# Roller Compaction Feasibility for New Drug Candidates

## Laboratory to Production Scale

**George W. Gereg* and Michael L. Cappola**

BOEHRINGER INGELHEIM PHARMACEUTICALS

**The authors developed a method to determine whether a drug candidate, excipient, or formula mix is suitable for dry granulation by roller compaction. Process parameters were determined with this model at laboratory-bench scale, and these parameters were translated directly to large-scale process equipment, thus saving time and materials during early product development. Various lactose materials, available as lactose monohydrate or spray-dried lactose monohydrate, were used as the model compounds. Results indicated that a parametric correlation can be made between laboratory-bench and production scale and many process parameters can be transferred directly.**

George W. Gereg is a research associate and Michael L. Cappola is a principal senior scientist at Boehringer Ingelheim Pharmaceuticals, PO Box 368, Ridgefield, CT 06877-0368, tel. 203.798.9988, fax 203.791.6197, ggereg@rdg.boehringer-ingelheim.com.

*To whom all correspondence should be addressed.

Roller compaction is a very attractive technology in the pharmaceutical industry. This methodology is an environmentally friendly process that has been the focus of heightened interest in recent years because of increased concern about environment effects and stringent regulations about the use of organic solvents (1).

Many components of solid dosage forms must be subjected to multiple processes, including those involving excipients and drug substances, before manufacture of the final product. Each excipient has a specific function, which requires that the product blend be homogeneous and provide good powder-flow characteristics. The particle size and density of the final blend must be suitable to promote this bulk powder flow. In general, fine powders do not have such characteristics. A process known as *granulating,* which masses fine powders into larger, denser granules, may be required for powder blends with poor flow. Dry granulation by roller compaction is a useful and efficient method of accomplishing these necessary powder characteristics (2). Other techniques, which also may be considered, include dry granulation by slugging and wet granulation.

Choosing the process of dry granulation by roller compaction has both product- and process-related advantages. In general, a major advantage of dry granulation over wet granulation is that no water or organic solvents are required, thereby making this methodology especially attractive for use with moisture-sensitive drugs as well as being environmentally friendly (1,3). In addition, the use of a roller compactor as the process equipment provides easy automation and efficiency.

This article describes a feasibility study that was performed to develop a method for identifying candidates that could be dry granulated by roller compaction. In these studies, the objectives were to characterize properties of the material, to identify process parameters suitable to achieve the necessary particle size and density using the dry granulation process, and then to translate laboratory information to a production-scale roller compactor.

### Materials

The following materials were used: lactose monohydrate (Granulac 200, type EPD80, Meggle, Germany); lactose monohydrate, modified, spray-dried, (Fast Flo 316 Grind, Foremost Farms

USA, Rothschild, WI); starch, pregelatinized (Starch 1500, Colorcon, West Point, PA). Materials were *USP–NF* grade. In this article, lactose monohydrate will be referred to as *regular lactose* or *regular-grade lactose.*

## Methods

**Material characterization.** The material bulk density was determined by filling a tared 100-mL graduated cylinder with powder to approximately the 70-mL mark and recording the exact volume. The cylinder was then weighed to determine the net powder weight. The bulk density, ρ, was calculated using the following equation:

$$\rho = \frac{w}{v_1} \quad [1]$$

in which ρ is the bulk (apparent) density, $w$ is the weight of the test material in the cylinder, and $v_1$ is the volume occupied by the powder (4).

The tapped density is the packing density after tapping a bed of powder until there is little or no change in the packing (2). Tap density was determined by tapping the graduated cylinder containing the powder for 1000 taps using a tap density tester (model 50-1200, Van Kel North America, Edison, NJ). The tap density, $\rho_t$, was calculated using the following equation:

$$\rho_t = \frac{w}{v_2} \quad [2]$$

in which $v_2$ is the volume occupied by the powder following tapping and $w$ is the original weight of powder in the graduated cylinder (4).

Samples were evaluated for their flow properties by using gravity flow through plastic funnels. The funnel sizes were 150-mm top inlet × 23-mm bottom outlet and 100-mm top inlet × 18-mm bottom outlet. Sample sizes were 50 and 25 g. The 25-g samples were evaluated in the smaller funnel. The amount of time it took for the funnel to empty the contents of material was recorded, and the flow rate was calculated using the following equation:

$$\text{Flow rate} = \frac{\text{sample weight}}{\text{elapsed time to empty}} \quad [3]$$

Results were the average of three trials.

An alternative expression used to predict powder flowability is the Carr or compressibility index, which is the ratio of the difference between the tap and bulk densities to the tap density, expressed as a percentage (2). The index has a direct correlation to the bulk granulation-particle packing ability. Carr index values between 15 and 25% usually indicate good flow characteristics, and readings above 25% generally indicate poor flowability (5). The Carr index was calculated using the following equation (2):

$$\text{Carr Index} = \frac{\text{tapped density} - \text{bulk density}}{\text{tapped density}} \times 100 \quad [4]$$

The static angle of repose, ϕ, is the maximum angle that can be obtained between a freestanding surface of a powder heap and the horizontal plane. These angles were measured from the powder heaps generated in the previously described flow studies. This measurement provided a qualitative assessment of the internal cohesive and frictional effects under low levels of external loading such as tablet die-filling operations.

The angle of repose was calculated using the following equation:

$$\tan\phi = \frac{2h}{D} \quad [5]$$

in which ϕ is the angle of repose, $h$ is the height of the powder heap, and $D$ is the diameter of the powder-heap base (5). The determination of the repose angle was the average of three trials. In general, values of ϕ between 20° and 40° indicate good flow potential. However, values of $\phi > 50°$ may have limited or no flow (5).

Sieve analysis was conducted on the test materials using a 10-g sample size. The test was performed with a sifter setting of sift–pulse for 1 or 2 min and pulse amplitude of 7 (ATM Sonic sifter, model L3P, ATM Corp., Milwaukee, WI). The 2-min duration was used for materials that visibly appeared more cohesive.

The test powders were introduced into the following tared nested-wire mesh screens: 1000, 500, 250, 125, and 63 μm, respectively. The net weight of the powder retained on the screen was determined. The percentage of material retained on each screen was calculated using the following equation:

$$\text{Percent retained} = \frac{\text{net weight on screen}}{\text{total net weight of sample}} \times 100 \quad [6]$$

The particle-size distribution and shape of particles were evaluated by light microscopy. Using a stereo microscope (model SZH, Olympus Optical Co., Japan), the maximum particle size (longest dimension) was determined. A representative sample of the material was placed into a deep well slide that contained a few drops of mineral oil. The slide with the sample was viewed using a calibrated reticule, and the particles were rotated in the oil with a tungsten wire so that the major axis could be measured. The size of the largest particle was recorded. The particle-size distribution was determined using a polarized light microscope (model BH-2, Olympus Optical Co.). A few drops of mineral oil were placed on a hemacytometer slide, and a powder sample was dispersed in the oil. A cover slip was then placed over the oil–powder mixture. A total of 200 to 400 particles was counted for each sample, evaluating particle ranges 1–5, 5–10, 10–25, 25–50, 50–100, and >200 μm.

Particle morphology was determined using a scanning electron microscope (model S-4000, Hitachi Ltd., Tokyo, Japan). Samples were prepared for scanning electron microscopy (SEM) imaging by sprinkling the powder particles on an aluminum stub with double-sided silver tape. The particles were then coated with platinum using a sputter coater.

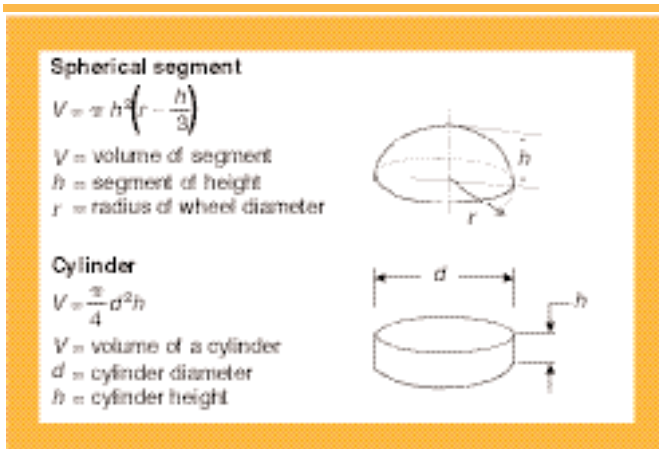


**Figure 1:** Diagram of compact volumes. Total volume of 1.2-cm compact = (2 × volume of spherical segment) + volume of cylinder. Total volume of 2.858-cm compact = volume of a cylinder.

**Compression evaluation; selection of compaction force–pressure.** The initial compaction profile of "neat material" was performed using 1.2-cm diameter, round, standard-cup concave punches in a special holding fixture. These compacts (1.2 cm) resembled tablets and could be evaluated with tablet-testing instruments. Approximately 500 mg of the material was weighed and transferred to the compact die where the material was compressed on a manual hydraulic press (Carver press model C, Carver Inc., Wabash, IN). Samples were compressed by applying a force from 500 to 10,000 lb in increments of 500 lb. The information recorded included compact weight, thickness, and hardness.

Compact volume, density, and pressure were calculated as follows: Compact volume (1.2-cm diameter compact) is described in Figure 1. The compacts comprised a midsectional cylinder and two spherical segments (reciprocal images of the upper and lower punches). The total volume was calculated by combining the volumes for all the segments as follows:

$$V = \frac{\pi}{4}d^2h_1 + 2\left[\pi h_2^2\left(r - \frac{h_2}{3}\right)\right] \qquad [7]$$

in which $V$ is the compact volume, $d$ is the compact diameter, $h_1$ is the cylinder or band height, $r$ is half the wheel diameter, and $h_2$ is the cup depth or height of segment (4,6). The wheel diameter was calculated as follows:

$$\text{Wheel diameter} = 4(D - \tfrac{1}{8}\text{ in.})$$

in which $D$ is the punch-tip diameter.

**Compact surface area (1.2- cm compacts), spherical segment.** The surface area of a spherical segment was calculated using the following equation (4):

$$A = 2\pi rh \qquad [8]$$

in which $A$ is the surface area, $r$ is half the wheel diameter, and $h$ is the segment height.

**Compaction pressure.** The compaction pressure was calculated using the following equation:

$$P = \frac{F}{A} \qquad [9]$$

in which $P$ is the compaction pressure, $F$ is the compaction force, and $A$ is the compact surface area (4).

**Compact density (laboratory compacts).** The compact density was calculated using the following equation:

$$\rho = \frac{W}{V} \qquad [10]$$

in which ρ is the compact density, $W$ is the compact weight, and $V$ is the compact volume (4).

**Compact density (roller compactor compacts).** The compact density was measured and calculated using an oil immersion technique. This method was used for "sticks" produced by the roller compacts because their density could not be calculated easily. Approximately 70 mL of a heavy mineral oil was added to a 100-mL graduated cylinder. The initial weight and volume were recorded. Approximately six sticks (compacts) were added to the oil, and the final weight and volume were recorded. Density was calculated as follows:

$$\rho = \frac{W_i - W_f}{V_i - V_f} \qquad [11]$$

in which ρ is the compact density, $W_i$ is the initial weight, $V_i$ is the initial volume, $W_f$ is the final weight, and $V_f$ is the final volume.

Compact thicknesses were measured using a handheld thickness gauge (model 1010M, Starrett Co., Athol, MA). Compact weights were measured using an analytical five-place balance (model AP250D Ohaus Balance, Analytical Plus, Ohaus Corp., Florham Park, NJ). Compact hardnesses were measured using tablet hardness testers (model 2E-106 and 6D, Dr. Schleuniger Pharmatron, Inc., Manchester, NH).

Compact friabilities of the 1.2-cm diameter compacts were measured using a tablet friabilator (Eberhard Bauer, Essingen, Germany) with five compacts. The initial weights of all five compacts were recorded. Compacts were placed inside the friabilator drum and rotated for 100 revolutions. After the test, the intact compacts were removed, and the final weights were recorded.

Percent friability of the compacts was calculated using the following equation:

$$\%\ \text{friability} = \frac{W_i - W_f}{W_i} \times 100 \qquad [12]$$

in which $W_i$ is the initial weight of the compacts and $W_f$ is the final weight (5).

**Laboratory preparation of regular-grade lactose granules. Selection of compaction force–pressure and milling conditions.** Compacts for the milling study were made on a hydraulic press using 1.125-inch (2.858 cm) round diameter, flat punches and matching

die. Approximately 4 g of the test material was weighed and transferred to the die and compressed. The lowest two forces to produce visibly nonfriable compacts were selected from the initial compression study. For the regular-lactose compacts, pressures were selected on the basis of a compact hardness range of 1.4–5.5 kp (kiloponds, in which 1 kp = 9.8 N) using 1.2-cm compacts. The compaction pressures for larger compacts were 10,000 and 15,000 psi, which were equivalent to 1500–2500 lb force of the smaller compacts. Several compacts at each pressure were made to evaluate granule integrity. These compacts were manually milled by rubbing them across an 18-mesh (1-mm opening) hand screen. Satisfactory granule integrity was accomplished if granules instead of fine powder formed from the compacts. Granule integrity was confirmed for these two pressures.

Using a mechanical cone mill (Comil model 193AS, Quadro Inc., Millburn, NJ) compacts (seven compacts) from each compaction pressure were milled alternately with the use of various mill screens (through 1.0- and 1.2-mm screens) to produce granules for evaluation. Granule properties were examined relative to bulk and tap density, Carr index, angle of repose (or flow), and sieve analysis. The final proposed compaction pressure was determined on the basis of the results of the milling study by selecting the most favorable granule properties.

Calculation of compact volume, density, and pressure were made on the basis of the compact size of 2.858 cm. Because the punches were flat, the equations for the compact surface area and volume were different from the initial tooling that was concave (see Figure 1).

The surface area of a flat-face circle was calculated using the following equation:

$$A = \frac{\pi}{4} d^2 \quad [13]$$

in which $A$ is the surface area and $d$ is the diameter (4).

The volume (cylinder) was calculated using the following equation:

$$V = A \times h \quad [14]$$

in which $A$ is the surface area and $h$ is the cylinder height. The pressure and density were calculated using Equations 9 and 10, respectively (4).

**Preparation of regular-grade lactose granules (production-scale roller compactor).** The selected compaction pressure, based on the results from the milling study, was translated from the hydraulic press (laboratory scale) to a production-scale roller compactor (model IR-520, The Fitzpatrick Co., Elmhurst, IL). The selected compaction pressure value was converted to total compaction force by multiplying the surface area of a compacted stick by the selected compaction pressure using Equation 16 below. This total compaction force then was applied to the roller compactor by converting it to pound-force per linear-inch of roll width, and finally, converted to hydraulic pressure using the manufacturer's conversion table (7). On the roller compactor, the roll gap was set for the desired compact thickness of 0.5 cm. The horizontal and vertical feed screws were adjusted to maintain a steady powder flow to the rolls.

The compact surface area was calculated using the following equation:

$$A = L \times W \quad [15]$$

in which $A$ is the stick surface area, $L$ is the stick length (roll width), and W is the stick width (axial groove width) (4).

The total compactor roll force was calculated using the following equation:

$$F = P \times A \quad [16]$$

in which $F$ is the total force between rolls, $P$ is the selected pressure, and $A$ is the compactor (stick) surface area (4).

The pound-force per linear-inch of roll width was calculated as follows:

$$F_1 = \frac{F_2}{W} \quad [17]$$

in which $F_1$ is the pound-force per linear-inch of roll width, $F_2$ is the total force between rolls, and $W$ is roll width (7).

The compactor hydraulic pressure was calculated as follows:

$$P = \frac{WF}{A} \quad [18]$$

in which $P$ is the compactor hydraulic pressure, $W$ is the compactor roll width, $A$ is the compactor hydraulic cylinder area, and $F$ is pound-force per linear-inch of roll width (7).

Milled compacts prepared by both the hydraulic press and the roller compactor were recompressed and evaluated. A compaction profile was prepared with increments of ~500 lb of force from 1500 to 10,000 lb. Compact hardness and density were determined for the recompressed compacts prepared on the hydraulic press and on the roller compactor. In addition, to evaluate formulation effects, 10% pregelatinized starch was added to each of the milled compacts. The mixes were recompressed and evaluated similarly for differences in density and hardness. Friability on the recompressed compacts from each method, with and without pregelatinized starch, was performed on the 5000-lb-force sample.

## Results and discussion

**Comparison of physical characteristics of regular-grade lactose versus spray-dried lactose.** Lactose was chosen as the model test material because it was available in more than one form (e.g., spray-dried and regular-grade lactose). The spray-dried lactose served as the reference material because it had the desired attributes of good flow and compressibility. Regular-grade lactose was selected to model a material that needed further processing to achieve desirable particle size, density, and flow (8). SEM photomicrographs and optical microscopy confirmed that the spray-dried lactose consisted of relatively uniform spherical particles as opposed to the regular-grade lactose par-

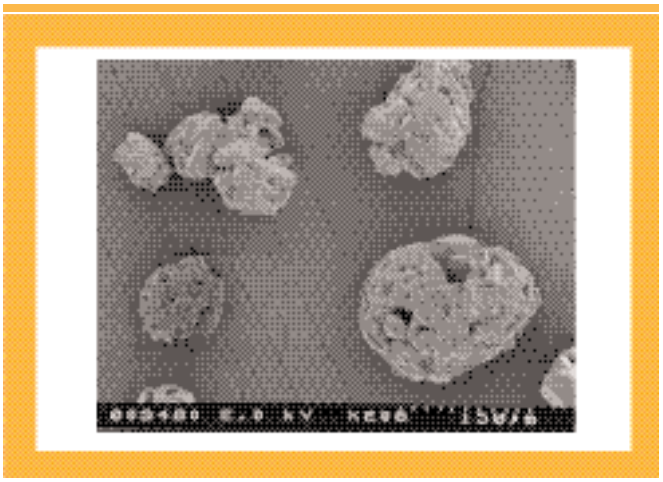

**Figure 2:** SEM photomicrograph of spray-dried lactose.

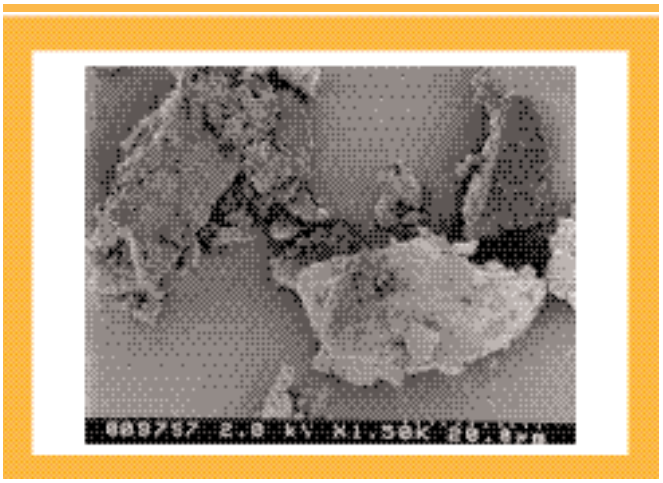

**Figure 3:** SEM photomicrograph of regular-grade lactose.

ticles, which were irregularly shaped and significantly smaller (see Figures 2 and 3).

Table I summarizes results of material characterization, including microscopy, bulk and tapped density, Carr index, angle of repose, flow rate, and sieve analysis. Comparison of the bulk and tapped densities indicated that the regular lactose had a greater difference between the bulk and tapped densities, resulting in a higher Carr index. The regular-grade lactose powder flow from a funnel was not possible without constant vibration from an external source. The majority of the regular-grade lactose particles (by microscopy) were sized <25 μm and irregularly shaped, and the majority of the spray-dried lactose particles were spherically shaped and sized ≥50 μm. Sieve analysis results paralleled those of microscopy, indicating a similar rank ordering. The spray-dried lactose showed excellent flow with a Carr index of 10.9%; however, poor flow was noted with the regular-grade lactose, which had a Carr index of 39%. The angle of repose for the spray-dried lactose was 8.6°, and those of the hydrous lactose was 41.4°. The angle of repose measurements again confirmed the much better flow characteristics of the spray-dried material.

**Compression evaluation of regular-grade lactose versus spray-dried lactose.** These studies were conducted to determine the compressibility of both regular-grade lactose and the spray-dried lactose. A density–compression profile for both materials was generated. Figure 4 shows both materials had an increase in density with an increase in compaction force. The spray-dried lactose was more compressible, achieving greater density after a force of ~3000 lb was applied. Maximum densities for the regular-grade and spray-dried lactose were 1.40 and 1.45 g/cm$^3$, respectively.

**Table I: Material characterization.**

| Test | Regular-Grade Lactose | Spray-Dried Lactose |
|---|---|---|
| Microscopy | Irregular shapes majority <25 μm | Uniformly spherical majority 50–100 μm |
| Bulk density (g/cm$^3$) | 0.54 | 0.63 |
| Tapped density (g/cm$^3$) | 0.89 | 0.70 |
| Carr index (%) | 39.0 | 10.9 |
| Angle of repose (°) | 41.3 | 8.6 |
| Flow rate (g/s) | 1.8* | 50 |
| Sieve analysis | 61% <63 μm | 82% 63–125 μm |

Required constant vibration to maintain flow.

**Table II: Granule characterization of regular-grade lactose: milled laboratory compacts.**

| Test | Starting Material | Compacts 10,000 psi Mill Screen: 1.0 mm | Compacts 10,000 psi Mill Screen: 1.2 mm | Compacts 15,000 psi Mill Screen: 1.0 mm | Compacts 15,000 psi Mill Screen: 1.2 mm |
|---|---|---|---|---|---|
| Bulk density (g/cm$^3$) | 0.54 | 0.58 | 0.60 | 0.57 | 0.64 |
| Tapped density (g/cm$^3$) | 0.89 | 0.97 | 1.0 | 0.96 | 0.98 |
| Carr index (%) | 39.0 | 39.7 | 42.8 | 40.9 | 34.2 |
| Angle of repose (°) | 41.3 | 29.3 | 28.8 | 28.3 | 29.8 |
| Flow rate (g/s) | 1.8* | 2.2* | 3.4* | 1.8* | 15.0 |
| Sieve analysis | 61% <63 μm | 38% <63 μm | 27% <63 μm | 31% <63 μm | 17% <63 μm |

*Note: required constant vibration to maintain flow.

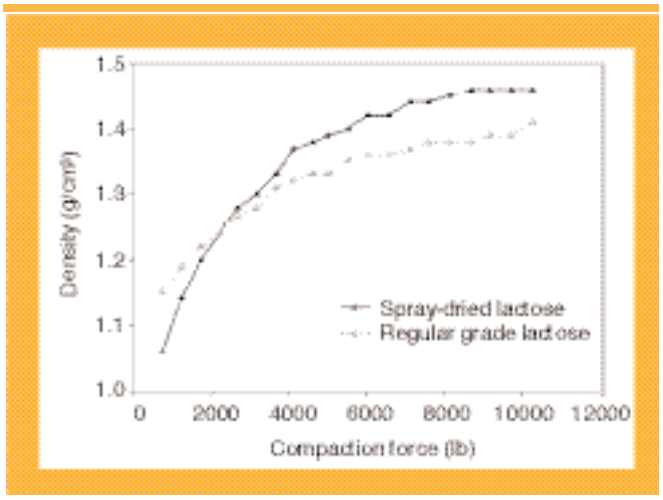


**Figure 4:** Compact density: regular-grade lactose versus spray-dried lactose.

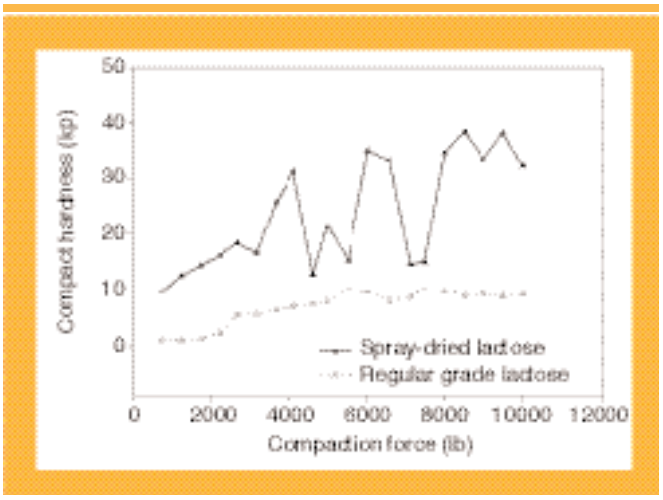


**Figure 5:** Compact hardness: regular-grade lactose versus spray-dried lactose.

Because the prepared compacts were round, they could be evaluated easily for diametrical crushing force (hardness). A hardness test provided a measure of the overall integrity of the compact and the potential of producing nonfriable granules (9). Figure 5 shows that the spray-dried lactose had a greater range (10–35 kp) of compact hardness than did the regular-grade lactose. Variation was greatest after a force of 3000 lb was applied, which may be a result of the various particle packing between the different forms of lactose upon compression. The regular-grade lactose had a lower maximum compact hardness of ~8 kp at 5500 lb with much less variability.

A compact should have sufficient hardness and density to be milled without pulverizing back into fine powder (9). This property was evaluated by a granule-integrity test. The test provided a method to predict the milling consequences for compact and associated compaction pressure. For the regular-grade lactose compacts, the pressures were selected on the basis of a compact hardness range from 1.4 to 5.5 kp using 1.2-cm compacts. Larger compacts (2.858-cm) compressed at corresponding pressures withstood the granule test and seemed acceptable visually. These forces were at the low end of the compaction profile and represented a conservative pressure for material to be further processed and recompressed.

**Preparation of regular-grade lactose granules. Selection of compaction force–pressure and milling conditions.** Using the compaction pressures that showed good granule integrity for the regular-grade lactose, a milling study was performed to select the best compaction pressure and screen size for mechanical milling. The compacts were milled separately with rasp screens of 1.0 and 1.2 mm.

The selection of compaction pressure and screen size was determined to be 15,000 psi and 1.2-mm screen, respectively. These conditions provided granules with the least amount of fines and the overall greatest potential for powder flow (see Table II). Although the Carr index was 34.2%, indicating the potential for poor powder flow, the angle of repose was 29.8°, conversely indicating acceptable powder flow characteristics. The measured flow rate was approximately one order of magnitude greater than that of the starting material, with the majority of

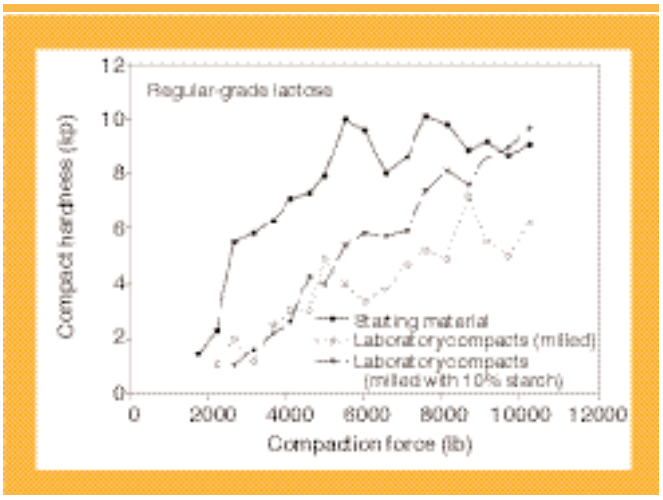


**Figure 6:** Recompression of regular-grade lactose granules from compacted lactose.

particles sized >63 µm. Consequently, the compacted and milled regular-grade lactose now had a greater density, larger particle size, and much greater powder flow.

**Granule recompression of regular-grade lactose.** Powders that have been compacted and milled are generally not as compressible after the initial compression (2). This is the reason for supporting the attempt to densify by compaction only to the degree necessary for nonfriable granules. Hence, the milled compacts prepared at 15,000 psi and milled through a 1.2-mm rasp screen were evaluated for recompression into 1.2-cm round compacts. Figure 6 shows that these recompressed compacts generally were softer than compacts made from the starting materials. This is a common effect that happens to powders after dry granulation. Although the compressed material does lose some compressibility after initial compaction, it is generally suitable for further processing into a final dosage form (2). Additional excipients also may be added to enhance compressibility. When 10% pregelatinized starch was added to the compacted–milled material, evaluation after recompression yielded

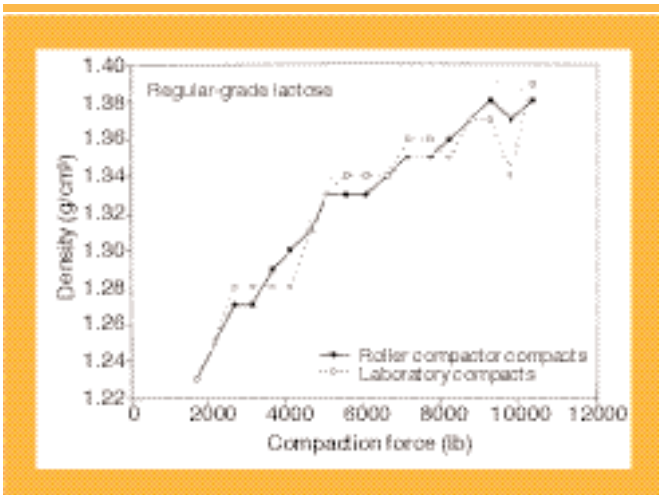


**Figure 7:** Comparison of compact density between recompressed regular-grade lactose from laboratory and roller compactor method.

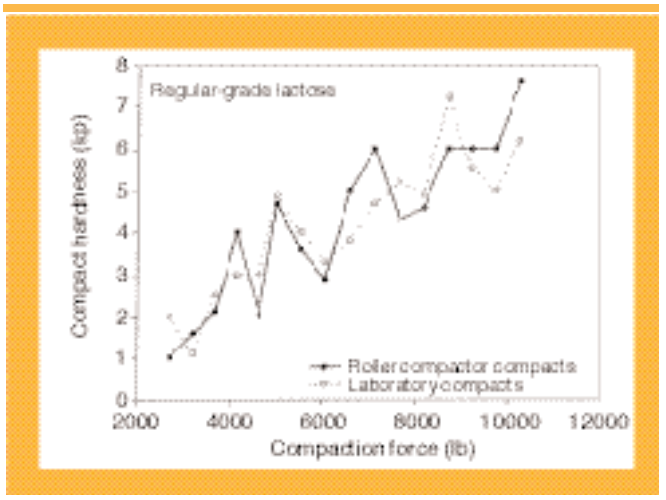


**Figure 8:** Comparison of compact hardness between recompressed regular-grade lactose from laboratory and roller compactor method.

**Table III: Granules comparison of regular-grade lactose: laboratory versus roller compactor compacts.**

| Test | Laboratory Compacts | Roller Compactor Compacts |
|---|---|---|
| Morphology SEM | agglomerated chunks | agglomerated chunks |
| Bulk density (g/cm$^3$) | 0.64 | 0.72 |
| Tapped density (g/cm$^3$) | 0.98 | 0.94 |
| Compact density (g/cm$^3$) | 1.3 | 1.3 |
| Carr index (%) | 34.2 | 23.7 |
| Angle of repose (°) | 29.8 | 28.7 |
| Flow rate (g/s) | 15.0 | 28.2 |
| Sieve analysis | 17.4% <63 μm | 14.0% <63 μm |

**Table IV: Compact friability comparisons: laboratory versus roller compactor.**

| Material | Laboratory Compacts % Friability | Roller Compactor Compacts % Friability |
|---|---|---|
| Regular-grade lactose | 1.5 | 4.9 |
| Regular lactose with 10% pregelatinized starch | 0.38 | 0.54 |

an increase in compact hardness of 30–40% (after 5000-lb force) (see Figure 6). Therefore, densification, by dry compaction, can be optimized with formula additives, if necessary.

This study confirmed that regular-grade lactose could be compacted, milled, and recompressed to provide the particle size, density, and powder flow needed for further processing. In addition, compression studies of the dry granulated–milled material suggested that although recompression yielded compacts of lower hardness values, this material was still very compressible and formulation additives such as pregelatinized starch could additionally increase compressibility.

**Preparation of regular-grade lactose granules (production-scale roller compactor).** Compacts were prepared from regular-grade lactose on the roller compactor using conditions determined in the laboratory with the hydraulic press. The rolls on the roller compactor were full axial rolls that produce compacts in the form of "sticks" (10). Unmilled compacts of both types (laboratory–roller compactor) had the same density of 1.3g/cm$^3$.

Table III lists a comparison of granules after milling using each method. Both materials were very similar, with the major difference being in the bulk density and, correspondingly, the Carr index. The geometry of the starting material (compacts) probably was accountable for the difference. Milling of sticks generated a slightly greater population of larger particles, whereas milling of the round disks from the laboratory work produced a greater number of fines. The flow rate for the milled roller-compacted material was approximately twice as fast as that for the laboratory material, with both flow rates being acceptable.

Both methods for densifying regular-grade lactose produced material with similar density, compressibility, and suitable powder flow. For all practical purposes, these methods can be considered equivalent.

**Granule recompression of regular-grade lactose (laboratory versus roller compactor).** Figure 7 shows that both the recompressed laboratory-scale and roller-compactor material yielded similar densities. Recompressed compacts made from both materials had a similar hardness profile (see Figure 8). When the compacts were subjected to friability testing, both materials had friabilities >1% (see Table IV). Figure 9 and Table IV show that when 10% pregelatinized starch was added, compacts produced by either method had similar increases in hardness with a reduction in friability.

**Summary of process.** Figure 10 presents a summary of the method from initial evaluation of material to production on a roller compactor.

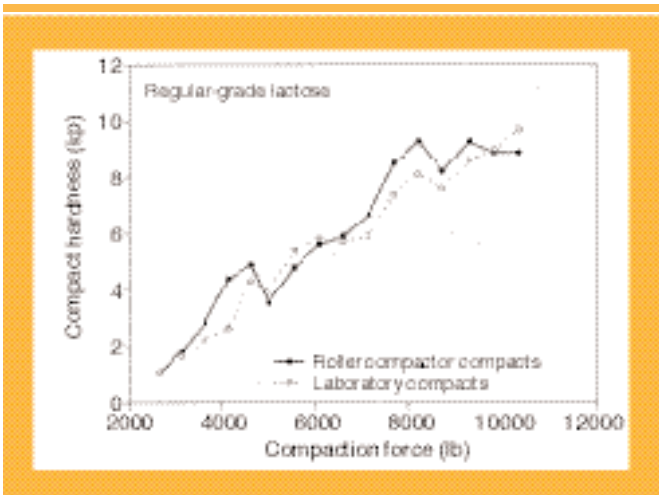


**Figure 9:** Comparison of compact hardness between recompressed regular-grade lactose from laboratory and roller compactor method with 10% pregelatinized starch added.

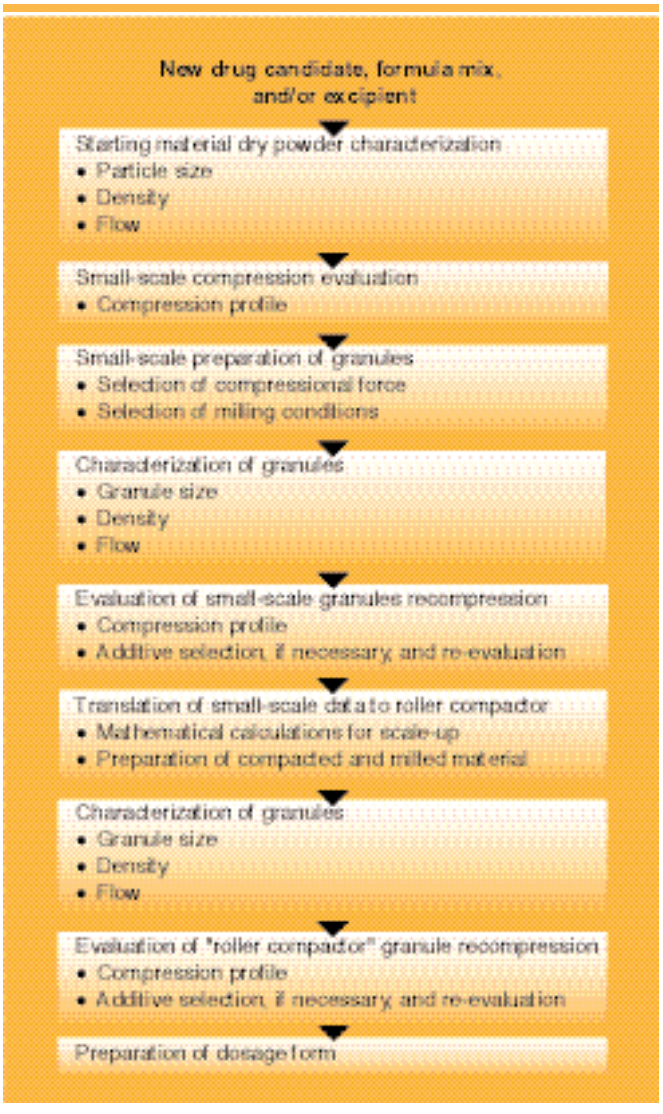


**Figure 10:** Flow chart of feasibility study.

## Conclusion

This study provides a method to predict whether a material is suitable for dry granulation. For a material to be dry granulated, it must be compressible, have a consistent increase in density with force, and be suitable for milling and possible recompression. Information generated in the laboratory on a hydraulic press can be correlated and scaled up to a production-scale roller compactor to produce dry-granulated material that has very similar powder–granule characteristics.


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