The functions of single- and bi-layer tablet presses are similar, but bi-layer presses pose unique challenges. If you don’t address them, you risk wasting material and extending formulation development and manufacturing times. This article describes some of the techniques and tools you can use to increase product yields, identify setup issues, and improve the process to get your product to market.

Bi-layer tablets have become popular in the pharmaceutical, dietary-supplement, and other industries. Advantages include their ability to control release, combine otherwise incompatible APIs and excipients, and differentiate brands. In controlled-release applications, formulators use novel techniques that take advantage of the functional properties of one layer to control the release of the other layer. Osmotic release is one example.

Bi-layer tablets can also improve patient compliance by reducing the number of daily doses required and simplifying regimens. In fact, as the population skews older, more people will need more medicine so the future of bi-layer tablets grows brighter.

But with the many advantages of multi-layered tablets comes the challenge of successfully producing them on the tablet press. While the principles of making bi-layers are similar to those of single-layer tablets, the operation requires more attention to detail. Examples of these challenges include using the appropriate instrumentation to monitor and control force, keeping the APIs separated to avoid cross-contamination, and preventing excessive waste of material due to incorrect press setup.

In many cases, a tablet press that produces bi-layers can be converted to produce single-layer tablets, which extends the return on your investment in the equipment. You can also set up the tablet press to produce bi-layers that comprise the same formulation, which enables you to achieve a higher-weight tablet than would be possible using a single-layer setup.
Characterizing the individual layers

Before jumping into bi-layer tabletting, understand the characteristics of each tablet layer. How do you determine which layer is going to be the first layer and which second? Due to the design of bi-layer tablet presses, it may be better to designate the material requiring a higher fill depth as layer one. But when the material can be formed as either layer, use the material that benefits more from pre-compression as layer one. Pre-compression is essentially a de-aeration stage that consolidates the particles and helps produce a more robust tablet.

The graph in Figure 1 shows the results of a compaction profile study of individual layers. Compaction profiles are a very effective tool for developing formulations because they help you understand the physical properties of the materials and tablets when compressed at different force levels. The conventional way of presenting compaction data is to show the relationship between the applied compression force and the resulting breaking force, which is erroneously but commonly referred to as tablet hardness. This relationship between compression force and breaking force changes, however, as the geometry of the tablet changes. Thus, a more meaningful approach is to convert the applied compression force to compression pressure and convert breaking force to tensile strength.

In Figure 1, Material A reaches its maximum compactability at 218 megapascals (MPa) of compaction pressure, and during breaking force tests, capping was observed in tablets produced at higher pressures. Capping refers to tablet failure on the horizontal plane (not the diametrical aspect). There are many causes of capping, including excessive fines, entrapped air, and too much lubricant. In a repetition of the study that included the addition of a small amount of pre-compression pressure, Material A performed better. Compactability increased and capping was not observed until force exceeded 255 MPa.

Material B showed higher compactability and did not benefit from the addition of pre-compression force. In this case, Material A is the clear choice for layer one since it will undergo two compression events, with the layer-one compression rollers providing the pre-compression.

Figure 2 shows the results of a strain rate study performed on individual layers. The strain rate study helps you understand the compaction properties of materials compressed at different loading rates or dwell times. Tablets made from some excipients and APIs are acceptable (i.e., good mechanical strength) when made on a small R&D press, but fail when made on a high-speed, large-scale manufacturing press. Such materials are said to be strain-rate sensitive. Studying strain rate is helpful because it can indicate the potential for problems when you scale up to a commercial press.

In the graph in Figure 2, the bottom axis is normalized for the turret’s pitch circle diameter, which allows you to compare data from studies that used different turret sizes. The left axis is the tablet strength, and the results have been normalized for any weight loss stemming from shorter feeder dwell times.

The red trace represents a material that is strain-rate sensitive. This material is characterized as a plastic or ductile-dominant material. The material represented by green trace does not show significant adverse effects and can be characterized as a material in which brittle fracture dominates. In this case, the plastic material would perform better as the first layer because it would benefit from pre-compression.

Most modern bi-layer tablet presses have compression rollers of equal diameter but in the past most used a smaller roller for layer one (pre-compression). Today’s larger rollers increase the loading rate and can help make good tablets from a strain-rate sensitive material because they allow more time for the material’s particles to consolidate and for interstitial air to be tamped out.

Proper setup maximizes yield

The fill cam is one variable among many that influence product yield and it is often overlooked. Located under the lead section of the feeder, the fill cam pulls the lower punch down to enable the feeder to deliver powder into the die. The size of the fill cam (photo) indicates the maximum
depth of the void it can create, and that depth should slightly exceed what the final weight cam allows. The deeper void causes overfilling, which promotes tablet weight uniformity. But if the overfill is too great or if the settings of the fill cam and weight cam differ excessively, too much material will recycle to the feeder, where it can become over-blended. And should the feeder get full, the excess material can be lost to the vacuum collection system. In fact, some powders can jam the paddles and drive motor.

Note the difference here between single- and bi-layer tablet presses. A single-layer press directs excess powder to the center of the turret and, as the turret rotates, the material can re-enter the leading side of the feeder. But a bi-layer tablet press cannot allow material to rotate with the turret because that would contaminate the other layer. It is thus very important to select a fill cam of the appropriate size or you will diminish product yields.

Fill cam selection is based on the tooling geometry, material bulk density, and tablet weight. First, calculate the tablet volume by dividing the tablet weight by the bulk density of the material:

\[
\text{Tablet volume} = \frac{\text{Tablet weight}}{\text{Bulk density}}
\]

Next, calculate the weight cam setting by dividing the tablet volume by the cross-sectional area of the punch tip:

\[
\text{Weight cam depth} = \frac{\text{Tablet volume}}{\text{Punch tip’s cross-sectional area}}
\]

Once you know the weight cam depth, select the fill cam that will allow a slight overfill. Table 1 provides a guideline for selecting fill cams.

When making bi-layer tablets, the penetration of the upper punch for layer one dictates the maximum weight of layer two. In other words, the upper punch penetration of the first layer acts as the fill cam, creating the void in the die that accepts the second layer. Be sure to optimize this setting in order to minimize the problems that ensue from excessive overfills as described above.

Once the weight cam is dialed in and the proper fill cam selected, you might have to make minor adjustments to the weight cam to compensate for the rotation of the turret, which affects feeder dwell time. Feeder dwell time is the period during which the lower punch remains under the feed system to allow the die to accept a charge of material.

The equation on the next page is a simple formula for fine-tuning the weight cam depth based on the initial weight cam depth and tablet weight.

<table>
<thead>
<tr>
<th>Required weight of fill (mm)</th>
<th>Fill cam (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 to 5</td>
<td>6</td>
</tr>
<tr>
<td>5 to 8</td>
<td>9</td>
</tr>
<tr>
<td>8 to 11</td>
<td>12</td>
</tr>
<tr>
<td>11 to 14</td>
<td>15</td>
</tr>
<tr>
<td>15 to 18</td>
<td>19</td>
</tr>
</tbody>
</table>
Initial or actual weight \[ \text{Target tablet weight} = \frac{\text{Initial or actual weight}}{\text{cam depth}} \times \frac{\text{Target tablet}}{\text{weight}} \frac{\text{cam depth}}{\text{Initial tablet weight}} \]

Over-blending in the paddle feeder can also affect tablet compactability, especially in formulations with a high amount of lubricant. Over-blending can also affect disintegration times. If either becomes a problem, see how slowly you can operate the paddle feeder while still producing tablets of correct weight consistently.

**Cross-contamination**

Cross-contamination is the intermingling of the first and second-layer powders or vice versa. Dust collection goes a long way toward preventing cross-contamination but it needs to be balanced against excessive material loss. There are several steps you can take to prevent loss:

- Ensure turret run-out is less than 0.003 inch;
- Set the feeder table at a height that prevents excessive powder from reaching the turret;
- Examine the scraper bars for wear and replace as necessary;
- Ensure that the dies fit tightly and don’t allow powder to lodge in crevices;
- Verify that the vacuum is set as the manufacturer recommends. If the vacuum is too strong, it will pull powder from the feeder. If set too low, it will allow the powder to contaminate the other layer; and
- Secure all vacuum hoses and ports tightly.

**The importance of instrumentation**

Making good bi-layer tablets consistently requires using force instrumentation during development and manufacture. Without high-quality data acquisition, you cannot know how the press is running. In fact, you’ll waste time, effort, and powder as you test tablet samples just to discover that the press needs adjustments. After that, it may take you hours to optimize the operation.

Opt for a high-quality data-acquisition system instead. While a complete system has many aspects, let’s focus on the importance of dedicating a compression transducer to monitor the creation of the tablet’s first layer.

Most bi-layer tablet presses exert as much as 80 to 100 kilonewtons (kN) of compression force on both layers, and a force transducer rated for 80 kN typically has a full-scale error margin of 0.25 percent, a range of ±200 Newtons (N). Furthermore, the target tamping force for the first layer is typically in the range of 1 to 2 kN. Thus, an error of 200 N represents a measurement error of 20 percent at 1 kN of force.

To reduce the magnitude of this error:

- Use a force transducer designed for a full scale of 25 kN instead of 80 kN. You can do this by reducing the web thickness in the strain pockets, which results in a similar stress at a lower force;
- Change the transducer material from steel to a softer material, such as aluminum bronze, which will generate a greater electrical output due to a reduction in the modulus of elasticity;
- Use platinum-tungsten or semi-conductor strain gages instead of constantan (copper-nickel alloy) to generate a greater electrical output;
- Tighten the restraints on the software filter to improved the signal-to-noise ratio; and
- Install a mechanism that shuts down the tablet press when force exceeds 25 kN of compression to protect the transducer.

These improvements will provide the measurement accuracy you need to monitor and maintain the compression force of layer one. It’s also good practice to display force in real time because you can set up the press faster and quickly identify weight variations.

Figure 3 shows the real-time force readings of a simulated compression of layer one. Note that it shows 16 compression events and the average peak force is 994.7 N. By displaying each peak force, you can gauge the variability between stations. The relative standard deviation (RSD) percentage of the compression force appears at the bottom of the chart.

During development, the press commonly does not use an automatic weight control system, and thus any variability in tablet weight will directly affect the compression force. In this example, the compression forces are uniform, which means the tablet weights are consistent.

![Figure 3](https://via.placeholder.com/150)
During actual manufacturing, however, the tablet press commonly would use automatic weight control and a rejection gate so that you can collect tablets that are within specification. With today’s technology, tablet presses can control the tablet weight of layer stages, not just the final compression. Even so, there is no substitute for a thorough examination of the tablet press setup. The checklist above covers the basics. T&C

Robert Sedlock is technical sales manager at SMI, 1309 Route 22, East Lebanon, NJ 08833. Tel. 908 534 1500, fax 908 534 1546. Website: www.smitmc.com.