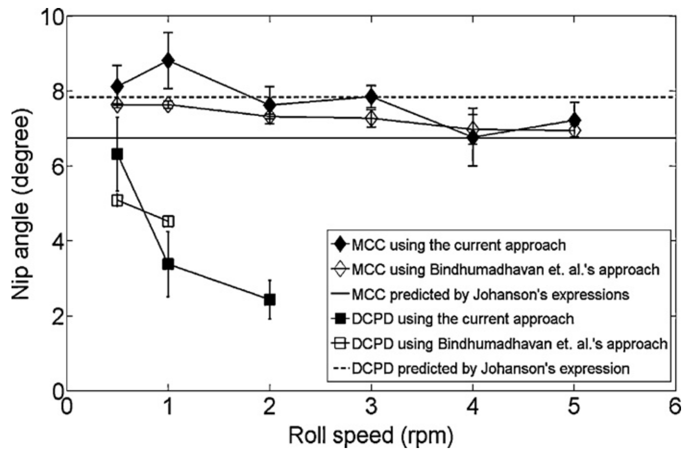


Fig. 7. The variation of nip angle with roll speed.

ascribed to the effects of the flowability of the feed powder in slip region. Johanson's model (Johanson, 1965) assumed a dense packing of the powders that required sufficient feeding. However, in practise, the feeding of the powders might be insufficient and be determined by the flowability and applied roll speed, which are not considered in Johanson's model (Johanson, 1965). This results in an inaccurate estimation of the friction angles.

3.5. Effects of roll speed on maximum pressure and nip angle

It was observed that ribbons could not be produced at roll speeds of greater than 2 rpm for DCPD, but were produced with MCC in a wider range of roll speeds. The maximum pressures for the powders at different roll speeds are shown in Fig. 6. At the lowest roll speed considered (*i.e.* 0.5 rpm), a high maximum pressure is obtained for DCPD, which has a larger effective friction angle and wall friction angle than MCC. As the roll speed increases, a rapid decrease in the maximum pressure is observed for DCPD, which is consistent with previous work (Inghelbrecht and Remon, 1998b; Petit-Renaud et al., 1998). Ribbons could not be produced at high roll speeds because the compaction pressure was too small. For MCC, the maximum pressure decreases slightly as the roll speed increases.

Using the proposed approach described in Section 3.4, the nip angles at the various roll speeds were determined and are shown in Fig. 7. The values calculated using the methods employed by Johanson (1965) and Bindhumadhavan et al. (2005) are also superimposed. It can be seen that the nip angles decreased with increasing the roll speed, which is consistent with the observations reported in the literature (Bindhumadhavan, 2004; Petit-Renaud et al., 1998). However, for MCC (i.e. the easy flowing powder), the values only decreased slightly, while for DCPD they decreases sharply. However, constant nip angles were obtained using Johanson theory (Johanson, 1965), as the effect of roll speed was not considered. In addition, this method slightly underestimate the nip angle for MCC but over estimate the value for DCPD, indicating that it is crucial to accurate determine the input parameters required in using this method. Similar results were obtained using the present method and that proposed by Bindhumadhavan et al. (2005). A close examination of Figs. 6 and 7 reveals that for both DCPD and MCC there is a correlation between maximum pressure and the nip angle as the roll speed increases. In other words, as the roll speed increase the nip angle decreases and so does the maximum pressure. This is consistent with the observations of Miguélez-Morán et al. (2008) who investigated roll compaction of MCC (PH 102) with various lubrication conditions at roll speeds of 3 and 5 rpm and showed that the maximum pressure increases as the nip angle increases.

3.6. Effects of flowability on maximum pressure and nip angle

In order to investigate the effects of the flowability on the maximum pressure and nip angle, binary mixtures of MCC and DCPD were roll compacted and the results are shown in Fig. 8. It is clear that the maximum pressure increases steadily with increasing mass fraction of MCC. The addition of MCC leads to an increase in the flowability and improves the feeding characteristics, which results in an increase in the nip angle. However, the nip angle is primarily determined by MCC when its mass fraction is greater than 75%.

3.7. Compacted ribbons

Compacted ribbons made from pure MCC and DCPD at a roll gap of 1 mm and roll speed of 1 rpm are shown in Fig. 9. The ribbons made from MCC are solid, with a regular shape and with approximately same width as the rolls. Those made from DCPD are brittle, and only fragments were produced with the width of the pieces being in a range 1–10 mm. This is due to the fact that DCPD is not ductile unlike MCC. Strong ribbons cannot be formed by DCPD which is less compressible, even at a high compaction pressure (>180 MPa) when the roll speed is low (0.5 rpm). Furthermore, the ribbons become weaker with increasing roll speeds. In contrast, the

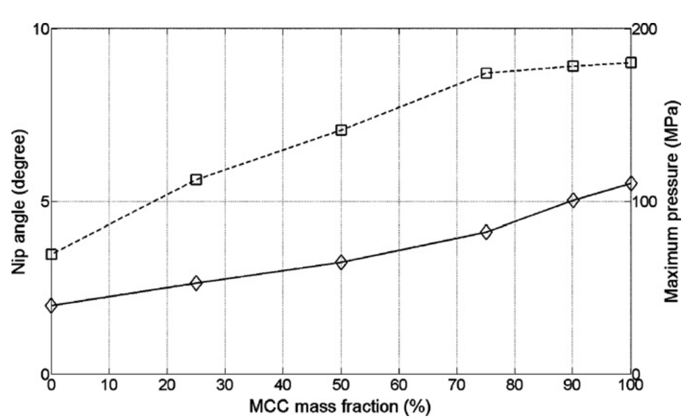


Fig. 8. The maximum pressure (◊) and nip angle (□) as a function of the mass fraction of MCC for MCC–DCPD mixtures (S = 1.0 mm, u = 1.0 rpm).

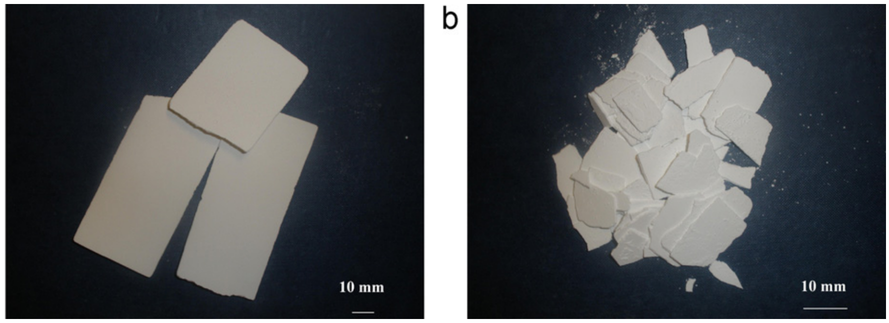
a b


Fig. 9. Compacts produced from roll compaction of (a) MCC and (b) DCPD (1 mm roll gap and 1 rpm roll speed).

strength of the ribbons made from MCC is greater and essentially constant at different roll speeds.

4. Discussion

4.1. Transition angle

For both MCC and DCPD powders, the maximum pressures were not obtained at the minimum roll gap (*i.e.* $\theta = 0$), but corresponded to a finite value of the angular position (Fig. 4), which was also found in numerical simulations (Cunningham, 2005) and the analysis of experimental data (Chekmarev and Vinogradov, 1963; Guigon et al., 2007; Lecompte et al., 2005). Radchenko (1974) suggested that a *neutral angle* could be introduced to represent the angular position for the maximum pressure with reference to the minimum gap. The angle at which the maximum pressure occurs hence corresponds to the condition that $d\sigma/d\theta = 0$ and $d^2\sigma/d^2\theta < 0$. The neutral angle was also defined as that at which the shear stress along the roll surface, τ_w, changes direction *viz.*, when $\tau_w = 0$ (Vinogradov et al., 1970). However, mathematically there is not an obvious interrelationship between the neutral angles defined by Radchenko (1974) and Vinogradov et al. (1970), in other words, $d\sigma/d\theta = 0$ and $\tau_w = 0$ are not necessarily satisfied simultaneously. This was demonstrated by experimental observation (Schönert and Sander, 2002) and numerical analyses (Cunningham et al., 2010; Michrafy et al., 2011). Schönert and Sander (2002) measured the pressure and shear stress simultaneously during roll compaction using a laboratory scale instrumented roll compactor and showed that the shear stress reached zero before the maximum pressure was obtained. Recently, Michrafy et al. (2011) and Cunningham et al. (2010) numerically investigated roll compaction using finite element methods and also found that this was the case. Therefore, it is more appropriate to introduce a parameter, the *transition angle* θ_{mp}, to represent the angle at which the maximum pressure is obtained, where θ_{mp} satisfies $d\sigma_{mp}/d\theta = 0$.

It is possible to argue that $\theta_{mp} > 0$ is related to the shear stress acting on the powder–wall interface and the elastic recovery of the compacted ribbon in the release region. The wall friction angle for DCPD is greater than that for MCC (Table 1). In addition, the yield stress of DCPD (431 MPa) is greater than that for MCC (49 MPa) (Rowe and Roberts, 1996). For the cases considered, it is unlikely that permanent plastic deformation was induced during the roll compaction of DCPD and it is anticipated that the magnitude of elastic recovery of DCPD is greater than that of MCC. Large elastic recovery of the compress DCPD powder when it leaves the minimum roll gap and high wall friction may shift the angular position for the maximum pressure further into the nip region, consequently a large transition angle θ_{mp} was obtained for DCPD, compared to that for MCC.

4.2. Nip angle determination

The three methods discussed in Section 3.4 have their advantages and limitations in determining the nip angle. Using Johanson's model, *i.e.* Eqs. (2) and (3), the nip angle can be predicted only if the frictional properties, ϕ_e and ϕ_w, and compressibility, κ, are accurately measured using techniques, such as shear cell tests and uniaxial compression. Since the wall friction angle, ϕ_w, is a parameter for a powder in contact with a given wall surface and depends significantly on the wall material, exactly the same wall material with the same surface finish as the roll surface should be used in measuring the wall friction angle. In practice, this is difficult to achieve. Furthermore, it is still questionable whether shear cell tests give an accurate value of the wall friction as it generally varies with the applied normal stresses (Cunningham et al., 2010). Moreover, the effects of roll speed are not considered in Eqs. (2) and (3), so that the method cannot be used to explore how the nip angle depends on this variable. This is demonstrated in Fig. 7, which shows that Johanson's method (Johanson, 1965) gives a close estimate of the nip angle for MCC, for which the nip angle is relatively independent of the roll speed, while it over-estimates the nip angle for DCPD. Furthermore, it cannot predict the dependence of the nip angle on the roll speed.

The method proposed by Bindhumadhavan et al. (2005) is convenient to use and has been employed by Miguélez-Morán et al. (2008) and Wu et al. (2010) but the result strongly depends on the threshold pressure, which was generally specified based upon previous experience on some well studied powders and is consequently of limited applicability for powders with unknown characteristics in this respect. Moreover, the potential errors are greater when the maximum pressure is small and a small threshold value close to zero has to be selected. Furthermore, the underlying physical concept is somewhat unclear as it apparently approximates the nip angle using both the data in the nip and release regions.

Although the nip angles obtained by the present approach are comparable to those obtained using the method of Bindhumadhavan et al. (2005), the present method has the following advantages: (1) it is based on the intrinsic features of slip and no-slip interactions between the powder and roll surface and is thus consistent with the physics of roll compaction, (2) it is applicable to any roll speed, even when a small maximum compression pressure is obtained. For example, it can be used to determine the nip angle for DCPD (i.e. the cohesive powder) at a roll speed of 2 rpm, for which the maximum roll pressure is very small (ca. 4 MPa, see Fig. 6), whereas the previous methods had limited success; and (3) the nip angle can be obtained directly from the pressure profiles obtained from roll compaction experiments without having to perform other complicated measurements, which have intrinsic difficulties, especially for wall friction measurements, as discussed above. However, caution needs to be taken in setting the initial values for the free fitting parameters, ϕ_e, ϕ_w and κ, when performing the multivariate fit.

4.3. The effect of material properties on roll compaction

The experimental results obtained using DCPD and MCC with distinctive material properties (friction, compressibility and flowability see Table 1) reveal that a number of factors contribute to the roll compaction performance in a much more complicated manner than that suggested in previous studies (Bindhumadhavan et al., 2005; Johanson, 1965). Among these, the frictional properties of the feed powder were regarded as the dominant parameters in roll compaction. Previous theoretical analysis (Johanson, 1965) and experimental investigation (Bindhumadhavan et al., 2005) showed that the nip angle and maximum compression pressure increase as the values of effective friction coefficient and wall friction coefficient of the feed powders increase, when other parameters are kept constant. For instance, Bindhumadhavan et al. (2005) evaluated the effects of wall friction on the maximum compression pressure by examining differently lubricated MCC powders. They reported that the maximum compression pressure increased substantially with increasing wall friction. Compressibility of the feed powders also plays an important role in roll compaction. Johanson (1965) found that as the value of the compressibility factor increases, the nip angle decreases but the maximum pressure increases. This explains why the nip angles for DCPD at different roll speeds are generally smaller than those for MCC (Fig. 7), since the compressibility factor of DCPD is much greater than that of MCC (Table 1). While the large values of the wall friction angle, ϕ_w, and compressibility factor, κ, for DCPD are primarily responsible for the relative high maximum pressure obtained at the lowest roll speed considered (i.e. 0.5 rpm, see Fig. 6).

Due to the dynamic nature of roll compaction, the performance is sensitive to the flowability of the feed powders, which may determine the efficiency of the powder feeding and therefore the compression pressure induced when a gravity feeding system is employed, especially at high roll speeds, as in the data reported here. It is clear that a larger compaction region (*i.e.* nip angle) and a greater maximum compression pressure is obtained for MCC and these parameters are not affected by the roll speed (Figs. 6 and 7), since this powder has better flowability. On the other hand, the poorer flowability of DCPD can result in insufficient feeding and a fluctuation in powder filling, as reported by von Eggelkraut-Gottanka et al. (2002), and therefore a reduction in the process efficiency. In theoretical models (Cunningham et al., 2010; Johanson, 1965), it is assumed that powder feeding is uniform and the powder mass is dragged primarily by frictional forces. However, the feeding of the powders is greatly affected by the flowability, especially for gravity feeding system. Thus, the size of the nip region is not only determined by the frictional properties and compressibility, but also by the flowability of the material. It can be seen from Fig. 10 that Johanson's theory (1965) overestimates the nip angle for DCPD and DCPD-MCC mixtures having relatively small mass fractions of MCC (say <50%) because of the relatively poor flowability. However, the theory underestimated the nip angle when the mass fraction of MCC is sufficient large and the formulation has good flowability. The maximum pressure for the mixture is determined by the extent of the compaction region characterised by the nip angle and compressibility of the feeding powders. It is clear that a steady increase in the maximum pressure with increasing MCC content is observed (Fig. 8), as a result of the increase in nip angle and compressibility.

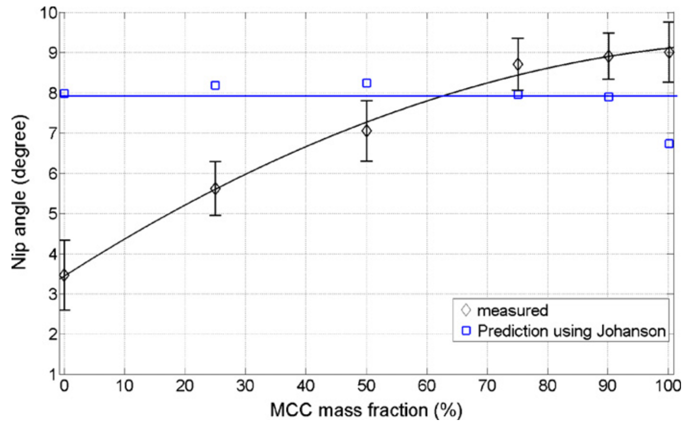


Fig. 10. Comparison of measured and predicted nip angle values for MCC–DCPD mixtures as a function of the mass fraction of MCC (S = 1.0 mm, u = 1.0 rpm).

4.4. Applicability of the proposed approach

The proposed approach for the determination of the nip angle from roll compaction experiments is able to scrutinise the effects of processing parameters, in particular the roll speed, which was not considered in Johanson theory. It reflects the physical factors that control the nip angle and provides a more meaningful interpretation of this parameter compared to conventional approaches. In addition, the present approach is more robust for determining the nip angles of cohesive powders, such as DCPD. This is important since the nip angle is an essential parameter for determining the extent of consolidation of powders in roll compaction. The approach can be used for accurate in-line measurements of the nip angle to enhance the process and for quality control. However, since the pressure gradient is used in the present approach, the method is very sensitive to small changes in the pressure. The data collected need to be processed carefully in order to avoid potential error due to fluctuation of pressure readings in factory scale equipment.

5. Conclusions

The roll compaction behaviour of two common pharmaceutical powders with distinctive material properties (MCC and DCPD) and their mixtures was investigated. It has been shown that the maximum pressure decreased with increasing roll speed for DCPD, while that for MCC is almost constant. A robust method for determining the nip angle based on the intrinsic features of slip and no-slip interactions between the powder and roll surface was developed. It has an advantage in determining the nip angle directly from roll compaction measurements for various processing conditions without resorting to wall friction measurements that involve contacting surfaces that may not be representative of those of the roll compactor. It was found that the flow properties of powders play a significant role and the nip angle depends strongly on the material characteristics for given processing conditions. In addition, the compacts made from MCC are solid ribbons with a regular shape. However, only brittle fragments of small pieces could be produced for DCPD.

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