

# Powder Hydrophobicity and Flow Properties: Effect of Feed Frame Design and Operating Parameters

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*The effect of feed frames, a device used in rotary tablet presses to drive the powders into compression dies, on the properties of the powders entering the dies is systematically described in this article. The work focuses on the effect of blend composition, feed frame parameters (blade speed and residence time), and rotary die disc parameters (die disc speed and die diameter) on powder overlubrication, the flow properties of the blends, and the resulting tablet properties (tablet hardness and dissolution). For lubricated blends, the feed frame had a large impact on powder hydrophobicity and powder flow properties. Hydrophobicity results demonstrated that the shear applied by the feed frame caused overlubrication of the powders, which improved the powder flow properties but affected adversely the tablet hardness and dissolution. © 2011 American Institute of Chemical Engineers AICHE J, 58: 697–706, 2012*

*Keywords:* powder feeders, die filling, shear rate, overlubrication, tablet hardness, dissolution

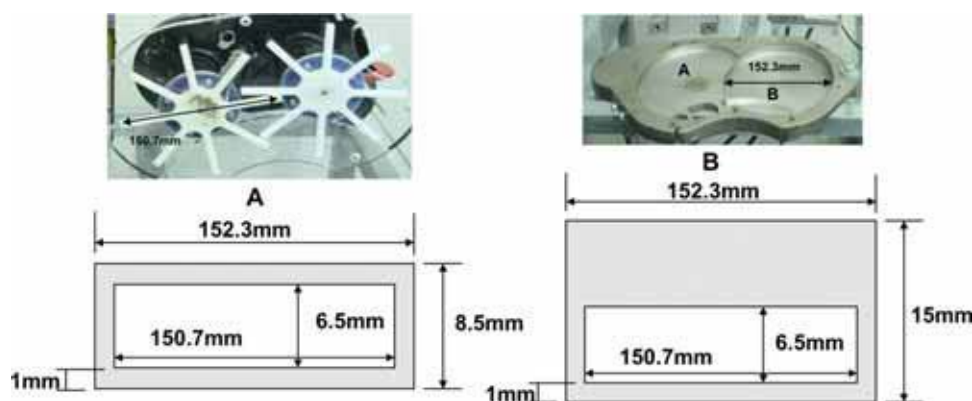
## Introduction

Oral solid dosage forms—tablets and capsules—account for ~85% of all medications, having an estimated market value in excess of \$300B/yr. Reasons for this include high patient compliance, dosage reliability, low cost, and superior physical and chemical stability compared to other forms. Thus, despite the significant academic interest in other forms of drug delivery, oral solids remain and are expected to remain, the most desirable and most prevalent route for drug administration to large populations. Tablets are the most

popular drug delivery system<sup>1</sup> and more than 70% of all pharmaceutical products sold worldwide are tablets.

Tablets are typically manufactured in high-speed compaction processes where several phenomena such as powder flow, die filling, precompression, compression, and ejection occur in rapid sequence. Most tablet presses are constant displacement machines, where the run of the punches is fixed. In such systems, the force at which a product unit is compressed depends exponentially with the die weight. As a result, several final properties of the compact, including its density and porosity and the amount of elastic stress stored in the compact, are affected by the amount of powder in the die. Therefore, (1) consistent filling of the tablet press die with a uniform weight of powder is often both critical to quality and rate-limiting for the entire process, and therefore,

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**Figure 1. Feed frame equipment and dimensions.**

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uniform die filling is a crucial control variable, and (2) the phenomena mentioned above affect the tablet drug content, and tablet hardness and dissolution. In addition, nonhomogeneous filling can contribute to many quality problems such as distortion, cracking, low strength, shrinkage, and chemical and physical instability.<sup>2</sup>

The ability of a powder to flow, especially into the dies, is a combined effect of the material's physical properties (particle size, particle size distribution, morphology, surface roughness, density, hydrophobicity, and cohesion)<sup>3–5</sup> and the equipment used for handling, storing, or processing the material.<sup>1,3,4,6–8</sup> Manufacturers often use mechanical assistance in the form of paddle feeders, wipers, blades, or agitator arms to maintain an adequate supply of powder to fill the dies. These devices force the powder into the cavity and/or aerate the powder so that it behaves more like a liquid than a powder. Other factors affecting the filling include: die table speed, distance between dies, dies size and shape, and operating conditions (humidity, temperature, shear rate, and total shear).<sup>2</sup>

Lubricant has been used for decades before the compaction process to improve the flow properties of the powder,<sup>9</sup> to reduce storage of elastic stresses, and to prevent material stickiness to the tooling.<sup>9–11</sup> However, exposition of the lubricated blend to extensive shear strongly affects powder flow properties.<sup>9</sup> Overlubrication inside the feed frame could potentially occur and hence affect the tablet hardness and dissolution rate.<sup>9,12</sup> In a previous work, we showed that the total shear applied depends on the residence time of the material in the feed frame, which is determined by the speeds of both the feed frame and die disc.<sup>13</sup> Lubricant can also reduce unfortunately interparticulate bond strength, making tablets softer, and it can make the blend hydrophobic, affecting the dissolution of resulting tablets.<sup>9,14–16</sup>

This article focuses on studying the effect of feed frame operating conditions and material's properties on the powder flow, and the resulting overlubrication effect, on tablet hardness and dissolution. Next section describes the material, equipment, and procedures used in the research. This section is followed by the results and discussion section, where results of basic material properties before and after the feed frame are presented. Results of hydrophobicity of the treated material and tablet hardness prepared from the treated material are also presented. The article ends with a conclusion and future work section.

## Experimental Procedure

The materials used in this study include lactose fast flow 316 monohydrate N.F. (Foremost Farm), magnesium stearate (MgSt) N.F. nonbovine (Mallinckrodt, NJ) as lubricant (sieved before use), and semifine acetaminophen USP/paracetamol Ph Eur powder (APAP, Mallinckrodt, NJ). The apparatus used in this study is composed of a standard two-stage controlled feed frame taken from a Manesty Betapress (Figures 1 and 2) and a Plexiglas die disc with the same actual dimensions of the tablet press. A completed description of the feed frame and simulated die system were presented in previous work.<sup>13</sup>

For the feed frame characterization, three feed frame speeds (24, 48, and 72 rpm) and three die disc speeds (29, 43, and 57 rpm) were used. All experiment started by setting up the respective feed frame and die table speeds and then the powder feed rate. After the system reached the steady state, ~2.5 kg of powder was collected for the characterization.

The powder density and the flow properties were characterized using 500 taps in the Quantachrome Instruments Autotap and a gravitational displacement rheometer (GDR).<sup>9,17–20</sup> The GDR was used to quantitatively measure the flow characteristics (flow index and powder dilation) of the blends before and after passing through the feed frame (Figure 3). Further details of the equipment, materials, and methods were previously published.<sup>13</sup>

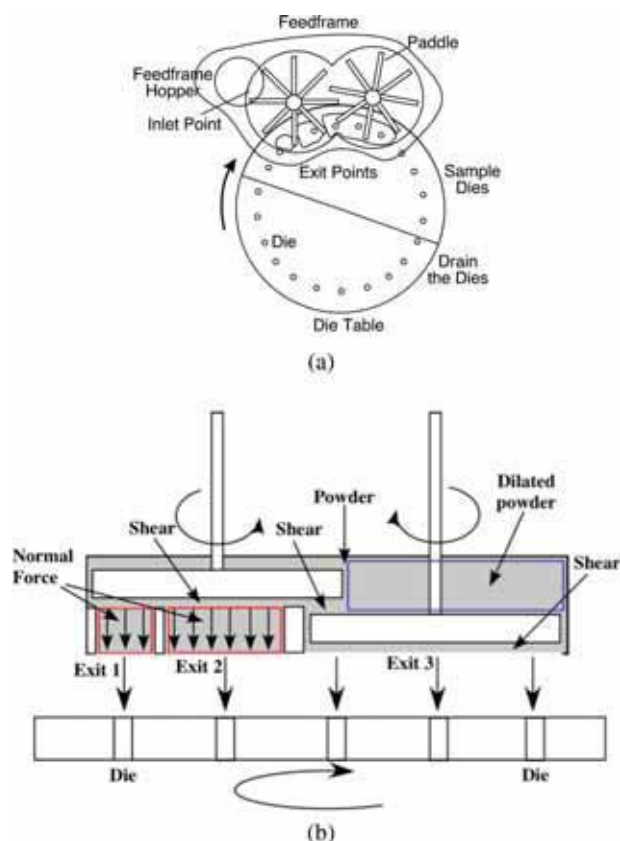
## Powder hydrophobicity

Hydrophobicity determines the ability of a solution to move by capillarity through a column of powders.<sup>21</sup> There are two different approaches to measure the capillary rise; one measures height, which are the classical method and the other the weight of the absorbed liquid.

The advantage of the weight measurements lies on the precision of the weighing equipment used vs. the visual observation of the height. The Washburn technique<sup>22–25</sup> uses Eq. 1 to quantify the hydrophobicity based on the mass of liquid absorbed by a vertical column of powder.

$$t = \frac{\eta}{C\rho^2\gamma \cos \theta} m^2 \quad (1)$$

where  $t$  is the time,  $\eta$  is the liquid viscosity,  $C$  is the geometric factor and is constant as long as the packing and the particle



**Figure 2. Feed frame and die disc system.**

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size remain similar,  $\rho$  is the liquid density,  $\gamma$  is the surface tension of the liquid,  $\theta$  is the contact angle between the solid and the liquid, and  $m^2$  is the quadratic mass of liquid that has penetrated by capillarity. The hydrophobicity is the slope of the line of time ( $t$ ) vs. the square mass ( $m^2$ ).

First, the powders of interest were placed in a glass cylinder with a sintered glass filter, to retain the powders, and in contact with a solution saturated with all soluble components

of the blend. The saturated solution was prepared at 25°C and kept constant thorough out all the measurements. Depending on the components of the blend, different solutions were used to analyze the sample. The first solution was prepared by adding 125 g of lactose and stirring at least 12 h to dissolve the maximum lactose possible to saturate the solution at room temperature. The solution was then filtered to remove the excess of lactose. For the blend with APAP, the solution was saturated using the same procedure above with lactose and APAP.

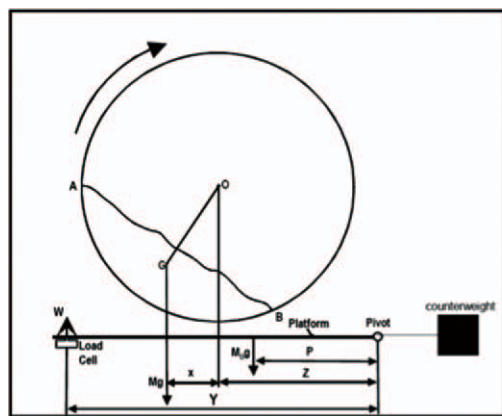
For the measurements, 30 g of powder was added to the cylinder and compacted using 500 taps. The cylinder with the powder was attached to a stand that was placed on a scale connected to a computer. The cylinder was then submerged in the solution at the same level of the powder. As soon as the cylinder was submerged, the scale was tare and measurements of the change in weight as function of time were recorded.

### Tablet compaction and characterization

Tablets were prepared from nontreated and treated blends (processed in the feed frame) of 3% APAP, 1% MgSt, and 96% fast flow lactose at three different compression forces: 6.8, 9.8, and 12.8 kN at constant thickness. The thickness of a tablet depends on the fill weight and the applied pressure. If the compression force is increased, then the thickness is reduced. The tablet density was assumed constant for each compression force because relatively small tablet weight variability was observed.

The lowest speed in the die disc generated the largest residence time.<sup>13</sup> The tablets were prepared in a Prester Model 252 with a IPT-B tooling type by Metropolitan Computing Corporation (East Hanover, NJ) simulating the roller conditions of a Fette PT 2090 IC 36 stations with a setup speed of 104400 TPH (tablets per hour; 48.3 rpm or 1.038 m/s turret speed) and a die diameter of 10 mm. The average weight of the tablets was 616 mg. The tablet press was connected to the computer to record the compaction pressure.

The tablets were characterized in terms of hardness and dissolution rate. Thirty tablets of each sample powder were analyzed using a Dr Schleuniger Pharmatron model 6D tester



**Figure 3. Gravitational displacement rheometer (GDR).**

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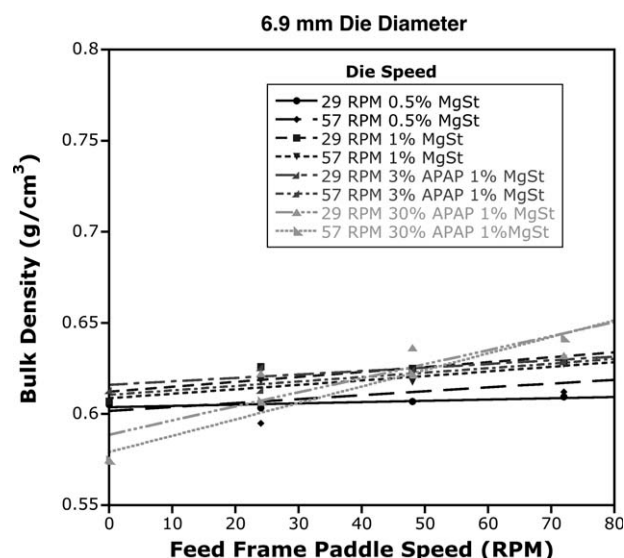


Figure 4. Powders bulk density before and after the feed frame.

to measure the tablet hardness. Dissolution tests were done on a Vankel VK7010 USP II apparatus with online reading in a flow cell Cary 50 spectrophotometer. The dissolution apparatus consists of eight vessels, each with a capacity of 900 mL with two paddles, which can rotate at different speeds. The operating time can be changed depending on the target tablet performance.

The first step of the test required adding the phosphate buffer solution (900 mL with a pH of 5.8) to each vessel with a fixed height of the paddles. After evaporation covers were set in place, the buffer was allowed to preheat to 37°C. Meanwhile, each tablet was weighed before placing it in its corresponding vessel.

After the vessel temperature reached steady state, the tablets were simultaneously dropped, and the absorbance was automatically read every 2 min for 90 min. The samples

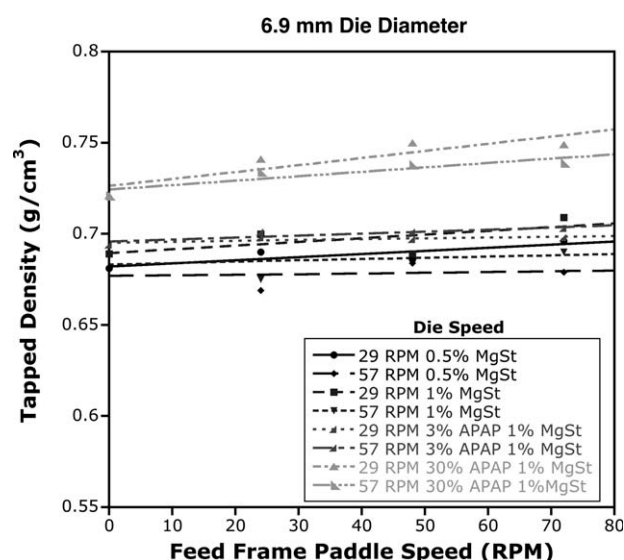


Figure 5. Powders tap density before and after the feed frame.

Table 1. ANOVA: Effect of the Lubricant Concentration, Feed Frame Speed, and Disc Die Speed on Powder Tapped Density

Source	DF	SS	MS	F	P
Feed frame speed	2	0.000206	0.000103	2.37	0.164
Die disc speed	1	0.000588	0.000588	13.54	0.008
% MgSt	1	0.000192	0.000192	4.42	0.074
Error	7	0.000304	0.000043		
Total	11	0.001290			

were tested in the UV spectrophotometer. The paddles rotated at 50 rpm for the duration of the test, with an infinity time point final spin of 250 rpm for 5 min. Sampling probes were fitted with 10- $\mu$ m filter tips. Absorbance readings were obtained at 243 nm in 5.0-mm flow cell cuvettes. For each tablet blend/shear sample, four tablets were tested. The tablet weight was used together with the percentage active concentration of the formulation and the amount released at each time point to derive a percentage release profile.

## Results and Discussion

### Powder bulk and tapped density

Figures 4 and 5 show the bulk and tapped densities for the untreated material (before entering the feed frame) and the treated material (exposed to three different shear conditions), respectively. As can be seen in Figure 4, the bulk densities for all blends except the one with 30% APAP are similar. The tap density (Figure 5) follows similar behavior. Comparing tap density to bulk density, the tap density is larger as expected. The increase in APAP concentration increases the powder cohesion of the blend especially at 30% APAP. Cohesive materials with lubricant, especially exposed to shear, show larger changes in flow properties and therefore in powder density due to the lower friction between the particles when compared with case with no lubrication.

There was not a statistically significant effect of the feed frame speed on the tap density for (1) fast flow lactose, (2) blends of fast flow lactose with MgSt, and (3) blends with low concentration of APAP and MgSt, and a statistically significant for the blend with 30% of APAP. Tables 1 and 2 include the analysis of variance considering the effect of the feed frame speed, die disc speed, and the concentration of lubricant or APAP on the powder tapped density. The statistical model, Eq. 2, includes only three factors and all interactions in the error.

$$y_{ij} = \alpha_i + \beta_j + \gamma_k + \varepsilon_{ijk} \quad (2)$$

where  $\alpha_i$  is the feed frame paddle speed;  $\beta_j$  is the die disc speed,  $\gamma_k$  is the lubricant concentration, and  $\varepsilon_{ijk}$  is the error.

Table 2. ANOVA: Effect of the APAP Concentration, Feed Frame Speed, and Disc Die Speed on Powder Tapped Density at Constant MgSt Concentration

Source	DF	SS	MS	F	P
Feed frame speed	2	0.0000315	0.0000158	0.63	0.560
Die disc speed	1	0.0000241	0.0000241	0.97	0.359
% APAP	1	0.0053341	0.0053341	213.87	0.000
Error	7	0.0001746	0.0000249		
Total	11	0.00556453			



**Table 3. Summary of Die Disc and Feed Frame System Results for 6.9 mm Die Diameter**

Material	Die Disc Speed (RPM)	Feed Frame Speed (RPM)	Hydrophobicity	Powder Flow Index	Powder Dilation
FF Lactose	Untreated			36.916	21.073
	29	29		35.552	18.928
	29	29		35.015	19.231
	29	29		40.605	19.542
	57	57		32.999	18.174
	57	57		33.755	17.799
	57	57		34.815	18.246
FF lactose + 1% MgSt	Untreated		0.218	36.309	20.224
	29	24	0.342	35.740	19.285
	29	48	0.385	32.740	17.664
	29	72	0.948	28.180	10.523
	57	24	0.284	31.130	19.221
	57	48	0.412	30.890	17.920
	57	72	0.490	28.930	15.165
FF lactose + 0.5 % MgSt	Untreated		0.147		21.520
	29	24	0.173	39.695	19.291
	29	48	0.191	40.596	19.075
	29	72	0.235	36.154	18.471
	57	24	0.175		19.342
	57	48	0.179		19.02
	57	72	0.211		18.693
FF Lactose + 3% APAP + 1% MgSt	Untreated		0.126	36.475	22.758
	29	24	0.243		19.238
	29	48	0.319		17.978
	29	72	0.440		13.151
	57	24	0.197		18.578
	57	48	0.292		17.012
	57	72	0.391		12.453
FF Lactose + 30% APAP + 1% MgSt	Untreated		0.143	37.136	27.470
	29	24	0.370	31.010	23.063
	29	48	0.587	25.910	21.658
	29	72	0.729	22.980	12.586
	57	24	0.266	31.660	21.496
	57	48	0.339	30.680	19.576
	57	72	0.527	27.330	14.285

Table 2 shows the results for blends without API with two concentrations of lubricant at three feed frame speeds and two die disc speeds. The results indicated that the effect of the die disc speed is statistically significant on the powder tap density for a 95% confidence level. The residence time and, therefore, the total shear applied to the powder inside the feed frame are function of the die disc speed. Table 3 shows the results for the blends with two concentration of APAP and constant concentration of lubricant at the same feed frame and die disc conditions. The results demonstrate that the APAP concentration had a statistically larger effect on the tap density. The reason for this is that the increase in APAP amount increases the powder cohesion, which makes the blend more sensitive to larger effect of lubrication and changes in flow properties.

### ***Powder flow index and dilation***

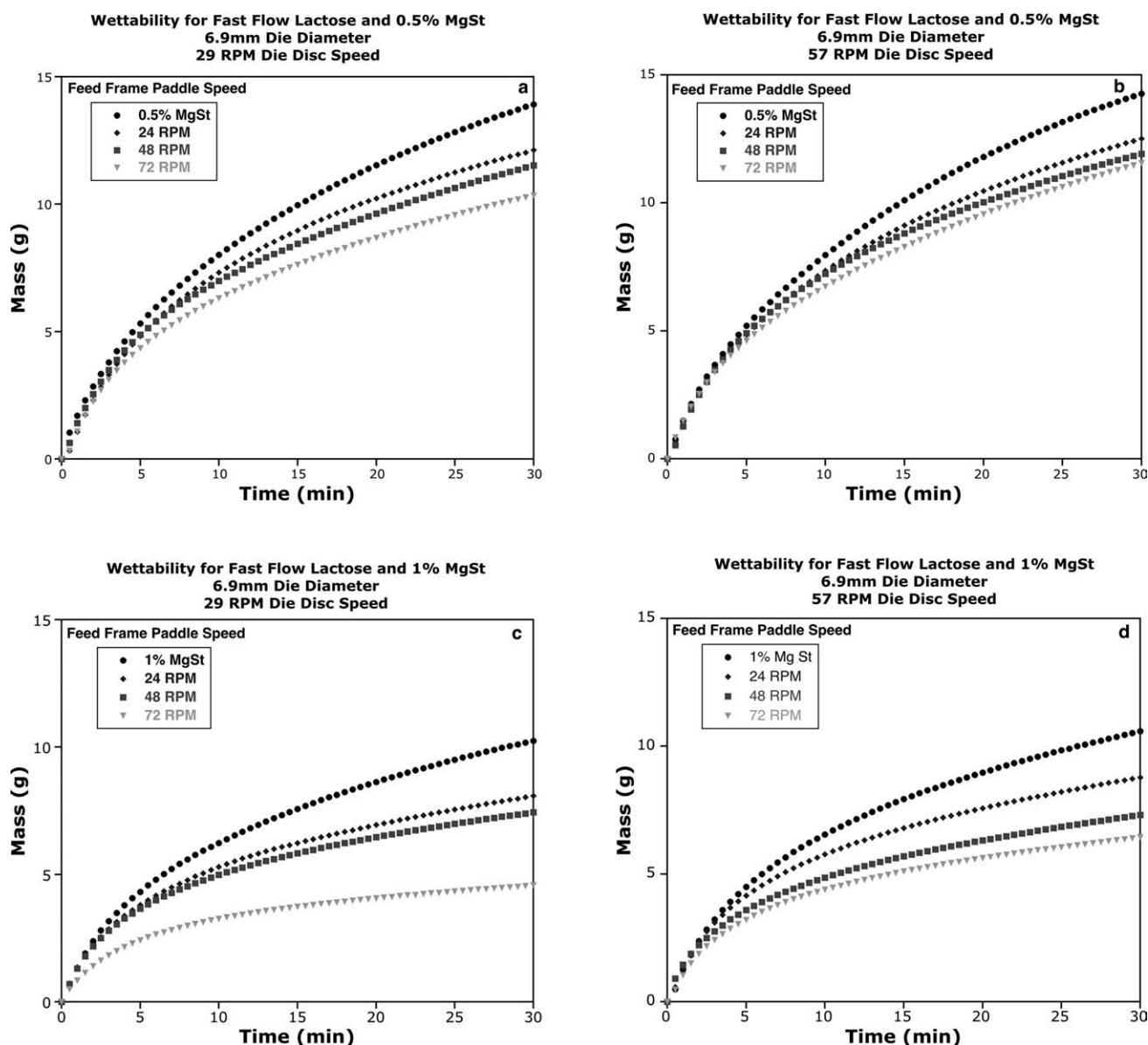
In a previous article,<sup>13</sup> we reported the effect of total shear in the feed frame on flow index and dilation of blends. In this article, we provide a summary of the main results for the sake of completeness listed in Table 1. For the nonlubricated blends, there is essentially no effect of the feed frame and die table speed on the flow properties of the powders, and the dilation results remain relatively constant as the feed frame speed increases. This demonstrates that the shear

applied to nonlubricated blend with this particle size distribution does not affect significantly the powder cohesion.

On the other hand, for the lubricated blends, there is a strong effect. Powders that have passed through the feed frame have significantly lower flow index and dilation, indicating a significantly lower cohesion than the one before passing through the feed frame. The results show a markedly dilation decrease as the feed frame speed increased (which increases both the shear rate and the total shear). The same behavior occurs for the lubricated blend with APAP. Therefore, lubricated powders with MgSt become shear sensitive. The results in this section demonstrate that such blends can experience enough shear in a feed frame to “overlubricate” them, leading to significant changes in flow properties.

### ***Feed frame effect on powder hydrophobicity***

The Washburn method was used to measure the effect of the shear applied in the feed frame on the hydrophobicity of fast flow lactose with magnesium stearate. The liquid mass penetration as a function of time for the lubricated blend in Figure 6 shows a reduction in the penetration rate of the solution as the feed frame speed increased. Based on Eq. 1, the shear rate applied to the powder increase the distribution of lubricant and increases the hydrophobicity by increasing the contact angle ( $\theta$ ). The largest reduction in wettability (or



**Figure 6.** Wettability curves for blends with 0.5 and 1% of MgSt as a function of the feed frame and die disc speed.

(a) Blend with 0.5 % MgSt at 29 RPM die disc speed, (b) blend with 0.5% MgSt at 57 RPM die disc speed, (c) blend with 1% MgSt at 29 RPM die disc speed, and (d) blend with 1% MgSt at 57 RPM die disc speed.

increase in hydrophobicity) was obtained for fast flow lactose with 1% MgSt, higher feed frame speeds, and lower die system speeds. The hydrophobicity is slope of the line when plot time as function of the mass square using the Washburn (Eq. 1). Figure 7 shows a good line agreement (for all the samples the square of the correlation factor is higher than 0.98) for fast flow lactose with 1% MgSt blends results, and the same results were obtained for other blends.

Figures 8 and 9 show that blends with fast flow lactose with 1% MgSt and blends with fast flow lactose, 3 or 30% APAP and 1% of MgSt, respectively, had substantially higher hydrophobicity (fivefold increase) after passing through the feed frame than the incoming stream. These changes in hydrophobicity correlate directly to the total shear applied to the powder in the feed frame. Presumably, more extensive

total shear affects the distribution of magnesium stearate over the surface of the larger excipients and API (active pharmaceutical ingredient) particles, and thus the powder contact angle. Figure 9 shows results for replicated experiments with fast flow lactose, 3% APAP, and 1% of MgSt showing reproducibility of the effect of total shear on hydrophobicity.

The total shear is the sum of the shear applied in the different zone inside the feed frame. In previous work,<sup>13</sup> we showed that the powders leaving the feed frame at different exit points are exposed to different shear histories due to differences in residence time. Therefore, the powders used in the measurements of hydrophobicity were a composite of powder exiting at the three different exits points. Furthermore, the dies were filled with powders coming off the three exits points; therefore, there is the possibility that the dies were filled with

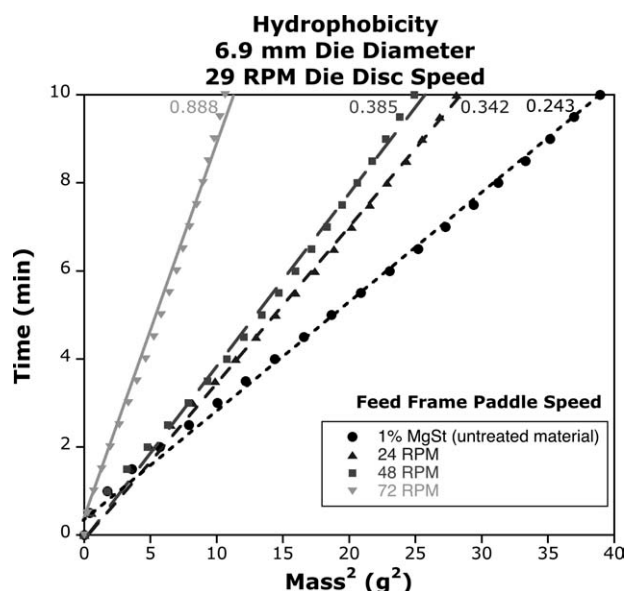


Figure 7. Time vs. mass square for blends with fast flow lactose and 1% MgSt as function of the feed frame paddle speed.

materials that experienced different total shears and that have different values of hydrophobicity. Moreover, if particle size and cohesion are also affected as a function of residence time, it is then possible to have the dies filled with material with nonuniform properties. This nonuniformity could cause problems with the tablet hardness and dissolution.<sup>14</sup>

Hydrophobicity measurements depend also on the packing of powders before starting the measurement. The reproducibility of packing is essential to obtain reproducible measurements.<sup>19,20</sup> As discussed above, most blends' packing was not

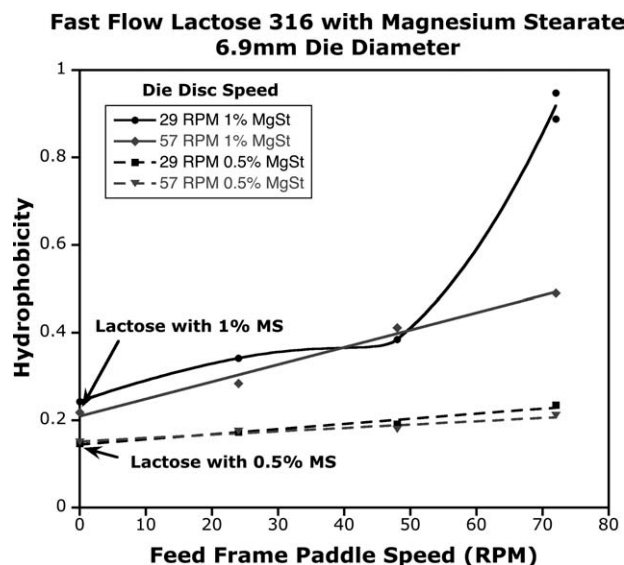


Figure 8. Powder hydrophobicity for blends with fast flow lactose and two different concentration of MgSt (0.5 and 1%) as function of the feed frame and die disc speed.

#### Fast Flow Lactose 316 with APAP and 1% MgSt 6.9 mm Die Diameter

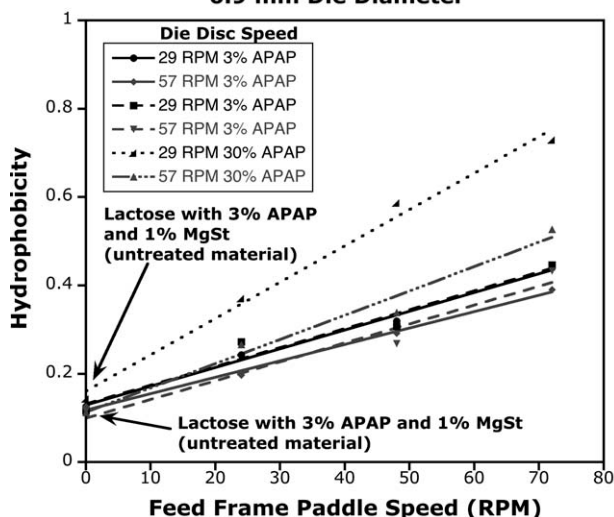


Figure 9. Powder hydrophobicity for blends with fast flow lactose, 1% MgSt and 3 or 30% APAP as function of the feed frame and die disc speed.

affected significantly by the processing it, therefore the hydrophobicity measurements must not be affected by packing.

#### Correlation between hydrophobicity and powder flow index and dilation

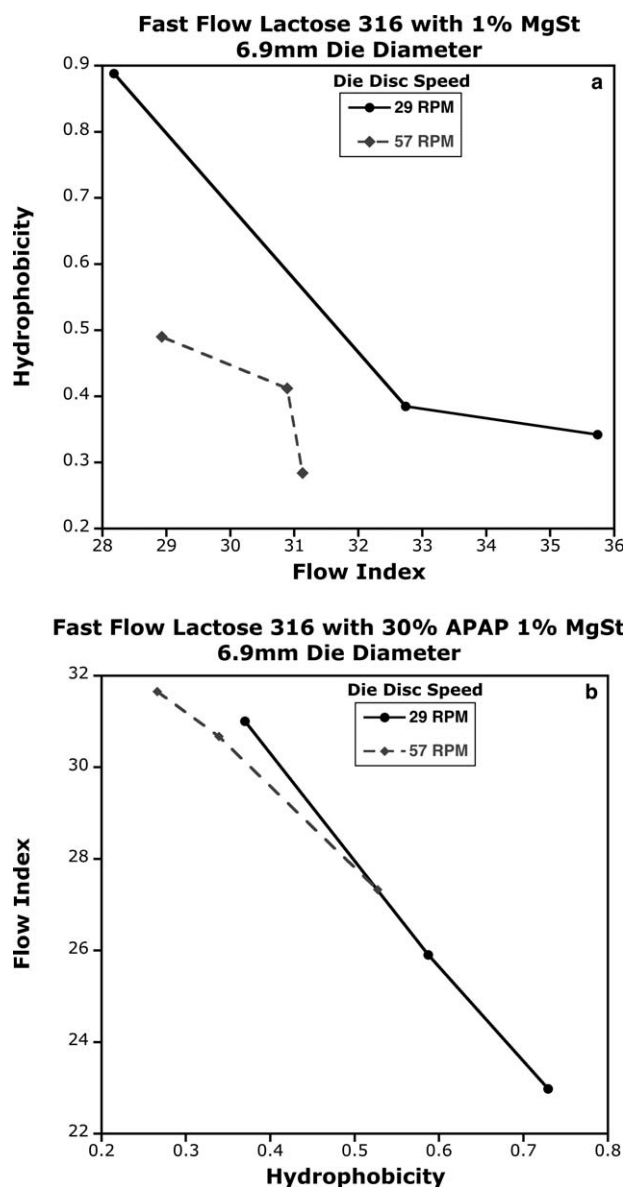
Previous work<sup>13</sup> showed the combined effects of the residence time and shear applied to the material on powder flow index for lubricated and nonlubricated blends. Figure 10 displays the correlation between the hydrophobicity of the blends and the powder flow index, both of which are affected by the feed frame operating conditions and the properties of the blend. The results demonstrate a marked decrease in powder flow index as the hydrophobicity increases, indicating that lubricated blends can experience enough shear in a feed frame to "overlubricate" them, leading to significant changes in flow properties.

Figure 11 depicts a correlation between hydrophobicity and powder dilation. Similar to the powder flow index, as the powder dilation decreases (i.e., as cohesion decreases), hydrophobicity increases. This indicates once again that the shear applied to the lubricated blend by the feed frame causes an overlubrication effect, decreasing the powder cohesion and the powder dilation.

For both the parameters, flow index and dilation, the changes in hydrophobicity were more significant for lower die disc speed and higher feed frame paddle speed. These conditions correspond to the higher shear applied and the lower flow index and dilation. These observations suggest that the main phenomenon inside the feed frame was the overlubrication of the powder by applied shear, which increased hydrophobicity while decreasing cohesion.

#### Tablet hardness and dissolution

Tablet hardness is one of the key attributes frequently used to describe and control the quality of pharmaceutical

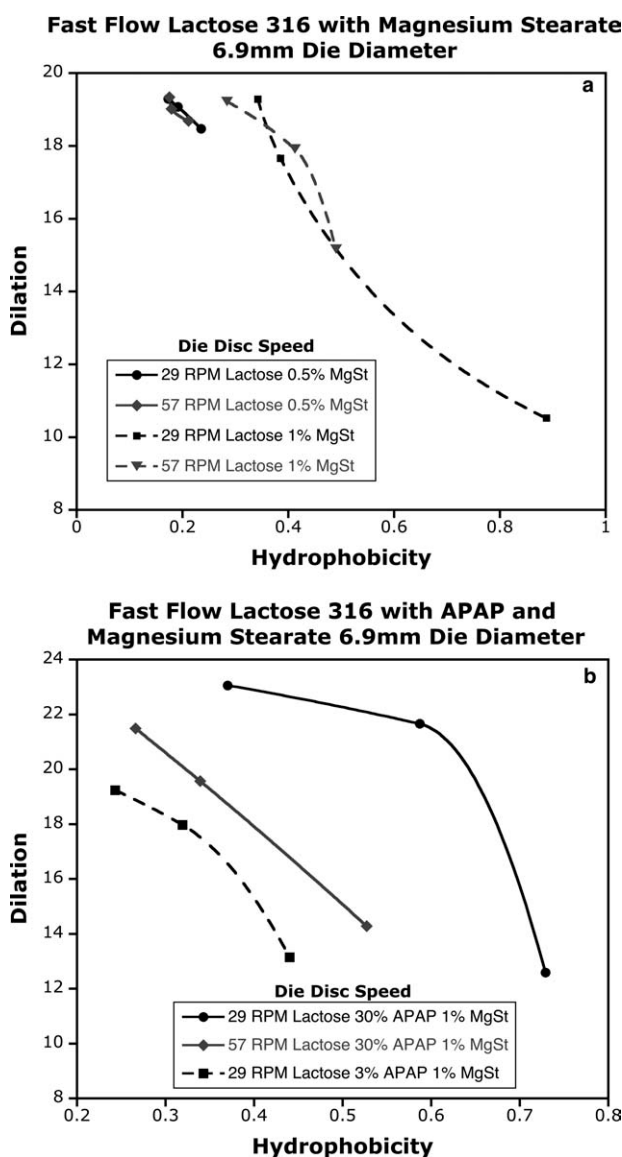


**Figure 10.** Correlation between the powder flow index and hydrophobicity for blends at different conditions of total shear applied in the feed frame for: (a) lubricated blends with fast flow lactose; (b) lubricated blends with fast flow lactose and APAP.

tablets. The effect of shear rate, total shear, and lubricant concentration, on tablet properties has been discussed quite extensively elsewhere.<sup>9</sup> The goal here was to study whether the total shear applied inside the feed frame at different operating conditions was enough to affect the quality of the tablets subsequently manufactured. To examine this issue, four samples, one collected before passing through the feed frame, and three additional samples collected after passing through the feed frame, subjected to different shear conditions, were used to prepare tablets. The weight variability and hardness of the tablets were then measured for a sample of 30 tablets from each operating condition. The tablet

weight variability was less than 1%. Figure 12 shows a linear behavior of the hardness for each of the four blends at different processing conditions for each compaction pressure. However, the results reveal a reduction in hardness only for a treated material relative to the nontreated blend, at constant compaction pressure. Table 4 includes the two-way analysis of variance of the effect of the feed frame paddle speed and the compaction pressure on tablet hardness and shows that the feed frame paddle speed does not impact significantly the tablet hardness.

Figure 13 examines the possible correlation between the tablet hardness and the hydrophobicity of the blend for three-compaction forces. The higher change in hardness was



**Figure 11.** Correlation between the powder dilation and hydrophobicity for blends at different conditions of total shear applied in the feed frame for: (a) lubricated blends with fast flow lactose; (b) lubricated blends with fast flow lactose and APAP.



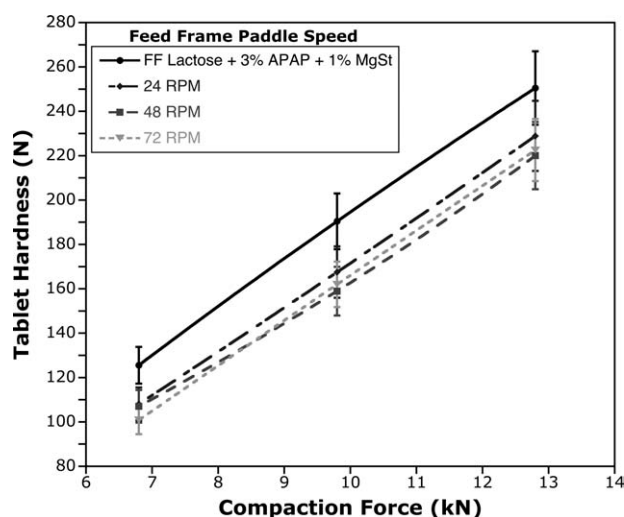


Figure 12. Tablet hardness for untreated and treated material inside the feed frame.

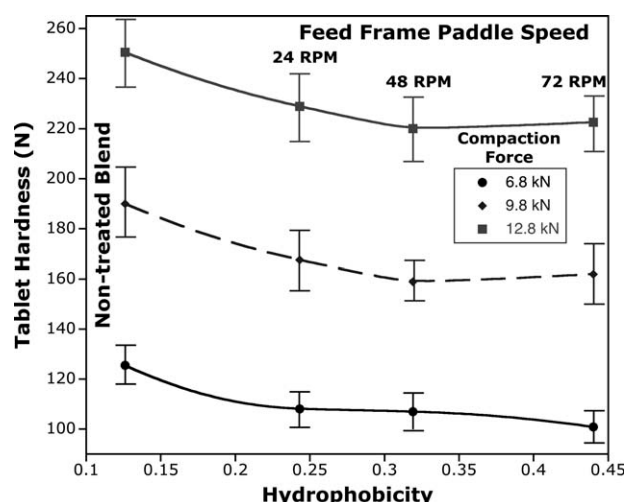


Figure 13. Powder hydrophobicity effects on tablet hardness.

observed between the nontreated and the material treated at 24 rpm in the feed frame, followed by the change between 24 and 48 rpm. Between 48 and 72 rpm, the values remained practically the same. Interestingly, the hydrophobicity effect on tablet hardness was similar for all the compaction pressures. The reduction in hardness between nontreated material and treated at 24 rpm is approximately 20 N for the three different forces.

Figure 14 compares the rate of dissolution of the tablets prepared with nontreated material lubricated with 1% MgSt to the tablets prepared with material exposed to three different shear conditions. The tablets were prepared at 12.8 kN compaction force. The results show a small reduction in the percent of drug released for the treated materials relative to the nontreated material. However, the treated material with three different applied shear rates produced similar dissolution rates.

## Conclusions

The effect of the feed frame on the powder blends properties depended on the blend composition, powder characteristics, and operating conditions. Results showed that the shear applied to the granular material inside the feed frame affected the final properties of the powder entering the dies. Hydrophobicity results demonstrated that the shear applied by the feed frame to the lubricated powder affected proportionally the overlubrication of the powders. The intensity of overlubrication effects also proportionally depended on the

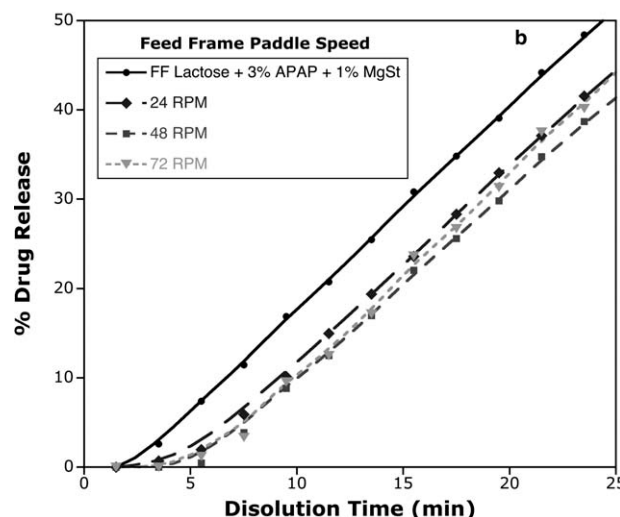
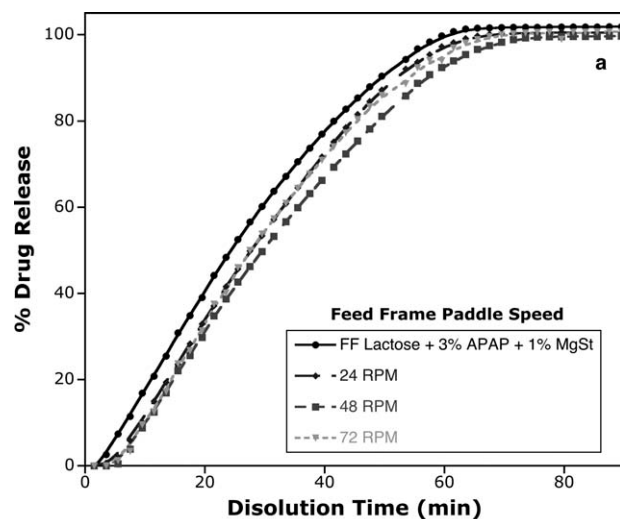


Figure 14. Dissolution rate at 12.8 kN for untreated and treated material inside the feed frame.

Table 4. ANOVA: Effect of the Feed Frame Speed and Compaction Pressure on Tablet Hardness at Die Disc Speed of 29 rpm

Source	DF	SS	MS	F	P
Feed frame speed	2	78.5	39.3	5.02	0.081
Compaction pressure	2	21077.8	10538.9	1346.91	0.000
Error	4	31.3	7.8		
Total	8	21187.6			

concentration of MgSt before entering the feed frame. A relationship with the hydrophobicity and the flow index and powder dilation was found and shows an increment in powder flowability when the hydrophobicity increases. The changes in hydrophobicity did not impact significantly the powder density of the blends studied. Large amounts of total shear applied reduced (1) the dissolution rate of drugs, (2) the hardness of tablets made from them, and (3) increased the powder flowability. The shear applied inside the feed frame had a small effect on the tablet hardness and dissolution results when compared with the nontreated material.

## Acknowledgments

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