Maintaining the correct bulk density is critical to manufacturing on-spec tablets. This article outlines the benefits of shear cell testing to measure the bulk density of powders and granulations.

To a layperson, manufacturing tablets must look simple. A powder flows into dies, gets compressed between two punches, and out pops a tablet. The process is more complex than that, of course, and a good deal of that complexity stems from the fickle nature of powders. Even small changes in their properties can affect how they behave on a tablet press. That's why it's important to measure the characteristics of powders and granulations during production. Once you see a change, you can adjust the powder and/or the process to maximize uptime and maintain yield.

Whether your tablets are pharmaceuticals, dietary supplements, or something else, the process to make them doesn't differ much. Nor does the goal: Produce high-quality products at high rates. After all, maximum production at maximum speed equals maximum profit. Yet each product's starting powder has unique characteristics, including flow properties, so they all need to undergo accurate, quick, and repeatable flow tests during production.

This article explores the flow problems associated with tablet making and how to conduct precise QA/QC tests that ensure maximum production while maintaining on-spec tablet weight and hardness. One test method, shear cell testing, can reveal your powder's flow metrics and support all facets of the tablet making process.

The tabletting process

Most readers need no explanation of the tabletting process, but if you're new to tablet making, it's important to understand this fact about it: The tablets you make must remain within the specified weight range, but the press itself operates without reference to weight. Instead, it depends on being fed a powder of consistent and uniform bulk density to fill the fixed volume of its dies. That's how—presuming the press is set up correctly—the tablets meet the weight specification.

In practice, however, things change and we must adjust for those changes to ensure we get a good product. Plus, because tablet presses can make hundreds of thousands of tablets per hour, just one misstep can lead to the production of a lot of inferior tablets in a very short time. Factor in the high value of today's active pharmaceutical ingredients (APIs)—perhaps millions of dollars per kilogram—and it becomes obvious that it's worth your time to prevent poor flow, changes in bulk density, segregation, or a jammed feeding system from upsetting production.

What's in a tablet

In addition to the API, tablets comprise a variety of excipients, including binders, disintegrants, flavorings, glidants, and lubricants. Ideally, we would blend these ingredients, send them to the press, and make good tablets. In reality, each ingredient can differ in particle size, size distribution, shape, density, and many other ways. Those differences can cause segregation, creating a nonuniform, poorly flowing powder. To avoid that problem, powder blends often undergo a wet or dry granulation process that increases homogeneity.

Wet granulation is the traditional and perhaps most popular method. It is extremely reliable and improves not only the flow but the compaction properties of powders. Typically, it entails combining the dry powder blend with a liquid binder inside a high-shear mixer. The material is then dried and milled to create particles of uniform size, density, and composition. With dry granulation, the API-excipient...
blend is compressed, typically in a roll compactor, and then milled and sieved.

At the tablet press, the granulation flows from a feed hopper and is fed by a gravity or paddle feeder into dies. The granules are usually small, and sometimes that leads to arches or jams in the feeding system. That's because, generally speaking—and there are many other variables that come into play—the smaller the particles, the harder it is for a powder to flow. As a rule of thumb, particles smaller than 50 microns are cohesive and hinder flow. Particles between 50 and 100 microns can be cohesive to easy flowing, and particles larger than 100 microns usually flow easily. Of course, the properties of the substance itself and environmental factors (temperature, humidity) can also affect how well a powder flows. Figure 1 shows the flow function of a powder, and the regions of flow are designated as very cohesive, cohesive, easy flowing, and free flowing.

Getting the correct amount of powder into the die is critical, because over- or under-filling it will lead to off-weight tablets and other problems. A jam during tabletting that starves the feeder and leads to empty dies can severely damage the press and its tooling. So again, it's worth your time to evaluate the powder's flow properties before and during production. In addition to checking flow behavior, you should measure the powder's bulk density and compare it to a target value. Only when it's on or very near that target can the tablet press apply the correct amount of pressure to produce a good tablet.

In fact, bulk density measurement defines the optimal force to apply, and if the bulk density changes for any reason—due to temperature, humidity, incorrect blending, or out-of-spec ingredients—and you don't adjust for it, the press might apply the wrong amount of force. Once you calibrate the press to apply the correct amount of force, monitor the bulk density of the powder. If it increases, the press will likely not apply enough force, causing the tablet to cap or laminate. If the bulk density decreases, the press is likely to apply too much force, crushing the powder and perhaps damaging the tooling or the press itself. While capsule filling machines operate differently from tablet presses, they too require powders with a consistent bulk density to ensure accurate dosing and smooth operation.

By quickly and accurately identifying a change in bulk density, you can adjust the tablet press to apply the correct amount of force. That's where a shear cell can help. It provides accurate, cost-effective, and timely flow measurement data—essentially an assessment of overall flow behavior.
The inaccuracy of common tests

Many different instruments can characterize or predict flow behavior, but most are fairly expensive—between $50,000 and $100,000—and some companies are reluctant to make that capital expenditure. Instead, they opt for inexpensive flow tests that aren’t up to the task.

The most common test is tapped density—described in USP General Chapter <616> and in ASTM D7481-09—which assesses the compressibility of a powder. To begin, a specified quantity of powder is placed in a cylinder of known volume. Next, a mechanical device repeatedly taps the cylinder, causing the powder to settle. Once the specified number of taps is delivered, you compare the settled volume to the original freely settled volume. The Hausner Ratio is correlated to the flowability of a powder or granular material. It is calculated by the formula

\[ H = \frac{\rho_T}{\rho_B} \]

where

\( \rho_T \) is the tapped bulk density of the powder and
\( \rho_B \) is the freely settled bulk density of the powder.

A Hausner Ratio greater than 1.25 is said to indicate poor flowability. But the Hausner Ratio is not an absolute property of a material; its value can vary depending on the methodology used to determine it. Nonetheless, it is used in a variety of industries to indicate powder flowability.

The Carr Index is also said to measure flowability and, like the Hausner Ratio, it uses the difference in the tapped and loose densities. It can be expressed as

\[ C = 100 \times \left(1 - \frac{\rho_B}{\rho_T}\right) \]

where

\( \rho_B \) is the freely settled bulk density of the powder and
\( \rho_T \) is the tapped bulk density of the powder.

A Carr Index greater than 25 is said to indicate poor flowability, and a value of 15 or less indicates good flowability.

The Hausner Ratio and the Carr Index are sometimes criticized—despite their relationships to flowability being established empirically—as not having a strong theoretical basis. Use of them persists, however, because the equipment required to perform the analysis is relatively cheap and the technique is easy to learn.

Another simple but flawed test measures angle of repose. For this test, you pour the powder onto a flat surface and then measure the slope (angle) of the powder relative to the horizontal. The higher the angle, it’s said, the more difficult it is for the material to flow. The problem with this test: It relies on human judgement and is thus prone to inaccuracy; many plant managers refuse to rely on it.

A better approach is to measure bulk density using a shear-cell-based instrument, as shown in the photo above and on page 27 [1]. Not only does a shear cell supply precise bulk density information, it measures important flow metrics that characterize bulk solids behavior, such as flow function, arching dimension and rat-hole diameter.

Flow characterization using a shear cell

The annular shear cell, developed in the 1960s, imparts a shearing action to a powder sample in order to evaluate the amount of force needed to overcome inter-particle friction. It allows shear data to be rapidly collected on bulk solids. This, in turn, allows quick analysis and timely QA/QC checks of powders used to make tablets and other products.

The shear cell simulates the conditions in a bin that affect the flow of material through the orifice of a hopper using two components: a shear cell lid and a trough. It does so by applying a series of defined compressive loads on a small sample of powder and then shearing the particles in the lid against the particles in the trough. This measures the inter-particle friction of the material and creates a predictive flow model of powder moving through a gravity discharge system.

It’s then possible to quickly derive flow function data. As increasingly compressive loads are applied to the small sample of powder, bulk density measurements are taken. The beauty of the shear cell is its operational simplicity and robust data output. Information from one flow function test provides enough data to calculate a flow function curve, arching dimension, final bulk density, rat-hole diameter, and internal friction angle.

The shear cell also performs a stand-alone bulk density test that you can run in as little as 100 seconds. The test can be used to characterize the bulk density of the material and to quickly and accurately check quality.
Bulk density testing in practice

To illustrate the value of these checks, imagine you’re the solid dosage manager at a pharmaceutical manufacturer who has just received a tote filled with an expensive formulation. All the qualification tests are done, and it’s time to make tablets. Because the product is known to be hygroscopic, the qualification process requires you to test the bulk density and conduct other quality checks during production.

In the early morning, when the humidity is low, production is smooth. Over the course of the day, however, the humidity rises and, as scheduled, you perform a quality check using a shear cell. As shown in Figure 2, the powder’s unconfined failure strength should be 4.0 kilopascals at a major principal consolidation strength of 9.0 kilopascals, and the bulk density should not exceed 925 kilograms per cubic meter.

But the flow function data indicate that the material has gained cohesive strength with the rise in humidity and that bulk density has also increased. Without some intervention, those changes could cause the powder to jam and a cascade of other problems could follow. In this case, the protocol might call for the addition of a flow aid and/or the adjustment of the tablet press. In so doing, you continue to make on-spec tablets throughout the day.

Reference

1. PFT powder flow tester from Brookfield Ametek, Middleboro, MA.

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