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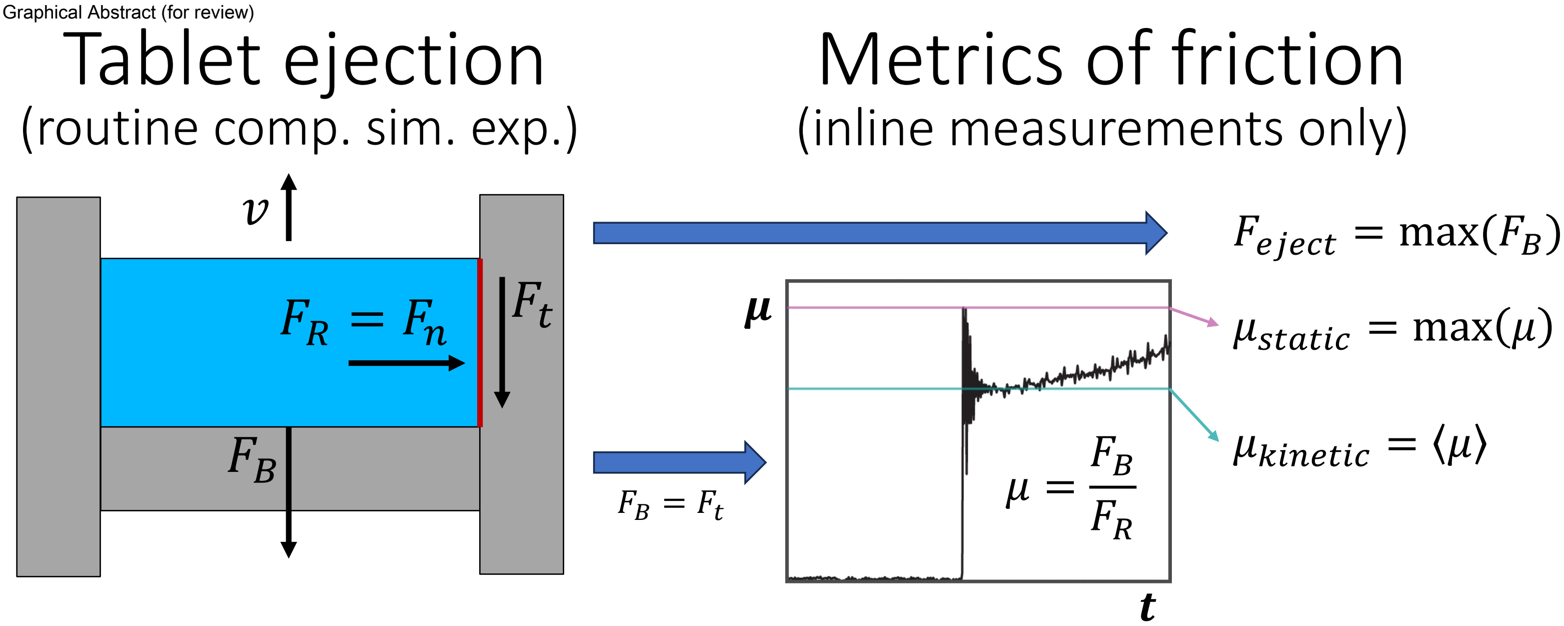
Graphical Abstract (for review)



Tablet ejection: a systematic comparison between force, static friction, and kinetic friction

Dingeman L.H. van der Haven[a], René Jensen[b], Maria Mikoroni[b], Umair Zafar[c], James A. Elliott[a,*], Ioannis S. Fragkopoulos[b,*]

[a]*Department of Materials Science & Metallurgy, University of Cambridge, 27 Charles Babbage Road, Cambridge, CB3 0FS, United Kingdom*
[b]*Oral Drug Product Process Development, Novo Nordisk A/S, Måløv, Denmark*
[c]*Oral Formulation Research, Novo Nordisk A/S, Måløv, Denmark*

Abstract

The magnitude of the frictional forces during the ejection of porous pharmaceutical tablets plays an important role in determining the occurrence of tabletting defects. Here, we perform a systematic comparison between the maximum ejection force, static friction coefficient, and kinetic friction coefficient. All of these metrics have different physical meanings, corresponding to different stages of ejection. However, experimental limitations have previously complicated comparisons, as static and kinetic friction could not be measured simultaneously. This study presents a method for simultaneously measuring the maximum ejection force, static friction coefficient, and kinetic friction coefficient *in situ* during tablet ejection in routine compaction simulator experiments. Using this method, we performed a systematic comparison, including variations of 1) ejection speed, 2) compaction pressure, 3) material, and 4) lubrication method. The relative importance of each variable is discussed in detail, including how ejection speed alone can be a decisive factor in tablet chipping. The reliability of the newly developed method is supported by excellent agreement with previous studies and finite element method (FEM) simulations. Finally, we discuss the suitability of friction coefficients derived from Janssen-Walker theory

*Corresponding authors
Email addresses: `jae1001@cam.ac.uk` (James A. Elliott), `ifra@novonordisk.com` (Ioannis S. Fragkopoulos)

and explanations for the phenomenon of die-wall static friction coefficients with apparent values far above one.

Keywords: Tablet, ejection, friction, static, kinetic, lubrication

1. Introduction

The production of pharmaceutical tablets is hindered by the occurrence of defects that are difficult to predict due to the complex nature of powders [1, 2]. Nonetheless, the consensus is that these defects occur either during the decompression or ejection stage of the process [2, 3]. As such, much effort has been devoted to better understand the effects of varying decompression and ejection conditions on the occurrence of tablet defects [2, 4, 5, 6, 7]. For ejection in particular, studies have investigated the effect of various ejection speeds [8], materials [9], lubricants [10, 11, 12], lubrication methods [13, 14, 12], and lubrication times [9] on either the ejection force [8, 9, 13] exerted by the lower punch on the tablet or the static [8, 9] or kinetic [15] coefficients of friction between the tablet and the die wall. However, all of these quantities have physically distinct meanings and no previous study has carried out a systematic comparison between the ejection force, static friction coefficient, and kinetic friction coefficient. The current study aims to address this gap within the scientific literature on tablet production.

Although the definition of the friction coefficient is straightforward, the direct measurement thereof can be challenging due to equipment limitations or highly dynamic settings, where the moment of interest is either very short or data becomes hard to interpret. Literature on tabletting therefore also reports a variety of methods for determining friction coefficients [8, 9, 15, 16]. Crucial to the computation of a friction coefficient is the radial force that the tablet exerts on the die wall. However, tablet compression machines are rarely equipped to be able to measure radial forces during ejection, leading many authors to use approximations for the radial force during ejection. The most common choice is to take the radial force at the end of decompression, when the bottom punch loses contact with the tablet [8, 9]. However, such an approach neglects the relaxation (after contact loss but before ejection) and recompression (on impact during ejection) of tablets [15]. In contrast, studies using the finite element method (FEM) typically use Janssen-Walker theory to estimate the friction coefficient from the compression stage [7, 17, 18, 19]. This approach in turn makes severe assumptions about the underlying physics and results in an ambiguity about whether the derived friction coefficient is a static or kinetic friction coefficient. A few studies have managed to obtain unambiguous friction coefficients but always required either specialised equipment or protocols [15, 20]. In summary, the literature appears to lack not only a systematic study on different metrics of friction but also a convenient and unambiguous method to measure friction coefficients.

In this study, we propose a new methodology to reliably and directly measure the ejection force, static friction coefficient, and kinetic friction coefficient in routine compaction simulator experiments. This provides significant advantages over previous methods, which either give limited information, rely on approximations, or require specialised protocols or equipment. To demonstrate the capabilities of this new methodology, the frictional behaviour of three strongly dissimilar excipients was studied under a broad range of varying conditions; compaction pressure, ejection speed, and lubrication method. The occurrence of chipping defects simultaneously allowed an investigation of the impact of ejection speed on the severity and frequency of defects. The newly proposed methodology thus allows frictional forces to be quantified as an integral part of regular formulation studies performed on compaction simulators, as well as directly in the relevant setting, allowing for the faster optimisation of powder formulations for the production of pharmaceutical tablets.

In addition, to provide deeper insight into the complex frictional behaviour of porous compacts, various theoretical frameworks were applied. Janssen-Walker theory was used to compute friction coefficient and tested against experimental values. Ejection was also simulated using FEM, making use of several different friction laws, to identify what frictional behaviours can and cannot be explained using a continuum elasto-plastic approach, providing valuable insights for future FEM modelling of tablet compression. Finally, we suggest a potential cause for the occurrence of extremely high static friction coefficients (well above one), which has important implications for the development of new formulations.

2. Experimental methods

2.1. Materials

The following three powders were used: micro-crystalline cellulose (MCC, Avicel PH200®, $D_{\mathrm{v}}50$ of 199 µm), dibasic calcium phosphate dihydrate (DCPD, Emcompress premium®, $D_{\mathrm{v}}50$ of 212 µm), and partially pregelatinized starch (Starch, SEPISTAB™ ST 200, $D_{\mathrm{v}}50$ of 192 µm). The effective true densities of these powders have been determined previously using the method by Sun [21, 7, 17]. These powders were blended with 1 wt% of magnesium stearate (MgSt) for the purpose of internal lubrication. Blending was performed using a 3D shaker TURBULA® T 2 F for 5 minutes at 25 rounds per minute.

The materials in this study have been chosen to represent a range of mechanical properties that is representative of powders encountered within the pharmaceutical industry. MCC and starch are extremely common excipients, respectively with predominantly plastic and (visco-)elastic behaviour. DCPD, on the other hand, is a common excipient with hard and brittle behaviour, more closely resembling the mechanical properties of a typical API. The selected materials therefore provide a decent sample of different mechanical properties whilst also providing a point of reference by having been extensively studied in the past.

2.2. Compaction and ejection

All tabletting experiments were performed on a compaction simulator; the STYL'One Evolution press (Medelpharm, Beynost, France), equipped with a 80 kN load cell, instrumented die, and flat-faced punches with a 11.28 mm diameter. The sampling frequency was set to 5 kHz. Compression (loading) and decompression (unloading) were the same for all experiments, using a V-shaped double-ended compression (DEC) profile with punch velocities of 2 mm s^{-1}, giving a total compression speed of 4 mm s^{-1}. The compression force was adjusted such that the final height of all the tablets was 4.0 mm. Punch positions were corrected for punch deformation using the Analis software (Medelpharm, Beynost, France). During decompression, the top punch retracts to fully detach from the tablet. The lower punch does not necessarily fully detach from the tablet because there is some freedom of movement between the lower punch and the actuator moving this punch. However, decompression is symmetrical and the force on the lower punch always reaches 0 ± 5 N at the end of decompression. Punch positions were also adjusted such that the radial pressure sensor in the die wall was always positioned at the centre of the band of the tablet.

Ejection speeds were varied on a logarithmic scale between 0.3 and 280.0 mm s^{-1} to give 5 different speeds in total. At any given ejection speed, tablets were made at 6 different densities with 3 replicates each. MCC experiments had 5 replicates instead to allow for the extra crushing experiments needed for the FEM parametrisation. To minimise experimental variability, all experiments of a single material were conducted on the same day, and all experiments were performed on the same machine. At the start of every day, the flat-faced punches had their punch deformation calibrated, as well as every time the punches had been taken out of the compaction simulator for e.g. cleaning. The lab environment was controlled to be at a temperature of 20 to 25 °C and relative humidity of 40% or less, according to EU Pharmacopoeia standards.

For a more complete comparison, a number of additional experiments were performed. First, a repeat of the starch experiments at one ejection speed (43 mm s^{-1}) and all densities but with an added 125 ms dwell time, where the dwell time is defined as the duration for which the punches remain static at the point of maximum compression. Second, a repeat of all original starch experiments but with external instead of internal lubrication. The die was cleaned (without solvent) after each compaction cycle to avoid build-up of leftover lubricant when using external lubrication. Third, externally lubricated MCC at a compaction pressure of 96 MPa and an ejection speed of 43 mm s^{-1} at six different sampling frequencies with six replicates for each frequency. Finally, the third was repeated, but with an added 125 ms dwell time.

The output data from all these experiments are the punch positions, the force on the upper punch F_T, the force on the lower punch F_B, and the radial stress σ_R. The axial pressure σ_z follows from the average of the forces on the upper and lower punches divided by their surface area.

2.3. Crushing

Diametrical crushing of the tablets produced in Section 2.2 was performed using a Texture Analyser TA.XT.plusC (Stable Micro Systems, Surrey, United Kingdom) equipped with a 50 kg load cell. All tablets, except for 3 of the 5 MCC replicates, were crushed diametrically. The diametrical or radial fracture stress is computed as

$$\sigma_d^f(\rho) = \frac{2F_{d,max}}{\pi D t} \quad (1)$$

where D is the tablet diameter, t is the tablet thickness, and $F_{d,max}$ is the maximum diametrical compression force.

The compaction simulator was also employed to crush the remaining MCC tablets, one replicate diametrically, and two replicates axially. Using the compaction simulator was necessary because the Texture Analyser was only able to crush the lowest density tablets for MCC. The axial fracture stress is computed as

$$\sigma_z^f(\rho) = \frac{4F_{z,max}}{\pi D^2} \quad (2)$$

where $F_{z,max}$ is the maximum axial compression force. Comparing the diametrical crushing forces of the compaction simulator with those of the Texture Analyser shows that the compaction simulator tends to overestimate the crushing forces. The difference between the two machines was quantified and turned out to be significantly smaller than the difference in fracture stress between the different materials and will therefore have no bearing on the results and conclusions reported in this work (supplementary material S1 & S7).

3. Computing the friction coefficient

This section provides an overview of the definitions used in this study and proposes a new method to simultaneously determine the static and kinetic friction coefficients during routine compaction simulator experiments.

3.1. Definitions

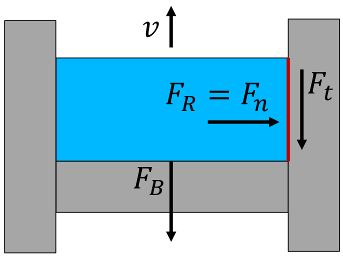


Figure 1: A schematic of the tablet within the die during ejection. The forces F and tablet velocity v are indicated. The tablet exerts a force F_B on the bottom punch and a force F_R on the die wall. The main frictional forces, F_n in the perpendicular direction and F_t in the parallel direction, are acting on the surface indicated in dark bold red.

The friction coefficient between two surfaces is defined as

$$\mu = \frac{F_t}{F_n} = \frac{F_B}{F_R}, \tag{3}$$

where F_t is the magnitude of the tangential force resisting movement lying in the plane in which the surfaces touch, and F_n is the magnitude of the normal force that is perpendicular to that plane (see Fig. 1). Strictly speaking, $F_t = F_B$ is only true at constant velocity. However, because the net force on the tablet due to acceleration is at most $\mathcal{O}(1)$ N, where $\mathcal{O}(x)$ indicates an order of magnitude similar to number x, this approximation is valid in general (see supplementary material S11.3). In a compaction simulator with an axisymmetrical cylindrical die of diameter D, the tangential force is given by

$$F_t = F_B = \sigma_B \pi \left(\frac{D}{2}\right)^2, \tag{4}$$

where F_B and σ_B are the force and pressure on the bottom punch, respectively. The normal force is given by

$$F_n = F_R = \sigma_R H \pi D \tag{5}$$

where F_R and σ_R are respectively the force and pressure on the die wall and H is the height of the tablet, assumed to be equal to the minimum distance between the punches when the punches are in contact with the tablet. When the punches are not in contact with the tablet, F_R is computed using the method described in Section 3.2 instead.

The maximum ejection force is

$$F_{ej}^{max} = \max\left(F_B\right), \tag{6}$$

being the maximum value of F_B during the entire ejection phase.

Ejection force is simultaneously the easiest and least informative quantity to measure. The punches in compaction machines are most often equipped with force sensors, directly providing the maximum force during ejection. However, the total maximum ejection force F_{ej}^{max} depends strongly on the contact area between the tablet and the tooling, i.e. F_{ej}^{max} is an extensive quantity. Formulating an ejection stress by dividing F_{ej}^{max} by the face area of the punch does not resolve the issue, as the thickness and geometry of the tablet also plays a significant role. Results are therefore not generalisable even if the powder formulation is exactly the same.

Friction coefficients are a better quantity of choice because of their theoretical independence of the tablet thickness and geometry, i.e. they are intensive quantities. However, a clear distinction has to be made between static and kinetic friction. The kinetic friction coefficient μ_k is related to the frictional forces when the tablet is sliding. μ_k is thus the relevant quantity at the moment the tablet leaves the die, a moment that is often associated with defect formation [1, 7]. The kinetic friction coefficient μ_k is defined as

$$\mu_k = \langle \mu_{v \neq 0} \rangle, \tag{7}$$

being the average of μ over a set of values for which the tablet is in motion ($v \neq 0$).

Conversely, the static friction coefficient μ_s is related to the frictional forces that arise when, just after decompression, the bottom punch starts to push on the tablet again to eject it. The static friction coefficient μ_s is defined as

$$\mu_s = \max\left(\mu_{v\approx 0}\right), \tag{8}$$

being the maximum μ of all the values for which the tablet has not moved yet ($v \approx 0$). In practice, it is difficult to accurately detect when the tablet starts to slide, and a small time window is used instead. Since μ_s is usually higher than μ_k, and the maximum ejection force typically occurs at this moment, μ_s and F_{ej}^{max} are closely related.

It should be noted that F_{ej}^{max} and μ_s are potentially sensitive to the sampling frequency, particularly at higher ejection speeds. Reducing the sampling frequency can cause a regression to the mean, resulting in a progressively lower F_{ej}^{max} and a smaller difference between the measured μ_s and μ_k. Reporting values of F_{ej}^{max} or μ_s without a sampling frequency can therefore strongly compromise the quantitative information provided, especially for comparison with other studies. The current study uses a sampling frequency of 5 kHz, meaning these quantities are averages over a 0.2 ms window. A brief test on the effect of the sampling frequency is presented in the supplementary material (S4).

3.2. Resolving the radial force ambiguity

The tangential force F_t directly follows from the force sensor in the bottom punch. However, obtaining the normal force F_n is non-trivial, because the radial force F_R is rarely measured directly. This has led to the use of a number of approximations as reported in the literature. For example, F_R can be approximated from the radial pressure at the end of decompression [8] or through a theoretical model [9]. These approximations compromise the accuracy of friction coefficients for a number of reasons.

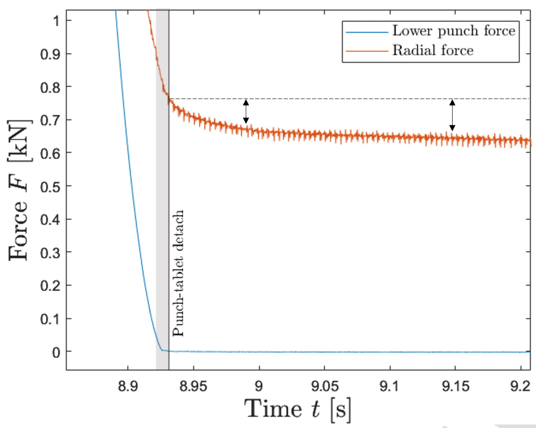


Figure 2: Lower-punch and radial forces at the end of decompression for an MCC tablet, demonstrating significant relaxation even after the punch has lost contact with the tablet. The moment of detachment occurs somewhere in the grey-shaded area. The residual radial force can differ more than 10% depending on the exact moment chosen. Radial forces were computed as described in the Section 3.2.

First, the viscoelastic behaviour of the tablet causes relaxation even after the end of decompression (Fig. 2). This affects both the height of the tablet and the radial force. Even without significant relaxation, the choice of a point at which to consider the punch attached or detached from the tablet is somewhat subjective, and this can lead to large differences in the radial force (see the steep slope in the grey area in Fig. 2). Second, upon impact with the lower punch, the tablet is recompressed, and the radial force changes. Third, both normal and tangential forces are often assumed to have their maximum value at the same time, which is not necessarily true. Finally, theoretical models such as Janssen-Walker theory are oversimplifications that were not developed to deal with inhomogeneous densities nor with dynamic situations. The radial force can thus only assumed to be correct if it is measured directly. Desbois et al. were able to do this, but only for kinetic friction coefficients, and required a specialised experimental protocol [15].

Most often, the radial pressure is measured using a strain gauge since the deformation field within the die wall is mostly independent of the tablet density or friction coefficient (supplementary material S6). This gauge is calibrated by the manufacturer, taking into account the distance between the punches and assuming that the punches are in contact with the powder compact (such as in Eq. 5). In this case, if punch deformation is accounted for, the distance between the punches can safely be assumed to be equal to the tablet height. The radial die-wall sensor thus gives a radial stress that can be converted into a force if the distance between the punches is known. When the punches are no longer in contact with the powder compact, the calibration is no longer valid and the sensor gives the incorrect radial stress values. However, due to clearance and tolerances, the punches do not touch the die wall and should not affect the measurements of the die-wall sensor. The punches can be assumed only to affect the radial stress or force by pressurising the tablet and not in and of themselves. Knowing the distance between the punches and the machine calibration method, the reported stress can thus always be converted into a force, regardless of the actual tablet height. This allows us to measure the radial force at any point during ejection, and thereby also allows us to compute the friction coefficient without having to know the height of the tablet.

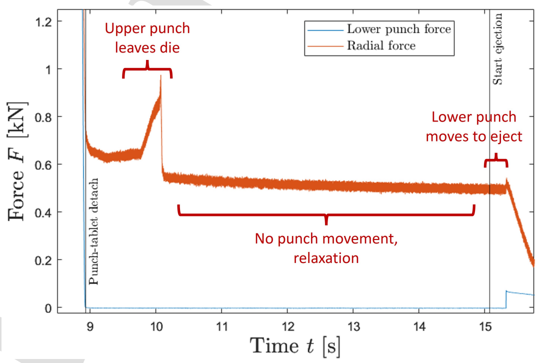


Figure 3: Lower-punch and radial forces at the end of decompression and during ejection, demonstrating that the radial force can be measured during ejection. Radial forces were computed as described in the Section 3.2.

After reverse engineering the calibration procedure of the STYL'One press, the radial force can readily be computed (Fig. 3). For reference, a figure of the uncorrected forces, also showing the effect of each step of the reverse-engineering process, can be found in the supplementary material (S2). (The machine scales the radial pressure by the distance between the punches but stops updating the position of a punch if the punch leaves the die or the ejection phase starts [22].) Closely inspecting Fig. 3, we see that there is relaxation, even when there is no punch movement. Moreover, when the lower punch starts moving to eject the tablet, the force on the lower punch remains negligible and the radial force is unperturbed. These observations confirm that the reverse-engineered radial force is consistent and that there is indeed clearance between the punch and the die wall.

3.3. Detection of impact and sliding

To reliably compute the friction coefficients and other ejection parameters, several critical events, such as the moment of punch-tablet impact during ejection, must be detected. In brief, the force on the lower punch after unloading is used to define a baseline for detecting punch-tablet detachment. The moment of punch-table retachment (or impact) upon ejection is determined using the (filtered) maximum ejection forces as a reference together with several heuristics. For example, the detection method is adjusted if the retachment would suggest the tablet has shrunk more than 4%. Full details on the detection method can be found in the supplementary material (S3).

A notable observation in Fig. 3 is that the radial force starts to trail off at longer times, even though the tablet is still well within the die. This is caused by the tablet moving away from the radial pressure sensor, whose calibration is only valid if the tablet is aligned with the sensor. For this reason, all data past a certain point are ignored when computing the friction coefficients. The maximum is set by the lower punch position at maximum compression plus 7.5% (for μ_s) or 15% (for μ_k) of the minimum punch separation (or tablet height) during compression. The static friction coefficient μ_s is therefore determined using the data within the first ∼0.3 mm after impact and the kinetic friction coefficient μ_k the first ∼0.6 mm. If the data are deemed to be extremely noisy (see supplementary material S3), which applies to 9.5% of the data, μ_s is determined using the data up until the lower punch passes the radial sensor position, giving a window of 2.0 mm at most. Since the total displacement within the selected data is minimal, we assume that our readings remain sufficiently accurate to determine friction coefficients reliably. Computing the maximum drift in radial force due to tablet sliding provides an overestimate of the maximum error, showing that it is 15.0% on average (see supplementary material S4).

3.4. Example friction profiles

Using the methods in Sections 3.2 and 3.3, the instantaneous friction coefficient μ can be determined throughout the entire ejection stage. Fig. 4 shows six examples. As the tablet density decreases and the ejection speed increases, the values of μ become more noisy. However, applying the definitions in Section 3.1 to a limited range of data (the shaded area) yields consistent results throughout with limited drift. The results are also consistent across different sampling frequencies, showing variations that are insignificant compared to the variations between e.g. different ejection speeds (supplementary material S5).

Another concern might be the influence of tablet flashing, where compacted powder is extruded into the tolerance gap between the tablet and the die, causing a premature force build-up before the lower punch fully comes into contact with the face of the tablet [23]. However, the maximum ejection force and static friction are only affected by the maximum force on the lower punch. Moreover, it can be seen in Fig. 4 that the maximum friction coefficient is reached very quickly, causing the potential influence of flashing to be confined to such a small region that its contribution to the kinetic friction coefficient would be negligible. Note that, as mentioned earlier, results for maximum force and static friction will always change as a function of the sampling frequency at very high ejection speeds.

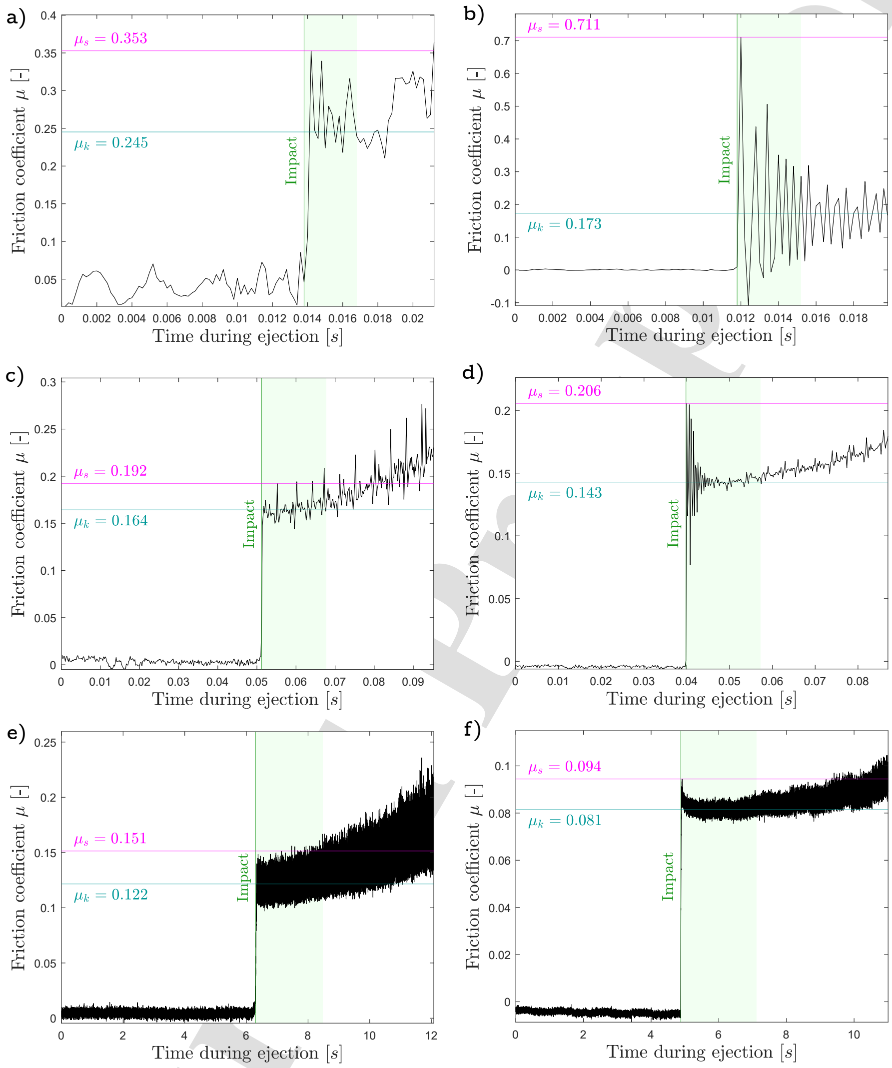


Figure 4: The instantaneous friction coefficients $\mu = F_B/F_R$ for six different ejection experiments with MCC, showing that consistent results can be obtained regardless of the ejection speed and tablet density. The maximum compaction pressures are 20 MPa (left column) and 368 MPa (right column). The ejection speeds are (a,b) 250.3 mm s^{-1}, (c,d) 43.2 mm s^{-1}, and (e,f) 0.3 mm s^{-1}. Green shaded areas indicate the data used to compute the friction coefficients μ_s and μ_k.

3.5. Janssen-Walker theory

Friction coefficients were also computed during the compression stage by using Janssen-Walker theory [24, 25]. Given a double-ended compaction profile, a friction coefficient can be computed as [7, 17]

$$\mu = \frac{D}{4zK} \ln\left(\frac{\sigma_T K_p}{\sigma_R}\right) \tag{9}$$

where z is the distance between the punch and the radial pressure sensor and K_p is Janssen's constant,

$$K_p = \frac{1+\sin(\beta)}{1-\sin(\beta)}, \tag{10}$$

with β being the internal friction angle, which is determined from crushing experiments in the same way as for the dDPC model [7, 17]. **Strictly speaking, Eq. 10 is only valid if $\sigma_T < \sigma_R$, but in practice violating this condition gives at most a 30% difference. For a more detailed discussion on the validity of Janssen-Walker theory as well as the calculation of the β values, the reader is referred to the supplementary material (S7).**

4. Numerical methods

The commercial software Abaqus 2019 by Simulia was used, using an implicit integration technique, to perform finite element method (FEM) simulations of the MCC compaction and ejection experiments [26]. Using the data from the compaction simulator and tablet crushing, the density-dependent Drucker-Prager Cap (dDPC) model was parametrised for MCC. The specifics of the parametrisation and model geometry are exactly as described in van der Haven et al. [7, 17]. For the purpose of this study, we used 5 replicates at 6 different final densities of MCC to parametrise the dDPC model. This amount of data is more than sufficient for an accurate parametrisation, because the parametrisation of the dDPC model is independent of the ejection speed, and the parametrisation was previously demonstrated to be stable and accurate even for a minimal data set with only one replicate per density [7].

The frictional behaviour between the tablet and the tooling was extended to include more accurate descriptions and allow for a comparative study. The following three friction laws were used: 1) a constant friction coefficient, 2) a density-dependent friction coefficient, and 3) a velocity-dependent friction coefficient. The constant friction coefficient is determined as the average Janssen-Walker friction coefficient (see Section 3.5) over all densities. The density-dependent friction law is given as a tabulation of the Janssen-Walker friction coefficient at each density, using linear interpolation for intermediate densities. The velocity-dependent friction law is given by

$$\mu(\gamma) = \mu_{k,\infty} + (\mu_s - \mu_{k,\infty}) \exp(-c\gamma), \tag{11}$$

where γ is the slip rate, μ_s is the static friction coefficient, $\mu_{k,\infty}$ is the kinetic friction coefficient at infinite slip rate, and c is the decay constant. In reality, these constants also depend on the final tablet density, so the constants in Eq. 11 were specified separately for each simulation. The value of μ_s was taken directly from experiment (as described in Section 3 and shown in Fig. 5) at ejection speed 8 mm s^{-1}. Similarly, $\mu(\gamma)$ was also taken from experiment with γ

equal to the ejection speed of 8 mm s^{-1}. The value of $\mu_{k,\infty}$ was then determined from c, μ_s, and $\mu(\gamma)$ by fitting Eq. 11. The constant c was set to 1, because it cannot be determined using the current data. This value of c gives a relatively rapid decay to $\mu_{k,\infty}$ such that at $\gamma = 8$ the value of $\mu(\gamma) \approx \mu_{k,\infty}$. The purpose of Eq. 11 is not to fully capture the true velocity dependence of the frictional behaviour, which is far more complex than the current expression suggests, but to create a continuous transition between static and kinetic friction regimes.

5. Results and discussion

5.1. Comparing friction metrics

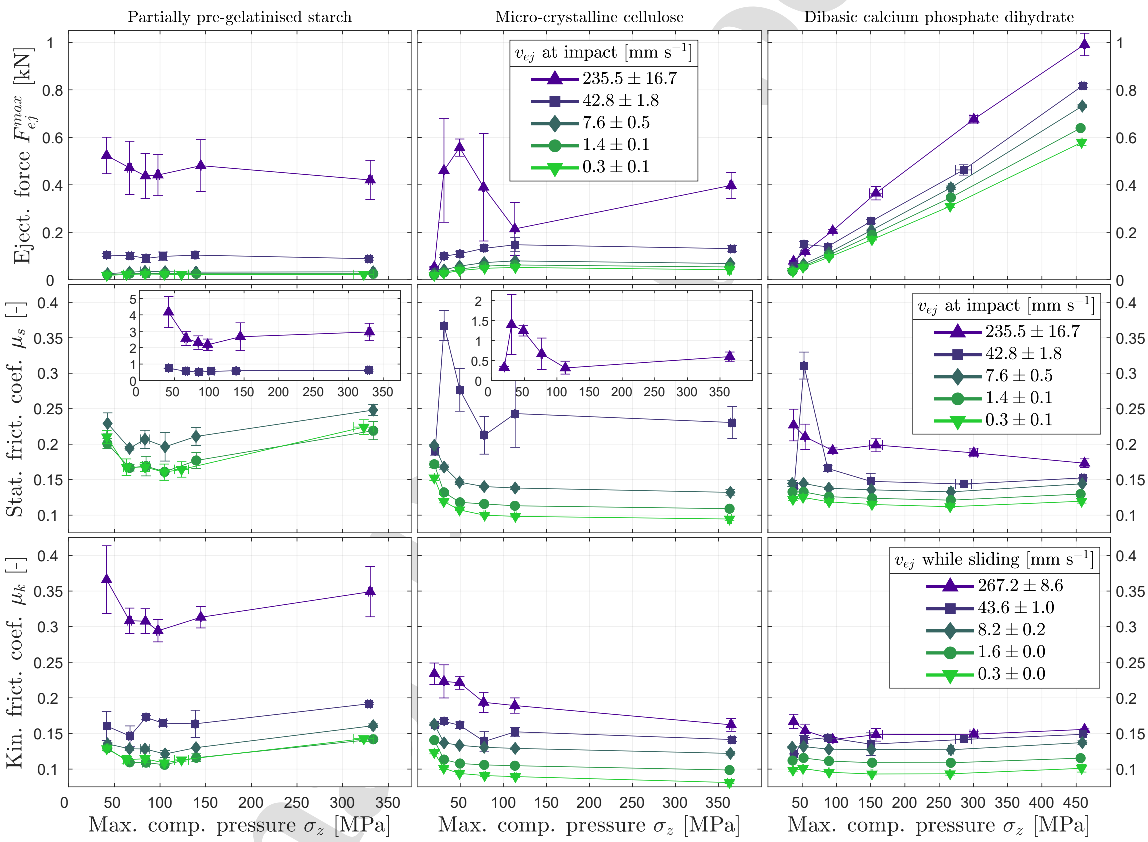


Figure 5: Experimentally determined friction metrics. The top row indicates the maximum ejection force, the middle row the static friction coefficient, and the bottom row the kinetic friction coefficients. Columns show the starch, MCC, and DCPD, respectively. Insets show the data of the same figure that fall outside the range of the encompassing figure. Legends indicate the lower punch velocity for the entire row. Reported velocities are based on the measured punch displacement.

The results of the series of compaction experiments varying the maximum compaction pressure, ejection speed, and material are shown in Fig. 5. All values were computed using the newly developed detection and analysis method described in Section 3. The fact that the error bars are small, despite using only 3 to 5 replicates per data point, shows that the developed method has a consistent performance and can reliably be used to obtain qualitative trends for the maximum ejection force, static friction coefficient, and kinetic friction coefficient all at once.

The first and most general observation is that increasing the ejection speed v_{ej} always produces increasing forces and friction coefficients. Another remarkable observation is that the static friction coefficients sometimes reach values much higher than unity, which will be discussed in detail in Section 5.6. However, regarding the dependence on ejection speed, there are strong qualitative differences depending on the material. Note that the ejection speeds were chosen on a logarithmic scale and that equidistant lines therefore imply logarithmic scaling. For the visco-elastic starch, the most striking feature is that all metrics seem to increase linearly with the ejection speed. On the other hand, for the plastic MCC and brittle DCPD, the maximum ejection force F_{ej}^{max} and static friction coefficient μ_s display a sub-linear (at lower pressures) to linear (at higher pressures) dependence on the ejection speed, but the kinetic friction coefficient μ_k consistently follows a logarithmic scaling law. This shows that the type of material can not only lead to different values but also to different scaling behaviours. Such information can be used to minimise risks when up-scaling to high-speed large-scale production settings. For example, keeping in mind that even at low densities the frictional forces in starch increase rapidly with ejection speed, DCPD may be favoured in a new low-density formulation to reduce frictional forces and reduce the probability of tablet failure when production speed is increased.

Aside from the ejection speed, the friction metrics are affected by the maximum compaction pressure or density of the tablet. Compaction pressure appears to have a much weaker effect on the friction coefficients; starch shows a shallow minimum at intermediate densities, MCC quickly levels off to a steady value, and DCPD shows near-constant values. Plotting Fig. 5 as a function of the final tablet density instead of maximum pressure reveals a linear dependency on the density for MCC (supplementary S8). Either way, Fig. 5 shows that the trend in F_{ej}^{max} does not necessarily reflect the trend in μ_s. The value of F_{ej}^{max} depends not only on μ_s but also on the radial force F_R. DCPD provides an excellent example, having a nearly constant μ_s at a given ejection speed and a density-independent Poisson ratio [7], F_{ej}^{max} increases linearly with respect to the compaction pressure. The final frictional forces depend strongly on the eventual radial force, meaning that the Young's modulus and Poisson ratio of the material being compressed are as important as the friction coefficients. In fact, having a lower friction coefficient may be of little use if the material properties lead to a much higher radial force. An accurate prediction of what tablet formulation leads to minimal friction requires a consideration of all of these factors as well as plastic deformation and falls outside the scope of this work. Although precise predictions of frictional forces remain difficult, taking the ejection forces normalised by the tablet-die contact area may provide a good overall metric of the resistance to ejection. This holistic metric, defined as $\tau_{ej} = F_{ej}/(\pi Dt)$, can be interpreted as the shear stress of ejection, which has already been investigated and validated by Pitt et al. [27]. This metric includes contributions both from the friction coefficient(s) and the elastic properties whilst supposedly remaining independent of the size of the tablet. Using τ_{ej} instead of F_{ej} would not change the conclusions drawn from Fig. 5 because the tablet thickness and diameter were chosen to be constant for this study, but it does provide a sensible method for comparing between studies. The newly proposed method nevertheless provides a useful tool for the assessment of tablet-die friction.

It is clear from the preceding discussion that the chosen material has a major influence on friction. However, the kinetic friction coefficient seem to depend only weakly on both the material and the compaction pressure (or density). Only starch deviates from this trend, which may be because the degree of lubrication is below a critical threshold. A possible cause is that starch has a fraction of extremely small particles (∼10 µm) that strongly increase the total surface area and may agglomerate around the bigger particles [28]. Desbois et al. similarly reported kinetic friction to be largely independent of the material

[15]. Their study made use of external lubrication whereas the current study uses internal lubrication. It therefore appears that both lubrication methods lead to similar frictional behaviour. This suggest that also for internal lubrication methods, the lubricant itself is the dominant factor determining the kinetic friction coefficient.

Overall, friction coefficients are less sensitive to density changes; the material and ejection speed are much more important. Caution should be taken in generalising these results as the currently study only used MgSt as lubricant, and even different types of MgSt have been shown to have different lubrication efficiencies [29, 30]. Uzondu et al. demonstrated that, for 1 wt% MgSt, blending past 5 minutes has a minimal effect on the static friction coefficient [9]. The concentration of the lubricant can be still increased, but only weakens the tensile strength further [9, 31]. Using excipients with inherently more favourable consolidation behaviour and friction coefficients may thus be a good solution to ejection force problems, especially if other options have already been exhausted.

5.2. The effect of lubrication method

The ejection experiments were repeated for starch but with external instead of internal lubrication. External lubrication is generally carried out by spraying the lubricant for a certain amount of time into the die. The exact amount of lubricant is therefore hard to determine, and comparing different lubrication methods becomes difficult due to varying lubrication levels. For example, external lubrication (Fig. 6) appears to result in generally higher ejection forces and friction coefficients, but this may be entirely due to external lubrication depositing a lower amount of lubricant in the die compared to internal lubrication. However, being able to measure both the static and kinetic friction coefficients at the same time enables us to make relative comparisons, focusing not on the absolute values obtained but on the ratios between the friction forces and coefficients.

If both lubrication methods are at similar values of μ_k, the values of μ_s and F_{ej}^{max} are lower for external lubrication (compare e.g. the curves for the

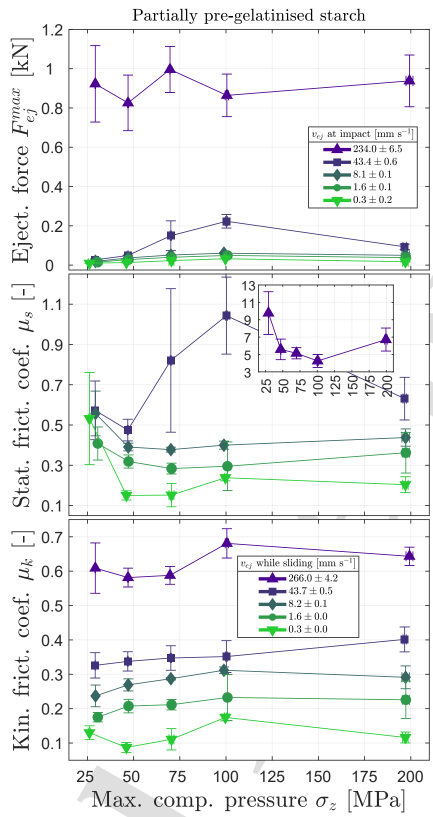


Figure 6: Experimentally determined friction metrics for starch, similar to Fig. 5, but here with external instead of internal lubrication. Values of v_{ej} at impact are the same for the top two figures.

second highest speed in Fig. 6 to those of the highest speed in Fig. 5). This suggest that external lubrication is relatively more effective at reducing the static friction and maximum ejection force than internal lubrication due to a lower μ_s/μ_k ratio. From a microscopic perspective, one might expect that external lubrication would lead to all die-tablet contact points being interfaced by lubricant. Conversely, internal lubrication would only lead to a fraction of the contact points being interfaced with lubricant. As a consequence, μ_s and F_{ej}^{max} can be expected to be higher when using internal lubrication if the same absolute amount of lubricant is used. Once the tablet starts to slide, the low-yield-strength MgSt starts to delaminate, coating most of the surface and dominating the die-tablet interaction, resulting in a consistent and material-independent friction coefficient [9, 15]. However, external lubrication may still lead to a significant number of clean die-tablet contacts as μ_s still shows a dependence on the material [14]. Such a simplistic microscopic view is thus unlikely to be completely accurate, especially since surface coverage is rarely total, but may nonetheless provide a reasonable explanation for the observed qualitative differences and aligns with the idea of different lubrication regimes [32, 33]. This again emphasizes that not only the lubricant but also excipient behaviour needs to be assessed prior to making formulation decisions if ejection forces are to be minimised.

Previously, it has been hypothesized that lubricant may migrate and be squeezed out of internally lubricated tablets due to the compaction pressure or dwell time [8, 15, 32]. Such an effect would likely improve the effective lubrication between the tablet and the die. However, trends with respect to the compaction pressure can be weak or even change direction depending on the materials (see starch and MCC in Fig. 5). Repeated compaction experiments of starch with an additional 125 ms dwell time also show no significant difference in friction metrics when compared to the compactions without dwell time (supplementary S5 & S9). These observations suggest that squeezing out of the lubricant is not significantly affecting the die-wall friction. However, it is possible that there is a critical migration time beyond which additional pressure or dwell time does not contribute to any further redistribution of the lubricant. Given that the compression speed in this study is low, the critical migration time might already have been surpassed. Sun does suggest there is a strong difference depending on the compression speed but did not explicitly state the ejection speed [8]. Compaction simulators often link the compression and ejection speed, therefore making it unclear whether the results were confounded by a change in the ejection speed. To conclusively deny or confirm the migration hypothesis, an extra set of experiments at constant ejection speed would be needed where only compaction pressure and compression speed are varied.

Overall, internal and external lubrication seem to give the same qualitative trends, only differing in the relative efficiency at which they provide a reduction in either the static or kinetic friction metrics. In practice, ejection forces can be brought to similar levels using either lubrication method [13]. However, internal lubrication can come with a significant penalty in the tensile strength or fracture stress and dissolution time of the tablet [13, 14, 31]. Up-scaled external lubrication may therefore be the most favourable method in general [34]. However, some excipients actually show longer disintegration times with external lubrication [14]. Quality control may also be more difficult for external lubrication due to the sensitivity on the spraying duration. It therefore nonetheless remains imperative to assess various lubrication methods.

5.3. Defect occurrence

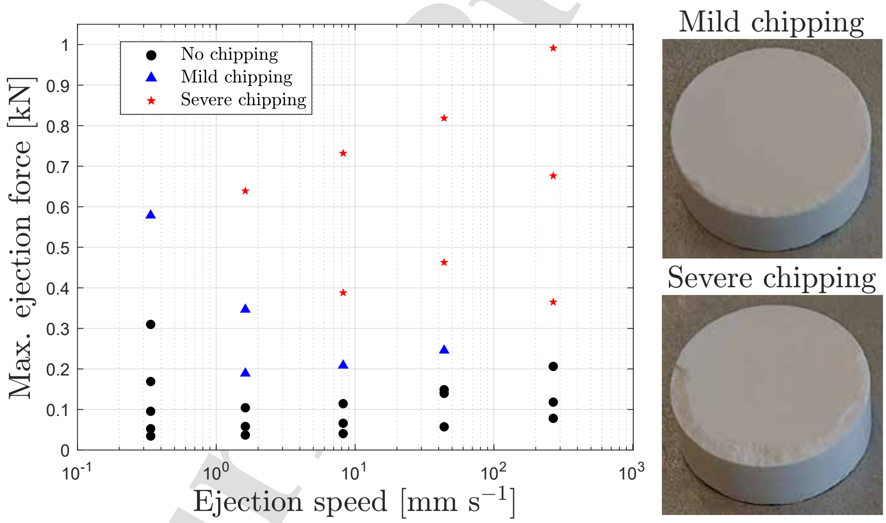


Figure 7: Ejection speed and force as decisive factors for the chipping of DCPD tablets. The ejection speed and maximum ejection force together determine the occurrence and severity of chipping defects. The indicated chipping severity applies to all replicate tablets.

The compaction experiments led to chipping defects in one of the three materials; DCPD. The occurrence and severity of the defect depends mainly on the maximum ejection force (Fig. 7). The tensile strength or fracture stress, a commonly used property to assess the resistance of a tablet to fracture, showed negligible changes depending on the ejection speed and is therefore not a contributing factor (supplementary S10). However, the ejection speed, with all other factors being equal, also appears to contribute to the defect occurrence and severity. For example, around 0.3 kN, ejection speed alone can cause a shift from no chipping to severe chipping. This might seem unexpected due to DCPD not showing rate-dependent behaviour, at least for compaction [35, 36, 37], but the lubricant MgSt can dominate the tablet-die interaction by forming a thin film and is known to show rate-dependent behaviour [15]. It is therefore possible that the ejection speed affects the shear forces near the edge of the tablet as the tablet leaves the die. Such behaviour again underlines that the behaviour of porous pharmaceutical compacts cannot be accurately understood without consideration of viscous behaviour. Although time-dependent stress or strain relaxation of the tablet itself (e.g. due to viscoelastic or viscoplastic properties) is unlikely in the case of DCPD, rate-dependent effects may still be induced by the lubricant. Combined with the lack of a significant change in the fracture stress, this not only conclusively demonstrates that ejection speed can be a decisive factor in tabletting defects but also that the chipping defect is dominated by local properties.

5.4. Testing Janssen-Walker theory

A common alternative to determine friction coefficients is to use Janssen-Walker theory, also known as the differential slice method [24]. It is straightforward and requires no additional experiments to those already required to parameterise the dDPC model and is therefore a convenient choice when only a basic description of friction is needed, despite not necessarily being valid for consolidated solids. Another advantage is that, in the case of a piezoelectric radial-pressure sensor, a friction coefficient can be estimated even if the tablet is not perfectly centred on the sensor. This method is used particularly often to determine the friction coefficient for FEM simulations [19].

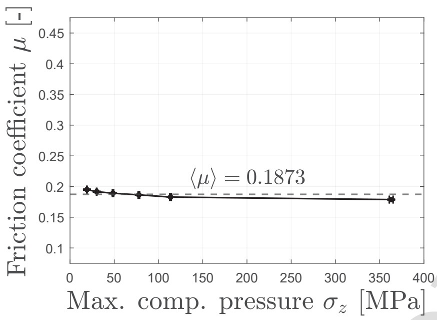


Figure 8: Friction coefficients for internally lubricated MCC at the end of compression as derived from Janssen-Walker theory. Since Janssen-Walker theory only uses data from the compression stage to determine friction coefficients, there is no dependence on the ejection speed.

Janssen-Walker theory is unique in the sense that it computes the friction coefficient only from data acquired during the compression stage. As such, the resulting friction coefficients depend on the compression speed instead of the ejection speed. Either way, it is not clear whether the resulting friction coefficients are static or kinetic. The theory was originally developed for the analysis of static silos [24]. However, during compression, depending on the chosen horizontal slice of powder, the powder is either moving at the speed of the punch or not at all. To avoid ambiguity and remain as close to the original assumptions as possible, the friction coefficient can be computed at the end of the compression stage, when the punches have stopped (or are just about to stop) moving. The friction coefficient computed by Janssen-Walker theory can then assumed to be a static friction coefficient. Similarly, this minimises any density discrepancies, which may also affect the friction coefficient, between the compression and ejection stage. This choice therefore allows for a valid comparison of Janssen-Walker theory with the static friction coefficients measured during ejection.

To test the validity of Janssen-Walker theory, the friction coefficients at the end of compression of internally lubricated MCC were computed (Fig. 8), giving an average of $\langle\mu\rangle = 0.187$. This value, at a compression speed of 4 mm s^{-1}, is generally higher than μ_s at an ejection speed of 8 mm s^{-1} (Fig. 5).

Janssen-Walker theory thus systematically overestimates μ_s even if the speeds are matched. An important difference is that the Janssen-Walker coefficient was computed under a higher pressure as the tablet still had to undergo unloading. Based on the trends in Fig. 5, the friction coefficients would therefore have been expected to be lower instead of higher than the measured μ_s, but this cannot be concluded because the effect of tablet density and pressure are overlapping here. Either way, differences between the Janssen-Walker and measured coefficients are not more than 0.05. Using the same material and model but with external lubrication, van der Haven et al. observed $\langle \mu \rangle = 0.180$, further demonstrating only minor differences depending on the lubrication method [7]. In sum, this suggests that Janssen-Walker theory systematically overestimates the friction coefficient when compared with direct measurement but only does so to a minor degree. Janssen-Walker theory therefore still provides a valid alternative, although there is little reason not to use directly measured friction coefficient, because coefficients can now be measured directly in exactly the same experiments. More conclusive statements would require a series of experiments varying the compression speed. It is not unlikely that Janssen-Walker theory may break down at high compression speeds, because direct measurements show that μ_s sometimes has values above unity that are the result of more complex physics than considered in Janssen-Walker theory.

5.5. Ejection simulations with FEM

Simulations using the finite element method (FEM) have become an important tool for understanding the complexities of pharmaceutical powder compaction, including the role of friction [19]. However, studies so far have only used a single constant friction coefficient in their simulations despite studies, including the current, showing that the friction coefficient is highly variable. This can explain, for example, the qualitative as well as quantitative differences observed between simulation and experiment reported by Mazel et al. [38]. Despite limitations, FEM simulations can still provide valuable insights into tablet ejection.

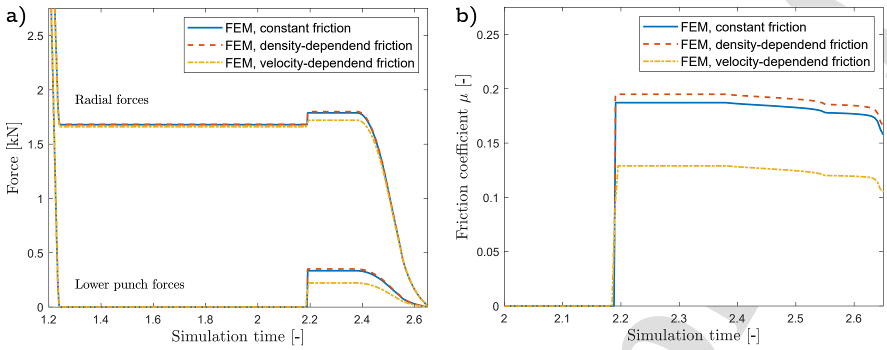


Figure 9: FEM simulation results with different friction laws for MCC with an ejection speed of 8 mm s^{-1}. The figures show a) the radial and lower punch forces at end of decompression and throughout ejection and b) the measured friction coefficient. The x axis shows the normalised simulation time, with $t = 2$ indicating the start of the ejection phase.

Simulating the tablet compaction MCC reproduces several characteristic features of tablet ejection. Fig. 9 shows that simulations capture the recompression effect upon punch-tablet impact during ejection, which is also seen in experiment (Fig. 3). Both the radial and bottom punch forces show a proportional increase. Taking a look at the radial force increase on impact, also called the recompression force, reveals a linear trend in FEM versus a sub-linear trend in experiment (Fig. 10). This difference is likely to be a consequence of the tablet being simulated as elastic instead of viscoelastic or hyperelastic, similarly leading to the absence of reasonable radial force relaxation in Fig. 9. Comparing the profiles demonstrates that, at least for ejection, the average friction coefficient dominates and the actual friction law itself is only of minor importance.

Conversely, the magnitudes in Fig. 10 show that the recompression force is very sensitive to the friction coefficient. The average coefficient of the velocity-dependent friction law is at most 37% lower than that of the constant and density-dependent law but already halves the recompression force. This sensitivity emphasizes the importance of an accurate parametrisation of the friction coefficients. Although Janssen-Walker theory leads to a reasonable estimate (constant and density-dependent law), the parametrisation from direct mea-

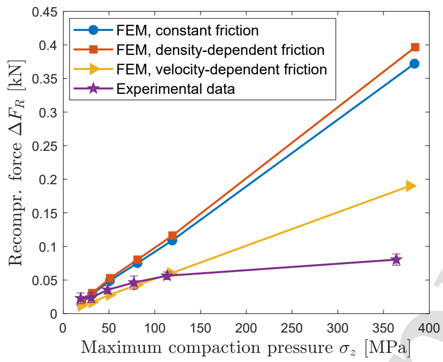


Figure 10: The radial force increase or recompression force upon punch-tablet impact during ejection for MCC at a maximum compaction pressure of 113 MPa with an ejection speed of 8 mm s^{-1}. The figure shows both FEM results for different friction laws and experimental results.

surements (velocity-dependent law) results in more accurate simulations, where the accuracy improvement is greater than would be expected based on a 37% difference. The magnitudes of the simulated and experimental recompression forces agree well when using direct measurements for the parametrisation of friction, only failing at high densities. This agreement between simulation and experiment further supports that the reverse-engineering method for measuring radial forces during ejection is valid and gives accurate friction coefficients.

The sensitivity of FEM simulations on the friction coefficient can raise some concerns regarding their validity, perhaps more so because of compression than ejection. For example, the level of friction between the powder and the die wall during compression has unambiguously been shown to strongly affect the resulting stress and density distributions [38, 39, 40]. Overall, increased friction seems to have a de-homogenising effect on the densities near the edge of the tablet, except for concave tablet that show a more complex dependency [40] However, qualitative stress and density profiles do not appear to change much for flat-faced tablets [38, 40]. In this study, different friction laws only led to small differences in the maximum compaction pressure and the relative density, the latter being no more than 0.03. Nonetheless, it is essential to properly parametrise the friction during compression, especially for tablets that are not flat-faced.

The friction coefficient during compression can indeed be measured experimentally, but only with a single-ended compaction (SEC) profile [16, 38]. This is a limitation because double-ended compaction (DEC) profiles are the industry default. Using any DEC profile necessarily requires extra experiments or using an approximation through a modified Janssen-Walker theory, which was shown in Section 5.4 to overestimate friction. However, even directly measured friction coefficients during compression suffer from the same deficiency as Janssen-Walker theory, i.e. that the resulting values are averages of the friction coefficients at different speeds. Proper parametrisation of friction during compression therefore remains an open problem within pharmaceutical powder compaction. The safest option would be to experimentally validate the density profile of the tablet with e.g. X-ray microCT [41]. The friction coefficient could then be adjusted until the density distributions match, at least providing correct results for similar tablet geometries. In the meantime, the most efficient option for simulating compression is probably to take the kinetic friction coefficient measured directly during ejection, measured at the same speed as the punch velocity during compression. This applies especially to concave punches, because powder movement near the punches will be important, which will approximately move at punch speed.

Further improvements in the representation of friction in FEM would likely require more advanced dynamic integration schemes. Current FEM simulations often apply the quasi-static assumption, which may also have been responsible for the lack of a clear static friction peak for the velocity-dependent case in Fig. 9. This need is also underlined by simulations being less stable when using the velocity-dependent friction law. Furthermore, including both the density and velocity dependence of the friction coefficient will require using a FRIC subroutine in Abaqus. Despite many opportunities for improvement of the numerical model, an accurate parametrisation of the average friction coefficient remains the most important.

5.6. Causes of extremely high friction

One of the more curious observations from Fig. 5 and 6 is that μ_s sometimes has values far above unity. Although there is no reason why this should not be possible, such high values require explanation, especially since even materials with very high friction coefficients rarely reach values above 1.5 [42, 43]. In the following discussion, we consider the potential causes that might lead to such high friction coefficients.

Separating the tablet from the die requires overcoming the cohesive energy between these two surfaces. Overcoming the cohesion requires a certain amount of work, and thus a faster ejection could lead to a higher ejection force. However, an estimate using the surface energy of MCC shows that such an increase in the force would be of $\mathcal{O}(10^{-4})$ N and therefore negligible (supplementary S11.1)[44].

If the punch would be in contact with the die, this could create additional friction that is not properly accounted for in the current calculations. However, earlier it was confirmed that there is punch-die clearance. This clearance is typically around 10 µm. Even at a compaction pressure of 500 MPa, the expected radial expansion of the punch would be 8 µm (supplementary S11.2). Any such effect would also be expected to occur in all materials but is completely absent in DCPD, which consistently shows $\mu_s < 0.4$ (Fig. 5). The interaction between the punch and the die to the friction coefficient is therefore unlikely to create a lot of additional friction.

Inertia may contribute to an increase in the ejection force. Although Sun applied a correction for the inertia of the punches, this should not be necessary [8]. Inertial forces only play a role upon acceleration or deceleration of the punches, but the punches do not slow down upon impact as would be indicative of a significant impact force or momentum transfer. In fact, the punch even accelerates slightly after impact (see the legends in Fig. 5). It is mainly the inertia of the tablets that could contribute to the ejection force. However, estimating the impact force shows that it is at most of $\mathcal{O}(1)$ N and therefore negligible (supplementary S11.3).

The strong oscillations in Fig. 4b show that there are mechanical waves upon punch-tablet impact. However, the frequency of the observed oscillations is at most of $\mathcal{O}(1)$ kHz. Given that the tablet thickness is only 4 mm, this excludes acoustic or phonon waves, which would be not be measurable at the current sampling frequency of 5 kHz as such waves would be orders of magnitude faster (supplementary S11.4).

Plastic deformation upon impact may dissipate energy, leading to a higher observed friction coefficient. This is possible at lower tablet densities and may explain why μ_s is generally higher at lower tablet densities. However, at high densities, the maximum ejection force does not reach the magnitude required (as estimated from the dDPC model) to cause significant plastic deformation. Energy dissipation due to plastic deformation at higher densities is therefore unlikely. Dissipation due to plasticity may thus explain the observed trend in μ_s but not the high values in general.

Elastic energy dissipation may provide a more feasible mechanism as the tablets contain a high amount of elastic energy. A rapid release of all elastic energy, potentially by relaxation just after recompression, could lead to forces of $\mathcal{O}(10^3)$ N (supplementary S11.5). However, the tablet remains constrained in the radial direction and still experiences friction, limiting the amount of elastic energy that can be released. This does not yet provide an explanation but does show that the tablet itself can have the energy or energy dissipation mechanisms needed to cause unexpectedly high resistance to ejection, which is also supported by the fact that only some materials show an unexpectedly high μ_s.

Looking for specific mechanisms causing oscillations and high friction coefficients, we finally identified stick-slip and oscillatory contact mechanics as candidates [43, 45, 46]. Stick-slip is a phenomenon in which a material sliding on a surface is elastically compressed, slips, and decompresses, only to recompress again shortly afterwards since the sliding velocity momentarily drops at the end of the decompression. This results in locally heterogeneous sliding velocities and thereby an oscillatory macroscopic friction coefficient. The entire phenomenon depends on the sliding velocity, further explaining why the strength of the oscillations (see Fig. 4 depends on the ejection speed [46]. Stick-slip provides a feasible explanation for the oscillations in μ, but would not yet explain very high values of μ_s.

A more complete view is given by the contact theory proposed by Persson, which is closely related to stick-slip [43]. Persson makes a strong argument that local oscillatory forces can lead to a highly dissipative mechanism, resulting in friction coefficients of $\mathcal{O}(10^1)$. However, despite the absence of a theoretical limit of the friction coefficient, reported values of $\mathcal{O}(10^2)$ or higher for tablet ejection should be met with scepticism, especially given the large length scale of the tablet-die interaction and the absence of strong attractive forces. Three factors are essential to this dissipative mechanism: 1) a stiffness mismatch between the sliding surfaces, 2) surface asperities, and 3) viscoelasticity in one material. There is a large mismatch between the stiffness of the tablet and the die wall, which can similarly aggravate stick-slip [46]. Asperities are naturally present in porous tablets or compacts. Viscoelasticity is present for starch with some $\mu_s > 3$, weakly present for MCC with some $\mu_s > 1$, and absent for DCPD with no $\mu_s > 0.5$. Interestingly, frictional heating may thus increase the friction coefficient as well by making powder particles at the surface more viscous through melting. Persson's theory thus not only provides an explanation for the high values of μ_s but also why μ_s is often higher at lower tablet densities, as the density is naturally related to the surface asperities and overall stiffness of the tablet. This leads to the counter-intuitive possibility that, depending on the case at hand, using a stiffer or less viscous excipient may actually lead to a reduction in ejection forces.

A problem with applying Persson's theory is that the original theory considers problems such as the friction between tires and roads, where small particles end up filling the larger cavities, causing smaller asperities to not contribute as much to the effective contact area and thereby energy dissipation, thus lowering the friction coefficient [43]. However, in tablet ejection, the surface area of the hard-material die is relatively smooth due to polishing. The asperities instead mainly come from the porous tablet, especially for starch, as it has a fraction of fine particles with a size of ∼10 µm that can coat the surface of larger particles

[28]. Nonetheless, a contribution by die asperities cannot be excluded, because hard materials such as DCPD may have worn down the die, creating surface asperities. Unfortunately, the current FEM simulations do not have the fidelity to provide any further insight into the matter. Discrete element method simulations may prove more insightful. In summary, Persson's theory aligns with all experimental observations but remains to be confirmed.

5.7. Operational limitations and recommendations

For static friction, the main source of error is a potential metal-metal impact between the lower punch and the actuator driving the lower punch influencing the measured ejection forces. Although a significant contribution of a actuator-punch impact is unlikely for the current study (see supplementary material S12), future studies may want to assure that this potential effect is excluded by retracting the lower punch extra far down (to assure the punch has detached from the tablet) and then moving it up a bit again (to assure the actuator and the punch are in contact again) before the start of ejection. This potential issue depends on the compaction simulator and ejection velocities used but is independent of how the static friction coefficient is computed. A potential actuator-punch impact may thus undoubtedly have occurred in other studies, which generally do not provide sufficient detail to exclude such an effect, but has been addressed in the present study. There may moreover not be any issues in practice, since the maximum ejection speed in this study exceed those commonly observed in production settings, and this artefact is predominantly limited to high-speed ejections.

For the kinetic friction, the main error comes from the drift or inaccuracy of the radial force due to the tablet moving away from the centre of the radial sensor. As stated previously, the average of the maximum radial force drift is 15.0% for the data presented in this study, with generally higher drifts at the highest ejection speed (see supplementary material S4). However, since the kinetic friction coefficient is computed as an average, and the reported drift is an overestimate of the maximum error, the actual error on the kinetic friction coefficients is highly likely to be smaller. Radial force drift may be avoided in future studies by using multiple piezoelectric sensors instead of a single strain gauge.

In both the static and kinetic cases, the aforementioned errors are largest at the highest ejection speed, where some of these systematic errors have been detected in a number of samples. This can partly be seen in the size of the error bars in Fig. 5. Friction coefficients at the very highest ejection speed thus need to be interpreted with a degree of caution until these errors can be excluded. However, their influence can also be relatively minor. For example, DCPD generally appears to show no metal-metal shock effect, since the actuator can be seen to make contact with the punch before punch-tablet impact, and has limited radial force drift. Friction coefficients at all other ejection speeds can be considered reliable as the errors had either been excluded or shown to be of a low magnitude.

Bearing in mind the aforementioned considerations, the newly proposed method for measuring the friction coefficients also overcomes several limitations, eliminating a number of errors. First, estimates of the tablet height **or tablet-die contact area** are not necessary. Second, force changes due to relaxation of the tablet between the end of unloading and the start of ejection are accounted for. Similarly, force changes due to recompression of the tablet upon impact are also included. Third and finally, friction coefficients can be measured in a regular compaction cycle, which may be important in and of itself, because friction can be path-dependent [47]. The overall accuracy of the proposed method is thus likely higher compared to other methods when measuring the static friction coefficient. When it comes to kinetic friction coefficient, there are equally valid arguments for the proposed method being either less or more accurate. Either way, the proposed method is more convenient by being usable in a regular compaction cycle.

6. Conclusions

We have presented the first method capable of directly measuring the ejection force, static friction coefficient, and kinetic friction coefficient in routine compaction simulator experiments. Finite element method simulations further demonstrated that directly measured friction coefficients using the method provided a significant improvement over those derived indirectly or approximated using e.g. Janssen-Walker theory. We suggest that this measurement of the static friction coefficient are more accurate with the new method. Whether measurements of the kinetic friction coefficient are more or less accurate than previously proposed methods is still unclear, as there are valid arguments on both sides. This new method, by requiring no additional assumptions or experiments, thus provides significant advantages over previous methods, particularly in terms of convenience.

A systematic study was performed using the aforementioned method to evaluate frictional forces under varying conditions. Internal and external lubrication exhibit the same qualitative trends with respect to maximum compaction pressure (or tablet density) and ejection speed. However, it appears that external lubrication is relatively more efficient at reducing the static friction and maximum ejection force. Friction coefficients appear to depend only weakly on the compaction pressure or tablet density. Ejection speed generally increases both the static and kinetic friction and can in and of itself be a decisive factor for chipping defects, meaning that commonly considered properties such as the tensile strength are insufficient to make claims about the structural integrity of the tablet and that chipping is a local defect. However, most of all, the choice of excipient plays a critical role in how quickly frictional forces scale with density or ejection speed. A careful consideration of excipient choices can therefore help reduce frictional forces and avoid potential problems when increasing tablet production speed. The proposed method therefore provides a novel tool for guiding the development of low-friction formulations for pharmaceutical tablet production.

Supplementary information

Supplementary information can be found with the online version of this article.

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- Method to measure friction coefficients in standard compaction simulator experiment
- Experiments conducted with different materials, speed, density, and lubrication type
- Ejection speed and excipient material are the dominant factors affecting friction
- Kinetic friction coefficients depend only weakly on the material
- Oscillatory stick-slip identified as potential cause for high friction coefficients

Declaration of interests

☒ The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.