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A Novel Method for Estimating Solid Fraction of Roller-Compacted Ribbons

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A simple method has been developed to estimate solid fraction or relative density of compacts using the weight of ribbons produced during roller compaction. The method provides an alternative to the commonly used dimensional measurement, especially for formulations not amenable to forming quality ribbons. Surface texture of the compaction rolls has been taken into consideration in our mathematical treatment along with correction for ribbon relaxation. Ribbon relaxation occurring upon ribbon exiting the compaction zone is estimated using roll geometry, roll gap, and ribbon thickness. Detailed experimental runs have been carried out to confirm the validity of the proposed theory. The predicted solid fraction was found comparable to that from actual dimensional measurement by caliper. In the case of the microcrystalline cellulose/dicalcium phosphate one:one formulation, the predicted solid fraction had an error sum of squares (SSE) of 2.64E-03 when compared to the dimensional method. When relaxation was included, the SSE decreased by four folds. Similarly, for the microcrystalline cellulose/lactose monohydrate 2:1 formulation, the SSE decreased twelfth folds when relaxation was taken into consideration. These results further confirm the utility of the proposed throughput method for estimating the solid fraction of ribbons.

Keywords roller compaction; dry granulation; solid fraction; Gerteis Mini-pactor®

INTRODUCTION

Roller compaction is a commonly used dry granulation process whereby powder densification is achieved by applying mechanical pressure to powders passing through two counter-rotating rollers (Inghelbrecht & Remon, 1998; Miller, 1994; Murray, Laohavichien, Habib, & Sakr, 1998; Murray & Sakr, 1996). The densified sheets (ribbons) are then dry-sized by an oscillating mill, a cone mill or an impact mill. The resulting granules are often blended with other extragranular excipients and compacted into tablets. Two main advantages of the roller compaction process are that it eliminates the need for a drying step and it is a continuous process (Hariharan, Wowchuk, Nkansah, & Gupta, 2004)

Solid fraction represents the normalized fraction of solid material in a compact and is associated with the mechanical property of materials. Solid fraction can impact particle size, size distribution of granules, and ultimately the quality of tablets produced from them. To maintain consistent ribbon quality, the compaction parameters can be controlled and the solid fraction monitored throughout the run (Lammens & Pörtner, 2000). Maintaining consistent solid fraction is also a commonly employed strategy in the scale-up of roller compaction processes.

Several methods are available to measure the degree of material densification of compacted ribbons. The ideal method must be easy to use and independent of formulation or manufacturing process. One widely used method is the displacement method. This method uses the volume of solid medium displaced by the sample to determine the envelope volume and apparent density of the solid object. The medium consists of small, rigid spheres that have high flowability and allows for close packing around the ribbon being tested. The sample cell in which the dry medium is placed is a precision cylinder. Preliminary compaction using a plunger with only the displacement medium in the cell establishes a zero-volume baseline. The compact is then placed in the cylinder with the dry medium and the compaction process is repeated. The difference in piston penetration distance during the test and the baseline is used to calculate the volume of the medium displaced. Hence for a known weight of sample, the apparent density and therefore solid fraction can be calculated. The method is however not popular as it is time consuming and the accuracy depend on the sample orientation.

Another commonly used method is a dimensional measurement, which requires a mini-saw, a caliper, and a balance. It involves preparing rectangular ribbon samples using a mini-table saw, weighing the ribbon sample and measuring the ribbon dimensions with a caliper. The relative density or solid

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fraction of the sample is then simply calculated as the ratio of compact apparent density to material true density (Tye, Sun, & Amidon, 2005). Though this method can be successfully used to estimate compact solid faction, there are instances when the small size and fragility of compacts undermine the accuracy of the method and present a safety hazard to persons preparing samples. The compacted ribbon may be of such quality that the dimensions cannot be measured to calculate the solid fraction.

These challenges underscore the need for a simpler method that does not rely on sample preparation to determine the solid fraction of compacts. We have developed one such alternative approach for estimating the solid fraction of ribbons produced during compaction operations. The proposed method uses ribbon production rate (compaction throughput) to estimate the solid fraction of the compacted material. By simply weighing the ribbons or granules produced in a known time interval, the solid fraction of the ribbons can be indirectly calculated during processing. The approach provides a simple yet robust method to characterize ribbons produced by roller compaction. In this article the authors elucidate the full mathematical treatment and demonstrates how the method may be implemented.

THEORY

Represented in Figure 1 is a simple schematic of the roller compaction process. The following arguments may be constructed assuming that the rolls of the compactor are rigid bodies undergoing purely rotational motion.

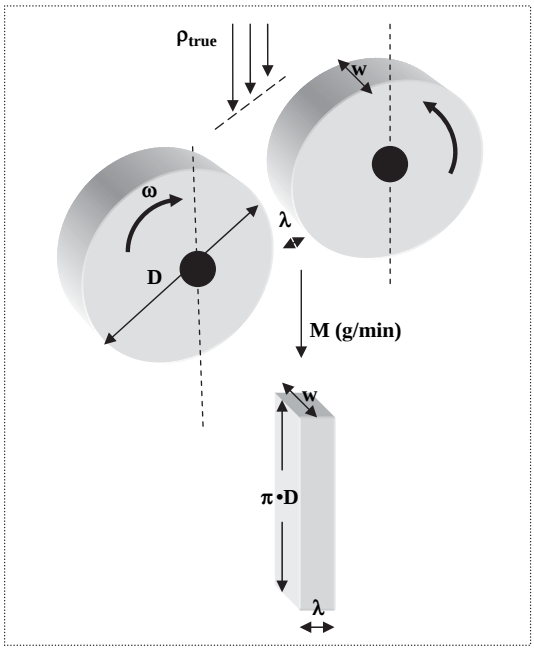

FIGURE 1. Schematic of roller compaction mechanism.

From the relationship for material density (mass per unit volume), the ribbon weight is deduced:

$$M \equiv \rho_{app} \times V = (SF \times \rho_{true}) \times V \tag{1.0}$$

For **ω** revolutions of the rolls, the volume of ribbon produced per minute is:

$$V = (\pi \times D \times W \times \lambda + Vsurf\_TM) \times \omega \tag{2.0}$$

Equations (1.0) and (2.0) are combined and a correction for slip on roll surface (ξ) is introduced to give a generalized equation for compaction throughput:

$$M\,(kg/min) = SF \times \rho_{true} \times (\pi \times D \times W \times \lambda + Vsurf\_TM) \times \omega \times (1 - \xi) \tag{3.0}$$

At steady state and assuming no-slip condition (ξ = 0), the following is obtained:

$$SF = \left[\frac{1000 \times M}{\rho_{true} \times (\pi \times D \times W \times \lambda + V_{surf\_TM}) \times \omega} \right]$$

Generalized form (4.0)

$$V_{surf\_TM} = 0 \qquad \text{Smooth roll} \tag{4.1}$$

$$V_{surf\_TM} = V_g \times N \qquad \text{Serrated roll} \tag{4.2}$$

$$V_{surf\_TM} = V_v \times N \qquad \text{Knurled roll} \tag{4.3}$$

This approach is independent of imperfections on the ribbon surface. The method assumes steady state and that the compacted powder does not stick or accumulate on the surface of the rolls. Also, a no-slip boundary condition is imposed. These conditions are generally met during standard compaction operation. Finally, the method does not take into account compact viscoelastic relaxation. However, a relaxation term may be introduced to correct for relaxation after compaction. This is treated in the next section.

Correcting for Ribbon Relaxation

Equation (4.0) provides the solid fraction *SF(0)* of ribbons at the time of compaction and Eq. (5.0) the solid fraction *SF(t)* after compaction. Note that Eq. (5.0) is the generalized form of the equations for the dimensional method (Tye et al., 2005).

$$SF = \frac{\dfrac{m}{(w \times l \times h) \pm V_{surf\_CM}}}{\rho\ true} \qquad (5.0)$$

Generalized form

$$V_{surf\_CM} = 0 \qquad \text{Smooth roll} \qquad (5.1)$$

$$V_{surf\_CM} = C_g \times w \times n \qquad \text{Serrated roll} \qquad (5.2)$$

$$V_{surf\_CM} = C_\kappa \times w \times l \times \kappa \qquad \text{Knurled roll} \qquad (5.3)$$

A correction factor (R) is now introduced to account for the relaxation of compacts such that:

$$SF(t) = SF(0) \times R \qquad (6.0)$$

Now suppose the press rollers undergo a single rotation such that ω equals unity and the resulting ribbon has roll dimensions: $l = \pi \times D$, $w = W$ and $m = M$. The assumption here is that the relative viscoelastic expansion along the width and length of ribbons are small compared to the relaxation in thickness. This assumption is consistent with compaction data. Equations (4.0) and (5.0) are solved simultaneously and Eq. (7.0) is obtained.

$$SF(t) = SF(0) \times \left[\frac{(\pi \times D \times W \times \lambda + Vsurf\_TM)}{(\pi \times D \times W \times h \pm Vsurf\_CM)} \right] \qquad (7.0)$$

where *SF(0)* is given by Eq. (4.0). Comparing Eqs. (6.0 to 7.0) provides the correction factors for smooth, serrated and knurled rolls:

$$R = \left[\frac{\lambda}{h} \right] \qquad \text{Smooth roll} \qquad (7.1)$$

$$R = \left[\frac{\pi \times D \times W \times \lambda + (Vg \times N)}{\pi \times D \times W \times h + (Vg \times N)} \right] \qquad \text{Serrated roll} \qquad (7.2)$$

$$R = \left[\frac{\pi \times D \times W \times \lambda + (Vv \times N)}{\pi \times D \times W \times h - (Vemboss \times N)} \right] \qquad (7.3)$$

Knurled roll

For this study and in general for Gerteis Mini-pactor® knurled rolls, the following relaxation equation is obtained by combining Eqs (4.0) and (7.0):

$$SF(t) = \left(\frac{1000\,M}{(\pi \times D \times W \times h - (Vemboss \times N))\ \rho_{true}{}^{\omega}} \right) \qquad (8.0)$$

$M \equiv$ ribbons/granules mass flow (g/min)	$D \equiv$ roll diameter (mm)
$m \equiv$ sample weight (mg)	$\xi \equiv$ slip on roll surface
$SF \equiv$ compact solid fraction	$\omega \equiv$ roll speed (rpm)
$\rho_{true} \equiv$ material true density (g/cc)	$W \equiv$ roll width (mm)
$\rho_{app} \equiv$ ribbon apparent density (g/cc)	$\lambda \equiv$ gap (mm)
$R \equiv$ relaxation correction factor	$C_k \equiv$ knurled volume correction (mm^3/mm^2)
$w \equiv$ mean ribbon width, in direction of width (mm)	$k \equiv$ number of sides of ribbon with knurled pattern
$l \equiv$ mean ribbon length, in ribbon direction (mm)	$C_g \equiv$ grooved roll volume correction (mm^2)
$h \equiv$ mean ribbon thickness (no embossments for serrated) (mm)	n ≡ total number of grooves/ serrations on both sides of ribbon
$V \equiv$ volume of ribbon (mm^3)	$N \equiv$ number of serrated or knurled rolls
	$V_{surf} \equiv$ total volume of roll grooves, voids, embossments (mm^3) [$= N*V_g$, $N*V_v$, $N*V_{emboss}$]

EXPERIMENTAL

Materials

Two model placebo formulations, one containing dicalcium phosphate and the other lactose monohydrate were used in this study. Each formulation contained Microcrystalline cellulose (Avicel PH 102) from FMC (Philadelphia, Pennsylvania),

Sodium starch glycolate (Explotab) from Penwest (Danbury, Connecticut), Magnesium stearate (nonbovine) from Mallinckrodt (St. Louis, Missouri), Dibasic calcium phosphate anhydrous (A-Tab) from Rhodia (Cranbury, New Jersey) or Lactose monohydrate (Fast Flo) from Foremost Farms (Baraboo, Winconsin). All materials were used as supplied.

Methods

Formulation Preparation

Two powder mixes were prepared for these experiments. Each blend contained three identical components with the fourth excipient being either Dibasic calcium phosphate anhydrous (Formulation I) or Lactose monohydrate (Formulation II) in 1:1 and 2:1 ratios respectively, relative to the amount of microcrystalline cellulose. The formulation compositions and amounts prepared are provided in Tables 1 and 2. The blends were prepared by blending all the materials in a blender and subsequently passing the blend through a Comil, equipped with round impeller and 0.062 inch mesh screen operating at 800 rpm. The true densities of the resulting blends were theoretically estimated to be 1.98 and 1.56 g/cm^3 for formulations I and II, respectively.

Roller Compaction Process

A Gerteis Mini-pactor® was setup with knurled rolls without the side rims. The no side rim configuration was used to ensure that the resulting compacts could be easily trimmed for dimensional measurements. Additional information is provided in Table 3.

TABLE 1
Formulation I

Components	% Composition	Batch Size
Microcrystalline cellulose, NF	48.0	960.0 g
Dibasic Calcium Phosphate, anhydrous	48.0	960.0 g
Sodium starch glycolate, NF	3.0	60.0 g
Magnesium stearate, NF	1.0	20.0 g
Total	100.0	2.0 kg

TABLE 2
Formulation II

Components	% Composition	Batch Size
Microcrystalline cellulose, NF	64.0	3840.0 g
Lactose monohydrate, NF	32.0	1920.0 g
Sodium starch glycolate, NF	3.0	180.0 g
Magnesium stearate, NF	1.0	60.0 g
Total	100.0	6.0 kg

TABLE 3
Summary of Relevant Experiment Information

	Prototype Formulations	
	I	II
Composition	MCC:DCP 1:1	MCC:LAC 2:1
True density (g/cc)	1.98	1.56
Roll configuration	Knurled (without side rim)	Knurled (without side rim)
Roll diameter / width (mm)	250 / 25	250 / 25
Roll gap (mm)	2.0	2.0

A simple procedure was employed in this study to cover typical solid fraction values. First, machine parameters were adjusted to produce viable ribbons. When the process reached steady state, the weight of ribbons produced after 1 min was recorded. From the production rate (g/min), the solid fraction of the ribbons was computed using the throughput method (described below). The solid fraction of the same ribbons was also estimated using the caliper method (also described below). Each run was repeated at the same processing condition (roll gap, force, speed, % tamp/feed). The process condition was however changed after each triplicate run to produce ribbons at different solid fractions. Again, the production rate (g/min) was recorded and the solid fraction determined. Procedures for throughput and caliper methods are summarized in the subsequent sections.

Solid Fraction via Throughput Method

The compaction throughput (g/min) was determined from the weight of ribbons collected 1 min after the compaction process reached steady state. Solid fraction was computed using the production rate (g/min), blend true density, roll geometry, and operating parameters. The procedure for the throughput method is as follows:

1. Place a scale under the granule collection bag attached to the roller compactor.
2. After steady state, record the weight of ribbons or granules produced in one minute.
3. Repeat step 2 for a total of 3 times and determine the average weight
4. Determine the solid fraction using equations 4.0 and 4.3, and finally equation 8.0.
5. Collect a few ribbons and follow the instructions for the caliper method.

Solid Fraction by Caliper Method

To determine the solid fraction of a ribbon sample, the blend true density, the ribbon mass, and dimensions are measured. The solid fraction of the sample is calculated simply

as the ratio of compact apparent density to blend true density. The procedure for estimating solid fraction using the caliper method:

1. Obtain true density of the powder blend or crushed ribbons.
2. After the weight of ribbons is recorded (see throughput method), collect a few ribbons.
3. Prepare three rectangular ribbon samples using a mini-table saw.
4. Weigh ribbon samples.
5. Use calipers to measure width, length and height of ribbon samples.
6. Determine solid fraction of each sample using equations 5.0 and 5.3.

RESULTS AND DISCUSSION

Summarized in Tables 4 and 5 are experimental results. The solid fractions estimated using the throughout method were compared to values obtained using the caliper method (measured solid fraction). Our initial estimates of solid fraction did not account for viscoelastic relaxation of the compacts. When relaxation was neglected, the predicted solid fraction values underestimated the measured values in almost every instance. The predicted solid fractions without relaxation had error sums of squares (SSE) of 2.64E-03 and 7.24E-03 for formulations I and II, respectively. To refine the method, a relaxation correction factor using information on roll geometry, roll gap and ribbon thickness was introduced into the calculation (Eq. 7.3). Taking relaxation into account (Eq. 8.0), the SSEs were reduced to 6.44E-04 and 6.15E-04 for formulations I and II, respectively. The predicted solid fractions were in close agreement with measured values (Figures 2 and 3). The results also demonstrated that roll force exerts the most effect on ribbon mechanical strength, whilst roll speed has the most influence on the compaction throughput. The effect of roll speed on ribbon density is thought to be negligible within the range of speeds tested. As a matter of general consideration, roll speeds typically used during development (3–10 rpm) are not significant enough to affect ribbon quality. However at the speeds encountered during production, roll speed can become important. This is analogous to the influence of press speed and dwell time on tablet properties during compression.

A more general application of the methodology presented in this paper for predicting ribbon solid fraction (with relaxation) involves using Eqs. (4.0) and (6.0) and the applicable relaxation factor (Eqs. 7.1–7.3). In other words, provided the roll gap, initial solid fraction (solid fraction at time-zero) and compact thickness are known, the solid fraction after relaxation can be accurately predicted. It is worth mentioning that the measured total thickness includes the relaxation of the ribbon. Only the void volume correction portion is estimated from drawing dimensions which does not include the adjustment to changes due to ribbon relaxation. Roll machining precision and accuracy of the balance used to weigh ribbons may also introduce error

TABLE 4
Summary of the Predicted Average Relaxation Factor, Throughput and Solid Fraction for Formulation I

Run Number	Parameters Gap (mm), kN/cm, RPM, %T/F	Thickness (mm)	Relaxation Factor	Throughput (g/min)			Solid Fraction		
				No Relaxation	With Relaxation	Measured	Predicted No Relaxation	Predicted With Relaxation	Measured By Caliper
1	2.0, 5.0, 3.0, 150	2.96	1.015	185.83	183.14	181.7	0.596	0.605	0.61
2	2.0, 5.0, 5.0, 150	2.94	1.023	304.64	297.89	295.2	0.581	0.595	0.60
3	2.0, 5.0, 5.0, 150	3.02	0.992	304.64	307.23	303.8	0.598	0.593	0.60
4	2.0, 7.0, 5.0, 150	2.91	1.035	324.95	314.02	302.7	0.596	0.617	0.64
5	2.0, 7.0, 5.0, 150	2.96	1.015	324.95	320.24	318.0	0.626	0.636	0.64

TABLE 5
Summary of the Predicted Relaxation Factor, Throughput, and Solid Fraction for Formulation II

Run Number	Parameters Gap (mm), kN/cm, RPM, %T/F	Thickness (mm)	Relaxation Factor	Throughput (g/min)			Solid Fraction		
							Predicted	Predicted	Measured
				No Relaxation	With Relaxation	Measured	No Relaxation	With Relaxation	By Caliper
1	2.0, 5.0, 3.0, 150	2.96	1.015	163.21	160.85	160.3	0.668	0.678	0.68
2	2.0, 5.0, 3.0, 150	2.90	1.039	168.01	161.72	160.4	0.668	0.694	0.70
3	2.0, 5.0, 6.0, 150	2.90	1.039	331.22	318.81	315.5	0.657	0.683	0.69
4	2.0, 5.0, 6.0, 150	2.99	1.003	321.62	320.66	317.3	0.661	0.663	0.67
5	2.0, 7.0, 6.0, 150	3.02	0.992	350.43	353.40	350.3	0.730	0.724	0.73
6	2.0, 7.0, 6.0, 150	2.94	1.023	355.23	347.36	344.7	0.718	0.734	0.74
7	2.0, 9.0, 3.0, 150	2.97	1.011	189.61	187.59	186.5	0.777	0.785	0.79
8	2.0, 9.0, 3.0, 150	2.90	1.039	192.01	184.82	183.4	0.764	0.794	0.80
9	2.0, 9.0, 6.0, 150	2.96	1.015	374.43	369.00	366.3	0.763	0.774	0.78
10	2.0, 9.0, 6.0, 150	2.97	1.011	374.43	370.44	367.8	0.766	0.774	0.78
11	2.0, 7.0, 6.0, 150	2.97	1.011	355.23	351.44	346.7	0.722	0.730	0.74
12	2.0, 7.0, 6.0, 150	2.94	1.023	355.23	347.36	344.6	0.718	0.734	0.74
13	2.0, 7.0, 3.0, 150	2.95	1.019	180.01	176.72	174.4	0.727	0.740	0.75
14	2.0, 7.0, 3.0, 250	2.90	1.039	180.01	173.27	171.8	0.716	0.744	0.75

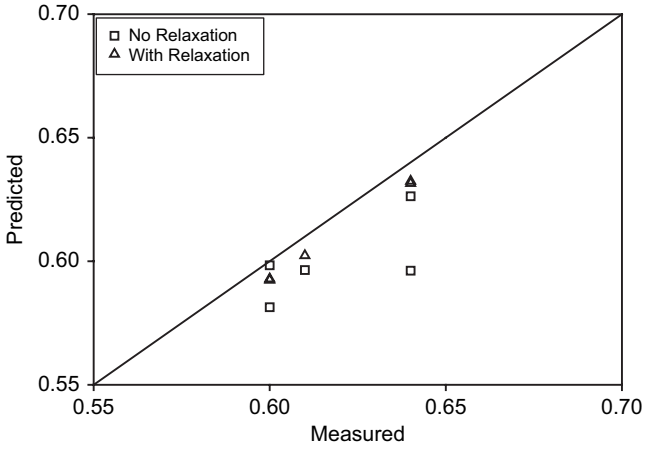

FIGURE 2. Solid fraction: predicted versus measured for formulation I.

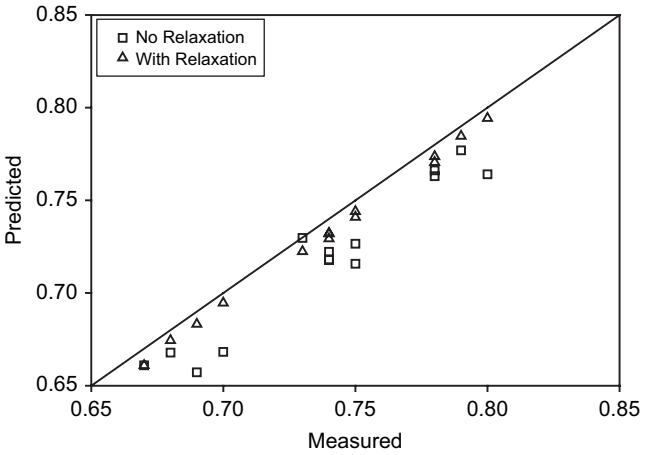

FIGURE 3. Solid fraction: predicted versus measured for formulation II.

into the solid fraction calculation. However the former is considered to have very little effect on the accuracy of solid fraction for a thicker ribbon, as the void volume accounts for only a small percentage in the volume calculation.

CONCLUSIONS

We report here the results of a proof-of-principle study of a simple method that uses compaction operating parameters to estimate solid fraction. The method assumes that gap-control and steady state conditions are maintained throughout the compaction process. Roll surface characteristics and ribbon relaxation are taken into account when calculating the solid fraction. The model appears to fit reasonably well with the experimental data. The results support the proposed method and demonstrate utility for formulation and process development and scale-up efforts. The method may be implemented on any conventional roller compaction platform that is equipped with a gap-control.

The throughput method may be employed in gap-controlled compactors as follows:

1. The machine is set at the desired gap (λ), roll speed (ω) and feed conditions.
2. From the blend true density (ρ_{true}), thickness (obtained from first few compacts produced), and target solid fraction (*SF*), the corresponding throughput (*M*) is calculated using equations 4.0 and 6.0 (note that equation 8.0 is the result when Gerteis knurled rolls are used).
3. The roll force is adjusted until the calculated throughput (*M*) is obtained.

The above iterative scheme is effective but may require at least 3–4 trials and 1–2 kg of material to achieve the desired ribbon properties. To minimize waste, the initial roll speed may be kept as low as possible (2–3 rpm) until the correct force-throughput combination is found. The roll speed may then be increased as desired and the corresponding throughput verified. Since low speeds have negligible effect on solid fraction, the new throughput should correspond to the solid fraction calculated at the original speed. No further adjustment of the roll force is needed thereafter. It stands to reason that if the roller compaction process is fully characterized prior to processing, solid fraction may be readily estimated with very little loss of the valuable product.

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