Understanding Powders

Over the 20 years that I've been working with powders significant advances have been made in powder testing technology and in the efficiency of powder processing. These advances come from a more developed and secure understanding of powders and how to control their performance.

The discussions I have with those in industry tend to focus around the following key themes:

- Why isn't my powder (process) performing well?
- How can I identify the right powder for my application?
- What testing technology will optimally support my activities?

This booklet collates a series of posts which appeared on LinkedIn that address these questions, from the standpoint of current knowledge and good practice. Beginning with material that summarises what we now understand about powders, focusing on powder flowability, a critical parameter for many processes.

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CHAPTER 1

Understanding Powders

Whether as raw materials, intermediates or final products, powders are integral to a diverse range of industrial processes, contributing to some 80% of all manufactured goods. Despite this ubiquity they continue to present challenges during product development, manufacturing, and in quality assurance. Powders are often labelled as 'bad' or 'erratic', when it would be more accurate to say we simply don't understand how they are behaving. Powders are neither intrinsically good nor bad, but they are unequally suited to different applications and environments. A powder that performs well in one process may have properties that give rise to poor performance in an alternative application.

Processing problems such as segregation, blockage of a line or flooding from a hopper are some of the most common practical manifestations of a powder ill-suited to its application. Powder formulators and processors need to understand the causes of such behaviour to ensure compatibility between the properties of the material and processing conditions. Reliably measuring properties that comprehensively characterise powders, in ways that relate to their processing performance, is a productive way to address such problems.

Powder processing and characterisation are both complicated by the fact that critical powder properties including flowability are influenced by so many different variables. Primary parameters such as particle size and shape, porosity, surface roughness and sensitivity to electrostatic charge are all influential, but system variables and environmental conditions can also have a profound effect. Air and moisture content are especially important.

This sensitivity explains why making a seemingly unimportant operational change can easily have a major impact. For example, the ease with which material discharges from a hopper may be influenced by how the hopper is initially filled, and the running level maintained. The filling method can affect the amount of air entrained within the powder, while the height of the material bed in the hopper will determine the stresses acting on the exiting material. Highly compressible powders are more susceptible to changes in behaviour as a consequence of powder bed height.

Repeatable, reproducible and sensitive powder characterisation similarly calls for the close control of all relevant variables, making sample preparation and procedural consistency extremely important. For example, a sample that deaerates on the bench top, prior to measurement, may exhibit quite different flowability from one analysed immediately, unless the method directly addresses this issue.

These complexities of behaviour cannot be adequately captured using a single parameter and multivariate powder characterisation is now widely recognised as a necessary and superior approach. The most valuable powder characterisation tools allow researchers to investigate a range of powder properties by measuring bulk and shear properties and the dynamic flow properties of consolidated, moderately stressed, aerated and fluidised powders. The resulting data extend understanding well beyond the levels achieved using conventional methods such as angle of repose, Hausner Ratio and Carr's Index, allowing the more accurate prediction of process and product performance. Using this knowledge to ensure an optimal powder-plant combination builds quality into the manufacturing process from the outset and lays a foundation for high levels of manufacturing efficiency and product quality.

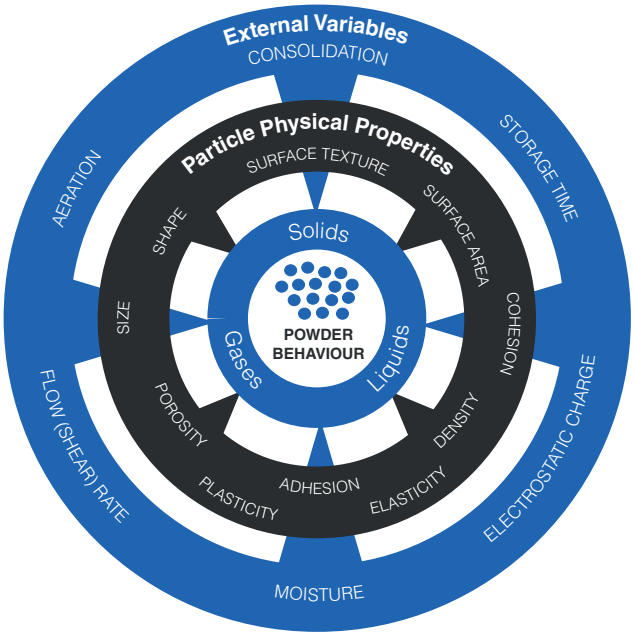
CHAPTER 2

2.2 | Focusing on Powder Flowability

In this chapter we will consider some of the many variables that influence powder behaviour, focusing on those that impact flow, often a critical performance attribute. Poor flowability lies at the heart of many powder processing problems, including sub-optimal throughput, unplanned shutdowns, erratic operation and inconsistent product quality. In many instances, achieving the desired flowability is therefore an effective way to enhance process efficiency and optimise product performance.

The Complexity of Powders

Although the terms ‘particle’ and ‘powder’ are often used interchangeably there are distinct and important differences between them. Powders are more than just particles alone and more accurately described as bulk assemblies, containing particles. They also consist of gases, normally in the form of air, and liquid, usually water, on the surface of the particle or within its structure.



The properties of each phase of a powder, and the interactions between them, define bulk powder behaviour. This means that behaviour is influenced by many variables and an array of potential interactions, as well as process or ‘external’ influences. The resulting behaviour is complex, and powder performance cannot be accurately predicted from measurements of particle physical properties alone.

Knowledge-driven Approach

A knowledge-driven approach to powder processing requires a strategy of manipulating particle and system variables that are known to influence powder behaviour to achieve process and product-related goals. This relies on understanding two things. Firstly, which powder properties are important in defining process and product performance, and secondly, which variables to manipulate, and how, to control these properties.

Better Understanding

Historically, there has been a limited and predominantly qualitative understanding of which properties influence powder behaviour. For example, the link between particle size and powder flowability has long been recognised, with powders consisting of smaller particles being generally more cohesive. For many years, a lack of reproducible, reliable powder property data prevented significant progress beyond this level of detail. However, significant advances were made around the turn of the century with the introduction of modern, more sophisticated testing instruments, notably dynamic powder testing technology.

In the intervening years, detailed studies of the impact of primary particle characteristics such as size, shape, surface roughness and charge, and system variables such as air or moisture

content, have become increasingly common. Advances in particle characterisation technology have also played an important role, notably the development of imaging as a routine tool for particle shape measurement. Today, the most successful powder processors typically have a robust specification that defines product performance and a secure understanding of how to control those properties that are critical to quality.

Powder Flowability

Dynamic powder testing involves precisely measuring the axial and rotational forces acting on a specially shaped blade as it rotates along a helical path through a powder sample, to generate values of flow energy which directly quantify powder flowability. Well-defined methodologies and a high degree of automation make dynamic testing, carried out using instruments such as the FT4 Powder Rheometer®, highly reproducible. Furthermore, tests can be carried out on consolidated, moderately stressed, aerated or fluidised powders. Modern instrumentation has also brought greater precision to shear and bulk property measurement.

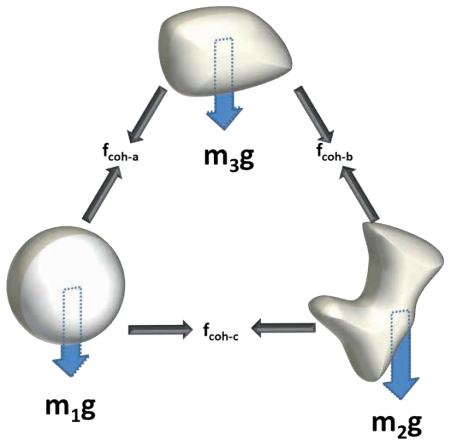
In upcoming posts I'll be looking at how this technology has been used to study some of the variables that most influence powder behaviour: particle size; particle shape; aeration; moisture content (humidity) and surface charge. Equally importantly such technology generates data that has proven process relevance so both requirements for a knowledge-driven approach to powder processing can now be met. Evidence suggests that this approach is extremely beneficial when it comes to accessing the highest levels of process efficiency.

2.2 | Exploring the Impact of Particle Size on Bulk Powder Properties

Controlling powder properties, particularly flowability, is essential for efficient handling and processing, and is made much easier by some understanding of which variables to change, and how, to achieve desirable behaviour. In this post he focuses on particle size, one of the most widely recognised variables affecting powder flow properties.

The Effects of Decreasing Particle Size

The effect of particle size on bulk powder properties stems principally from its impact on the relationship between the strength of inter-particle bonds and the motive forces of gravity that act on the particles.



The schematic to the left shows the forces acting on and between three adjacent particles. When powder is required to flow under gravity (in contrast to forced flow), as in many process environments, it is the magnitude of the "mg" component relative to the restrictive inter-particulate forces "f" that dictates whether flow occurs. This relationship is often described as the Bond Number, Bo, the ratio of the inter-particulate forces to the weight of the particle. If the gravitational forces are large in relation to the inter-particulate forces (Bo is small), then particles will move, and the material flows. As particle size reduces, the associated reduction in particle mass directly influences the gravitational motive force acting on each particle, resulting in a more cohesive bulk material. In parallel, smaller particles have a relatively large surface area leading to higher surface energies and an associated increase in inter-particulate forces. Generally speaking, powders with a small particle size tend to be more cohesive for these reasons.

In terms of packing behaviour, large particles tend to pack closely to form beds with a homogeneous stiff structure. Such beds may possess substantial voidage between contacting particles but are generally free of large cavities. By contrast, the relatively strong inter-particle forces of finer, more cohesive powders make them prone to forming agglomerates and a heterogeneous structure. These differences in packing behaviour have a marked impact on the flow characteristics of the powder.

Impact on Powder Flowability

Powder flowability can be directly quantified by measuring flow energies. These are dynamic powder properties derived from measurements of the axial and rotational forces acting on a blade as it rotates through a powder sample. Specific Energy (SE), an unconfined flow property, is measured by rotating the blade upwards through the sample, imposing a gentle lifting action, while Basic Flowability Energy (BFE) which is measured in a confined flow regime, involves a downward traverse of the blade and the application of a compacting flow pattern.

To explore in more detail how particle size affects flow behaviour let's contrast some flow energy measurements for spray dried lactose with a Dv50 of 130 microns, with some equivalent data for lactose finely milled to a Dv50 of 20 microns.

	Spray Dried Lactose	Finely Milled Lactose
Specific Energy (mJ/g)	4.8	9.6
Basic Flowability Energy (mJ)	1200	635

SE values reflect how a powder flows when unconfined, or in a low stress environment, such as during low shear mixing or dosing into capsules or a die, and is a good measure of cohesivity. Here, for the reasons previously outlined, the finer, milled lactose is more cohesive, and the SE is correspondingly higher, as would be expected.

The BFE results show a different trend suggesting that under forced flow conditions, such as might be applied during screw feeding or in the feed frame of a tablet press, the finer lactose will flow more easily. This observation is attributable to differences in the structure and packing within the two beds, rather than just the cohesive forces. The bed comprising of finer particles absorbs the movement of powder displaced by the blade, because of the air trapped within it. This air makes the bed locally compressible, so less energy is required to establish flow.

The spray dried lactose, in contrast, can exert considerable resistance to a compacted, forced flow regime. The larger particles, mostly in contact with neighbouring particles, form a stiff bed, so force chains and frictional contact is high. The result is a much higher BFE. This mechanism can be visualised by considering the resistance observed when applying a vertical load on two different materials in a beaker. A more cohesive flour sample would compress easily, where by contrast, sand would greatly resist motion. Sand is more resistant to flow when in a confined environment.

Relevant Measurement

The results above provide some insight into how particle size affects powder flow behaviour and highlight the importance of characterising powders under conditions that relate to how they are being handled. They illustrate how different types of powder can exhibit markedly different flow behaviour depending on how they are being induced to flow.

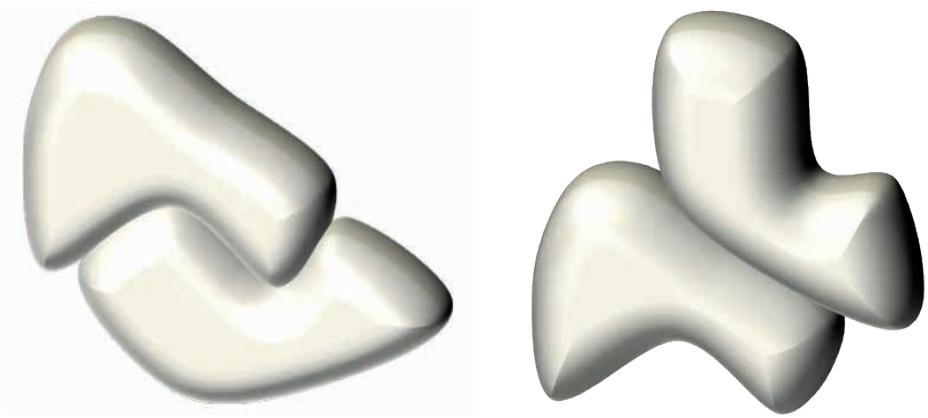
Reliable particle size information has been available for some time and so the influence of particle size on powder behaviour is relatively well understood and appreciated, as this discussion illustrates. In my next post I'm going to be considering the impact of a variable that has only become reliably and easily measurable in recent years: particle shape.

2.3 | Exploring the Impact of Particle Shape on Bulk Powder Properties

There are many variables that influence powder behaviour. In this section we look at the importance of another critical particle parameter - shape. Many powder processors recognise that particle shape influences powder behaviour, perhaps most significantly flowability, but until relatively recently it has been difficult to access any form of quantitative correlation. Modern advances in shape measurement, as well as those in powder characterisation, have transformed our ability to develop robust relationships between these properties and understanding in this area is now advancing rapidly.

The Mechanisms of Powder Flow

For a powder to flow, particles within it have to move relative to one another. Many factors influence the ease of this movement, with shape being one of the easiest to understand in a qualitative way. The particles in the figure below have a highly irregular morphology that makes them prone to mechanical interlocking. As this occurs, the particles will strongly resist further movement, even if their surface friction is low, an effect that will reduce the ability of the powder to flow.



The properties of each phase of a powder, and the interactions between them, define bulk powder behaviour. This means that behaviour is influenced by many variables and an array of potential interactions, as well as process or 'external' influences. The resulting behaviour is complex, and powder performance cannot be accurately predicted from measurements of particle physical properties alone.

The particles on the left are orientated so as to make interlocking likely. However, if reoriented, as shown on the right, the particles are now more likely to shear in a lower energy interaction. The extent of mechanical interlocking can only be reliably reduced by making the particles more regular in shape. A powder comprising completely spherical particles, for example, has minimal potential for mechanical interlocking, and, all other factors being equal, would be expected to flow more easily than a powder with irregularly-shaped particles.

Investigating Correlations between Particle Shape and Flow Energy

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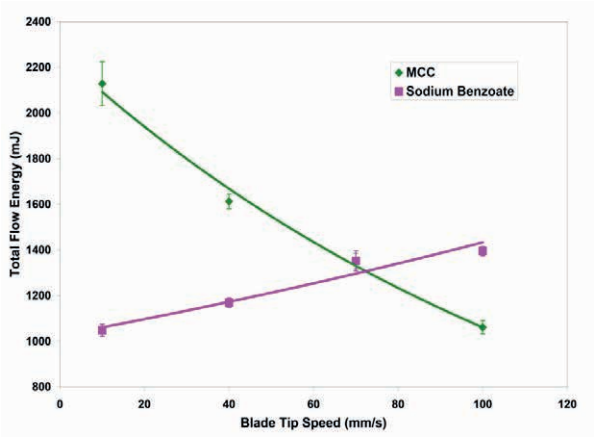
$$\textbf{HS Circularity} = (4 \times \pi \times \text{Area} / \text{perimeter})^2$$

Perfect spheres have a HS circularity of 1.0 while less regular forms have values closer to zero. In this study HS Circularity was measured for both samples using an automated image analysis system (Morphologi G3, Malvern Panalytical). The Flowlac 100 was found have a median value of 0.91, while the less regular Spherolac 100 had a median value of 0.83.

The flow properties of these two materials were quantified with the dynamic flow parameter Basic Flowability Energy (BFE) which was measured using an FT4 Powder Rheometer (Freeman Technology). In dynamic powder characterisation the axial and rotational force acting on a blade, as it rotates through a sample, is measured to generate flow energy values that directly quantify the ease with which the material flows. The BFE value measured for the Flowlac 100 was around 1200mJ compared to around 2500mJ for the Spherolac 100, illustrating that the flowability of one lactose grade is approximately half that of the other, solely as a consequence of differences in particle shape. If specified only in terms of particle size, measured by laser diffraction, as is often the case, these grades would appear almost identical. This illustrates the importance of measuring flow directly and having a range of particle measurement capabilities to thoroughly characterise these complex materials.

The Practical Relevance of Shape

This correlation between shape and flow is of very practical relevance since engineering powders with desirable flow characteristics is essential, both for efficient processing and in many instances for product performance too. For example, research has shown that the flow properties of particles correlate closely with blending performance. The figure below shows how the flow energies of microcrystalline cellulose and sodium benzoate change with shear rate (impeller speed) i.e. whether the powders flow more or less easily at higher shear rates.



The MCC, which has approximately spherical particles, flows more easily at higher shear rates. The sodium benzoate on the other hand, which has platelet shaped particles exerts more resistance to flow at higher shear rates with faster impeller speeds more energetically driving the platelets into an interlocked state. In blending trials, the MCC blended more rapidly at higher impeller speeds but with sodium benzoate the opposite effect was observed, where lower blending speeds resulted in faster blending to a uniform state. This shape-related result can be readily predicted from the flow energy data.

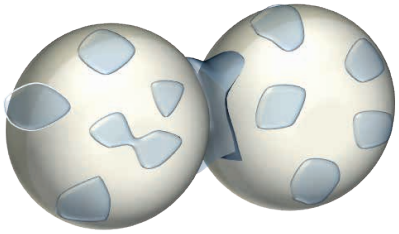
These examples illustrate how our understanding of the impact of shape on powder flowability is crystallising, and how that knowledge enhances our ability to control powder behaviour. Particle shape is increasingly taking its place alongside particle size as one of the variables that formulators routinely manipulate to meet flowability targets. This advance, which is underpinned by developments in both powder characterisation and shape measurement technology strengthens our ability to successfully achieve powder processing goals.

2.4 | Exploring the Impact of Humidity on Bulk Powder Properties

Having started by earlier examining the effect of various particle properties, including size and shape, we now turn to an external variable - humidity. Moisture can significantly influence powder behaviour, especially flow properties, and quantifying its effect is essential to develop effective control strategies for a specific application. There can be significant cost involved in removing water from the atmosphere in a processing environment, or indeed from within the powder itself. These costs must be balanced with the economic benefit of maintaining acceptable processing performance. The challenge is to understand a powder's appetite for moisture uptake and, more importantly, how moisture will affect its characteristics and performance.

The Mechanisms of Powder Flow

For a powder to flow, the particles within it must shear relative to one another. It is widely believed that introducing water results in powders flowing less freely, and there are mechanistic reasons to support this view. Water in a powder often forms liquid bridges between particles that would otherwise be subject to relatively low inter-particulate forces. Wet granulation exploits this mechanism, but when it occurs in routine operation such bridging can inhibit the movement of the particles, with a detrimental impact on performance.



The MCC, which has approximately spherical particles, flows more easily at higher shear rates. The sodium benzoate on the other hand, which has platelet shaped particles exerts more resistance to flow at higher shear rates with faster impeller speeds more energetically driving the platelets into an interlocked state. In blending trials, the MCC blended more rapidly at higher impeller speeds but with sodium benzoate the opposite effect was observed, where lower blending speeds resulted in faster blending to a uniform state. This shape-related result can be readily predicted from the flow energy data.

However, there are times when moisture improves flow behaviour. In the case of particles with a rough surface, for example, low levels of moisture can act as a lubricant, allowing the powder to flow more freely. Water can also improve the performance of electrostatically charged powder by improving its electrical conductivity. Dissipating electrostatic charge in this way can reduce the strength of inter-particulate cohesive forces with a dramatic impact on flow behaviour, especially for powders with a relatively small particle size.

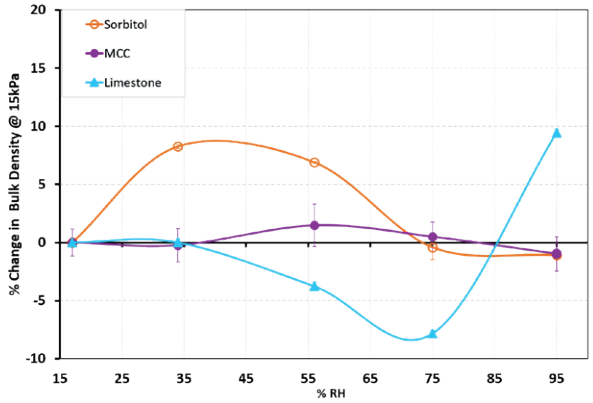
Since moisture can induce these very different effects, it is vital to accurately measure its influence. We've conducted extensive research in this area and have found dynamic powder testing, alongside bulk property measurement, to be particularly informative.

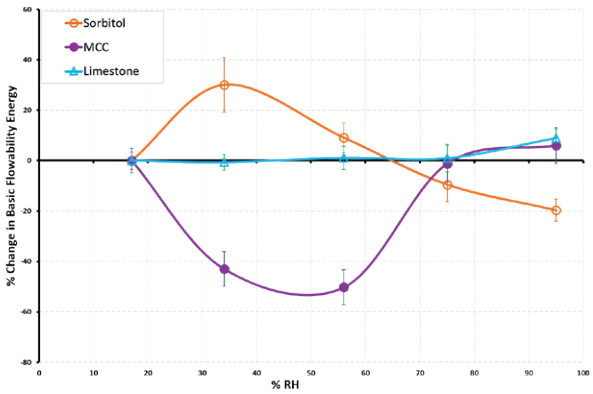
Measuring the Impact of Humidity

Dynamic powder testing involves measuring the axial and rotational forces acting on a blade as it rotates through a powder sample, to determine flow energies. Basic Flowability Energy (BFE) is the flow energy measured as the blade passes down through a powder sample of uniform, low to moderate packing density. One of the benefits of dynamic measurement is that it can be applied to consolidated, moderately stressed (as in the case of BFE), aerated, and even fluidised powders to assess how powders will behave in different processing environments.

The graphs below show how conditioned bulk density (CBD) and BFE change as a function of exposure to increasing Relative Humidity (RH) for microcrystalline cellulose (MCC) [PH200,

FMC], Sorbitol [C*Sorbidex S] and Limestone [BCR116] and provide an illustration of the extent to which powders vary in their response to moisture. All data were generated using an FT4 Powder Rheometer.





Focusing on the data for MCC, the results show minimal variation in density (approx. 2 – 3 %) indicating that in this instance changes in moisture have little impact on the packing behaviour of the powder. However, the BFE data show interesting and perhaps unexpected changes in flowability, passing through a minimum as moisture content increases from the initially desiccated condition. During the study it was observed that at low RHs, the sample had a tendency to coat the test vessel, suggesting significant electrostatic charge. This points to a rationale for the observed behaviour, where at low RH, the reduced moisture content means that surface charge is preserved, leading to cohesive behaviour before exposure to moderate RH introduces enough water to provide a conductive surface, thereby dissipating charge and improving flow. At the highest levels of RH capillary bonding occurs between particles, increasing adhesion and resulting in a higher flow energy. Clearly, these trends cannot be detected from changes in bulk density, highlighting a limitation of using bulk density methods to quantify flow performance.

The data for Sorbitol and Limestone reinforce this point. Both materials exhibit more significant changes in bulk density than MCC, approaching 10% at lower and higher levels of RH respectively. However, for Sorbitol this change is minimal when compared to the 30% change observed in BFE while in contrast, the flowability of limestone varies very little with RH. As with the MCC, changes in bulk density do not fully reflect all the mechanisms that influence flowability and therefore fail to accurately predict changes in flow behaviour.

Moisure - Good or Bad?

These results show that moisture is not always detrimental to powder flow behaviour and underline the importance of carrying out appropriate powder testing to quantify a material's sensitivity. The characteristics demonstrated by the MCC, which cannot be predicted from first principles, were a result of exposing samples to relative humidities in the range 17 – 95%, with the most significant changes observed within a narrower central range. This variation in material performance could therefore easily occur in routine industrial operation.

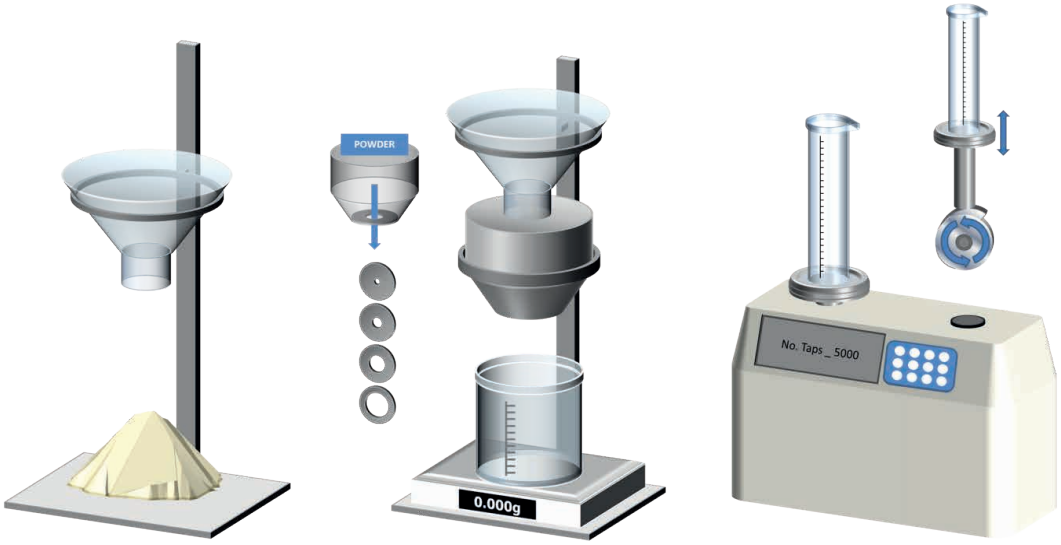
Of equal importance, the results show how different properties may help to identify and rationalise the mechanisms dominating behaviour. Our preferred approach is to measure shear, bulk and dynamic properties to address processing issues, but in this instance neither shear data nor bulk density changes were able to reliably identify the critical changes in powder behaviour. Though changes in density were observed they were relatively small (<5%) and not proportional to changes in flowability. It was dynamic data that provided the information needed to assess the impact of humidity in a process relevant way, to support effective process design and optimisation.

CHAPTER 3

3.1 | Reviewing the Traditional Powder Testing Toolkit

In this chapter we begin with an assessment of some traditional powder testing tools within the context of modern requirements for information.

Engineers have been devising ways to quantify powder behaviour for many decades and a wide range of testers enjoy routine use across powder processing industries. Flowability – the ease with which a powder flows – is arguably the most important characteristic of powder behaviour and often the focus of measurements. With all industry facing increasing emphasis on more efficient manufacture and consistently high product quality, the need for reliable, relevant and precise flowability measurement has steadily intensified which makes it timely to review the capabilities of traditional flowability test methods. Being realistic about the value and limitations of traditional techniques is essential for their appropriate use and supports the process of evaluating alternative powder testing solutions.



Simple test methods include (l to r): angle of repose; flow through an orifice; and tapped density methods.

The harmonised pharmacopoeial chapters on powder flowability testing (USP chapter 1174 and EP 2.9.36) describe four of the techniques most commonly applied within the pharmaceutical industry, and indeed elsewhere. These are: flow through an orifice; Compressibility Index/ Hausner Ratio; angle of repose; and shear testing. These chapters were released to encourage more standardised practice, for techniques that had inherent variability and little consistency in terms of the manufacture of test equipment. Three of the four methods listed above exemplify some of the simplest powder testing methodologies used to quantify behaviour.

Angle of repose is 'the constant three-dimensional angle (relative to the horizontal) assumed by a cone-like pile of material formed by any of several different methods' (US Pharmacopoeia chapter <1174>). Larger angles are associated with stronger inter-particulate forces and therefore poorer flowability, 'excellent' being the classification routinely reserved for materials with an angle of 25 to 30°.

Compressibility Index and Hausner Ratio are measured by comparing the unsettled volume of a sample with the tapped volume. As the sample is tapped the particles pack more closely, causing an increase in bulk density. Here, significant change on tapping is associated with poor flowability, with more free-flowing materials maintaining a more constant volume/density.

Flow through an orifice is perhaps the most intuitive method and simply involves measuring mass or volumetric flow rate through a given geometry. There is no general scale of flowability because the geometries used can vary considerably depending on the device selected.

Understanding the Limitations

These tests reflect certain aspects of powder behaviour. More cohesive powders have a greater tendency to form a steeply sided cone and do tend to flow relatively poorly. Greater cohesion may also result in stronger bridging within a powder sample inhibiting flow through an orifice. In addition, cohesive powders have a propensity to entrain significant amounts of air, which may be released by tapping, resulting in a dramatic change in volume. All three techniques therefore provide some insight into flowability and, for the most part, give a qualitative indication of comparative performance, when used appropriately. Where there is a need for more in-depth, process-relevant understanding, however, or a requirement to sensitively differentiate between two closely similar powders, these methods have less value.

For example, if a powder has a Hausner Ratio of 1.11 it would be classified as having excellent flowability, with an expectation of free-flowing behaviour. The question is: what does this mean in terms of processing? If this powder were blended under low stress conditions, it is likely each particle would disperse well and blend homogeneity would be readily achieved. However, when subjected to higher stresses and forced flow, such as in the feedframe of a tablet press, it could lock up and perform very poorly. The key to efficient powder handling is matching powder behaviour to the processing environment, so the classification of a powder with a low ratio as ‘excellent’ and one with a higher value as ‘poor’ can be misleading. Furthermore, a powder with a Hausner Ratio of 1.00 would be identically classified, although clearly not identical. If two such powders are capable of behaving differently in a process, then it is important to apply a technique that differentiates them.

Shear testing has evolved to support a scientific approach to hopper design and is based on fundamental mathematical principles (unlike other traditional methods), more specifically characterisation of the stresses associated with the no flow/flow transition required for discharge from a hopper. It remains valuable for hopper design and more generally for the assessment of flowability under moderate to high stress. However, in common with the other traditional techniques outlined here it does not allow testing under well-defined, low stress conditions. This is an important limitation for process relevant testing, particularly for the assessment of aerated or fluidised performance, that has become more critical as our need for information has increased.

3.2 | Reproducible Powder Testing

Reproducibility, measurement sensitivity and the usefulness of an analysis are inextricably linked. If a technique or instrument exhibits poor reproducibility then measurements are 'noisy', so only gross trends or differences can be detected. For industries working with increasing precision to rigorously optimise the performance of processes and products, poor reproducibility becomes increasingly limiting. In powder testing, achieving the required level of reproducibility is especially challenging, but is now essential.

The Impact of Processing History

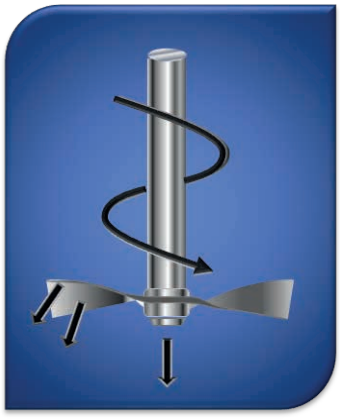
Many traditional powder testing techniques, such as angle of repose, Hausner ratio and flow through an orifice, remain largely manual. As a result, operator-to-operator variability can be a significant issue. In addition, imprecise definition of methods and equipment for such techniques may complicate data exchange across different areas of powder testing and industrial sectors. Beyond these generic issues we also have to consider additional challenges that are unique to powders.

The properties of a powder are not defined solely by the immediate environment, they are also influenced by processing history – an often under-appreciated but easily illustrated point. Imagine measuring the angle of repose of two samples, identical apart from their storage history. One has been held under consolidating conditions and the other extracted from a low stress, functioning process line. Even if the conditions applied during testing of the powders are identical, without appropriate sample preparation the results will be very different.

To accurately define and measure powder properties it is crucial to first establish and apply a reliable baseline state for testing. Eliminating processing history - as far as is possible and practicable - makes comparative testing much more informative, and more reliably differentiating.

The Importance of Sample Conditioning

In dynamic testing, with a powder rheometer, samples are analysed by measuring the forces acting on a helical blade as it rotates through the powder bed along a prescribed path. Values of flow energy, a dynamic parameter that quantifies powder flowability, are calculated from the resulting data. Methodologies are well-defined and testing is largely automated, both of which are important factors for reproducibility. In addition, the sample is conditioned prior to analysis. This conditioning takes the form of gentle agitation and results in a uniform, reproducible, loosely packed bed that defines a baseline state for measurement.

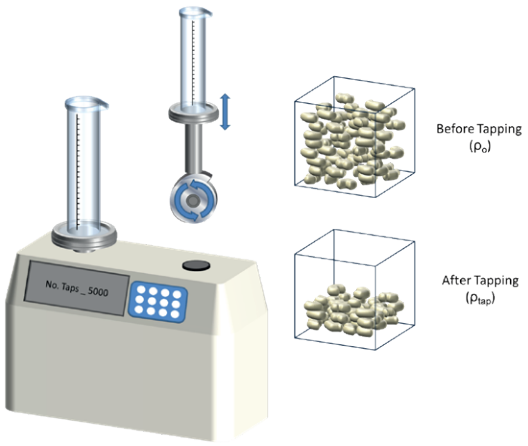


Dynamic testing offers a level of sensitivity that means any differences detected can be reliably attributed to a real difference in the sample. In fact, flow energy measurements can differentiate samples that other techniques classify as identical. Using conditioning during the application of other methodologies, such as bulk property measurement, also lends superior reproducibility to these measurements. From a practical perspective this boosts the effectiveness of investigations of how a powder will respond to the processing environment: to the introduction of air, for example, or to consolidation; to shear rate; to moisture; to storage – will segregation occur; or to aggressive handling - will attrition be a problem? All important questions during product development and into production. In answering them reliably, dynamic testing supports faster, more efficient commercialisation, and the evolution of better manufacturing practice.

3.3 | Evaluating the Powder Testing Toolkit: Tapped Density

Understanding Tapped Density Methods

Tapped density methods are based on measurement of the increase in bulk density induced by tapping a powder sample. Bulk density of the sample is first measured in a "baseline" state, and then again after a defined tapping process. Carr's Index and Hausner Ratio are alternative ways of representing the relationship between tapped and untapped density, and they enable classification of the powder according to a predefined scale: a Carr's Index of less than 15, for example, indicates "good" flowability.

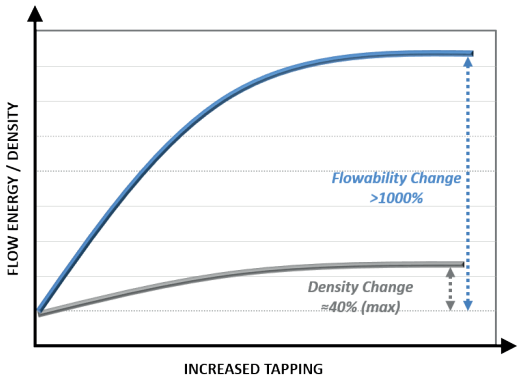


Such techniques have a number of practical advantages. They are quick, relatively easy to carry out and the associated instrumentation is typically inexpensive. Density change as a result of vibration or unidirectional tapping is an important aspect of powder behaviour and happens routinely during transport and processing. However, when it comes to assessing powder flowability, tapped density methods only coarsely differentiate cohesive from free-flowing samples. Moreover, attempting to apply such data to predict the flowability of different samples within the processing environment quickly highlights some important limitations of the technique.

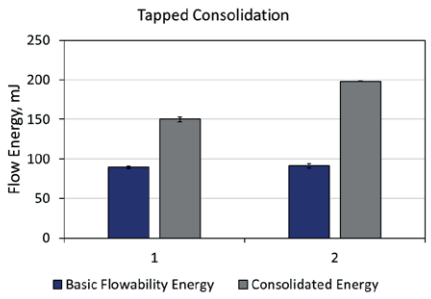
The Limitations of Inferring Flowability from Tapped Density Measurements

The use of tapped density measurements to assess powder flowability is based on the idea that the interactions that influence the packing or bulk properties of a powder are the same as those that control flow behaviour. I would argue that although this is broadly true it is not the whole story. The factors influencing bulk density and flowability are not exclusively matched nor do they impact both to the same extent, as the figure below shows.

In this simple experiment the change in bulk density induced by tapping is contrasted with the change in flowability measured directly by dynamic powder testing using a Powder Rheometer. Flowability changes by several orders of magnitude, while the change in bulk density is more modest.



This comparison highlights two important limitations of tapped density methods. Firstly, they are far less sensitive to changes in flowability than alternative techniques such as dynamic powder testing. And secondly, they may be misleading regarding the magnitude of the change in flowability following consolidation. Whilst such techniques may have a place in the modern testing toolkit, they are therefore less than ideal for detailed process design, optimisation, troubleshooting and QC to the standards now required for successful manufacture.

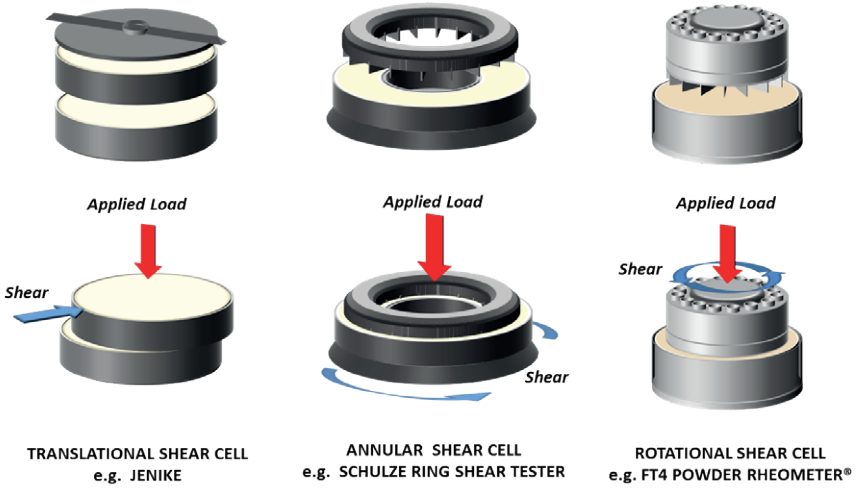


The flow energy data shown above also illustrates the limitations of tapped density methods. Here, two samples that exhibit almost identical flowability when in the low stress packing state, associated with a Basic Flowability Energy test demonstrate different flow energies when tapped (Consolidated Energy). The tapped density of the two materials are similar (data not shown) and yet they have different resulting flow energies, indicating that density changes aren't necessarily proportionate to flowability changes.

3.4 | Evaluating the Powder Testing Toolkit: Shear Testing

An Introduction to Shear Cells

Shear testing has its roots in the pioneering work carried out by Jenike in the 1960s to tackle the issue of discharge from storage vessels. The technique was developed to support design methodologies that brought a numerical approach to the specification of powder handling equipment for the very first time. The task of developing a design methodology for hoppers and silos to deliver controlled powder discharge was a major challenge, and the work has stood the test of time remarkably well. While discharge and hopper design remain an imperfect science, the theory and subsequent strategies developed fifty years ago have not been substantially improved upon and remain in use.

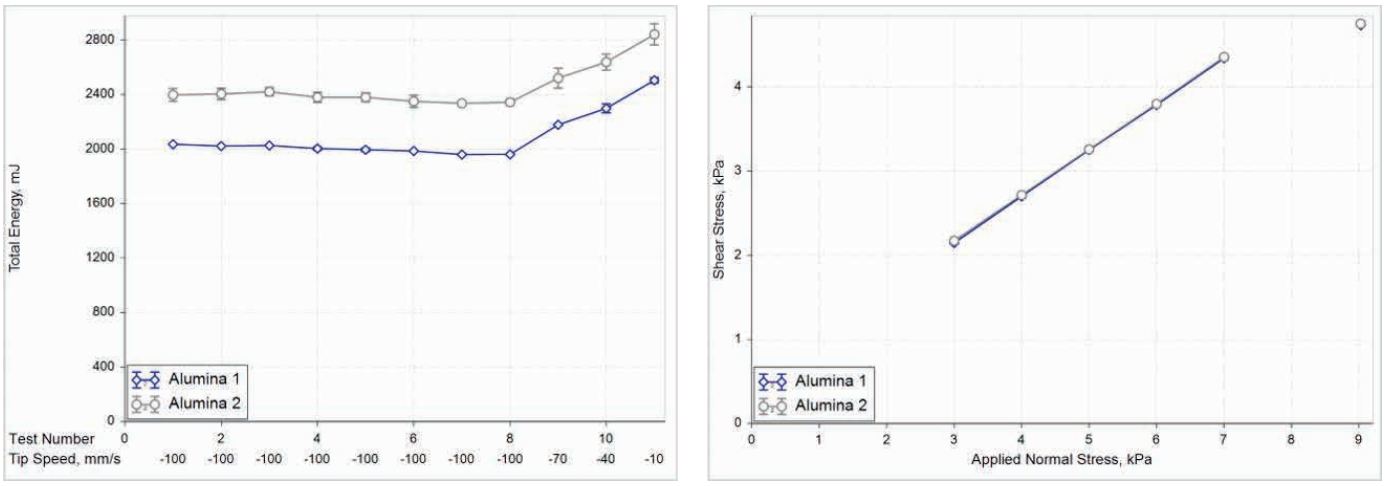


In simple terms shear testing involves measuring the forces required to shear one consolidated powder plane relative to another. Similar methods are applied to measure wall friction, the friction between the powder and a sample of the material used in the construction of a hopper or other piece of processing equipment. In combination these methods provide most of the data required for hopper design. At the base of the hopper, powder consolidated by the weight of material above is subject to normal and shear stresses as it flows within the powder bed, or relative to the vessel wall, so the relevance of these test methods is clear.

The Limitations of Shear Testing

Over the decades since shear testing was conceived the need for process-relevant powder characterisation has encouraged the application of shear testing well beyond this original intent. This is understandable but has brought into focus some of the technique's limitations.

One issue is that shear testing is most suitable and accurate for more cohesive powders. With a cohesive material the shear forces measured are relatively large but with less cohesive samples the forces become relatively small. The 'free-flowing' classification of Flow Function, a primary parameter derived from shear testing, in fact covers a broad range of flow behaviours, and shear testing is simply not as differentiating as, for example, dynamic characterisation (see over page).



Relatively free-flowing alumina samples are clearly differentiated by dynamic testing though classified as having identical flow characteristics by shear testing.

A second, arguably more important issue is that the conditions applied during shear testing are not representative of those that prevail in, for example, a fluidised bed, low shear blender, or during gravitationally induced filling. For certain processes, the response of the powder to air is of crucial importance and this is something that cannot be directly investigated via shear analysis. More broadly, trying to infer from shear data how a powder will behave under conditions that are very different from the test environment can be both inaccurate and unrealistic.

There is no doubt shear testing provides value for the purpose for which it was designed, and I would also argue that beyond this, shear testing has a role to play in providing insight into the nature of powders for more general study. I would however suggest that other techniques, specifically dynamic testing, are more appropriate for powder characterisation at low stresses and/or high strain rates, as shear analysis starts to reach its limits. Recognising these limits and bringing the most appropriate technique to bear are crucial as processors push towards greater manufacturing efficiency.

CHAPTER 4

4.1 | Powder Characterisation Techniques for Hopper Design

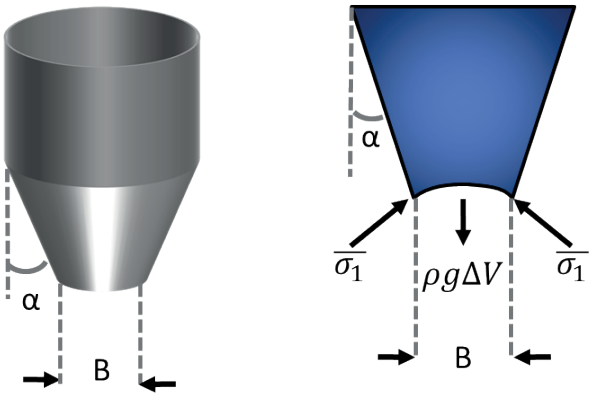
In recent years it has become increasingly evident that the value of measuring different properties is dependent on the extent to which they describe how a powder behaves in a given process or as a certain product. This understanding highlights the limitations of 'single number' powder testers and the enhanced value of instrumentation that offers multivariate characterisation. To begin here, we will start with hopper design, the only powder handling process where equipment geometry can be designed from measurements of powder properties. For many, the shear testing methodologies required for hopper design are their first, and for some, only, introduction to the world of powder characterisation. However, despite their longevity, shear cell testing, hopper design and hopper operation continue to present a challenge.

The Basics of Hopper Design

Getting powders to flow consistently from hoppers is an issue in many powder processing industries. Frequently encountered problems include: bridging, leading to no flow/erratic flow/ stoppages; flooding (uncontrolled flow); segregation; and funnel flow/ratholing (flow through the core of the hopper with an outer stagnant layer).

Flooding (left) and erratic flow/stoppages, as evidenced from hammer rash (right), are just two of the problems routinely associated with sub-optimal hopper design and/or operation.

Successful hopper operation relies on an efficient match between the in-process material and certain attributes of the hopper: material of construction; half angle (the steepness of incline of the hopper walls); and outlet size. Generally, smoother materials, steeper half angles and larger outlet sizes all tend to promote flow.

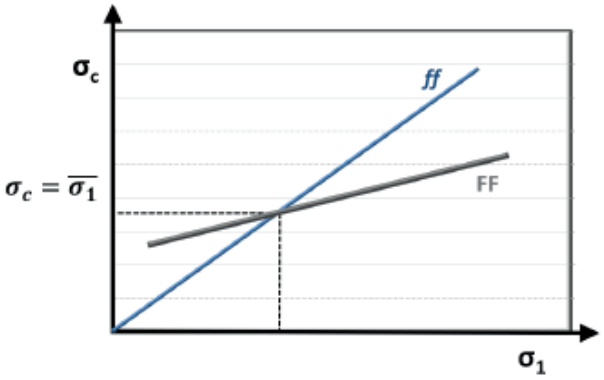


$$B = \frac{\overline{\sigma_1} H(\alpha)}{\rho g} \qquad \propto = \frac{\pi}{2} - \frac{1}{2} cos^{-1} \frac{(1 - sin\delta)}{2sin\delta} - \beta$$

Hopper design methodologies lead to specification of the steepness of incline of the hopper wall and outlet size on the basis of a stress balance.

The hopper design methodology developed by Jenike in the 1960's remains the standard today. For a more detailed discussion I'd refer you to 'Modern Tools for Hopper Design' but in summary it relies on calculating the flow function (FF) and flow factor (ff). FF depends purely on the shear strength of the powder, as determined from shear cell testing, while ff depends also on the characteristics of the hopper – material of construction, and shape. Hopper half angle and outlet size are calculated on the basis of these two parameters.

Because of these methodologies, many believe hopper design to be a relatively robust element of powder handling, and in relative terms it may be. However, operational problems are common, and at many companies hopper specification is an out-sourced expert task. Why is it that even with defined methods in place, robust hopper design remains challenging?



Hopper Troubleshooting

What emerges from Jenike's methods is that if the material of construction, shape or half angle of a hopper is different from that of another unit then a different outlet size might be needed to achieve mass flow, for the same powder. Equally importantly, using a hopper that works well with one powder to handle an alternative material, may not be successful. These points are relatively well-recognised, but what is less well-understood is that optimum values of FF and ff, and hence optimal hopper geometry, may change simply because of environmental conditions. For example, if the hopper is filled when the relative humidity is higher than normal, discharge behaviour may be compromised.

This observation suggests that conducting hopper design, and the associated testing in-house, may be advantageous. In-house capability makes it easier for engineers to fully scope the conditions over which the design may need to operate, and for troubleshooting teams to get to the root cause of a problem. The barrier is having the necessary expertise, but there are tools that can help. Automated shear testing, coupled with modern hopper design software guide the user through every step of the design process, from analysis through to computation. Using such tools helps powder processors to get the best out of existing hoppers (assessing whether new materials will work with existing equipment) and specify robust new units with confidence.

4.2 | Powder Characterisation Techniques for Capsule Filling

Capsules are widely used to provide metered doses for oral and pulmonary drug delivery. For oral administration fill weights are typically in the range 50 to 500 mg but for Dry Powder Inhalers (DPIs), dose size is far smaller, principally within the range 0.5 to 15 mg. These smaller quantities, in combination with the fine particle size of inhaler formulations, are particularly challenging. Characterising powders in a way that allows for a correlation between measured properties and the powder's behaviour in the dosing equipment is extremely helpful when it comes to developing optimised filling processes for all powders, but especially these demanding materials. Research has shown that multiple powder properties, in combination, define capsule filling performance, making powder testers that deliver multi-faceted powder characterisation uniquely applicable.

The Basics of Capsule Filling

Image courtesy of Harro Höfliger

Commercially applied capsule filling technologies include: dosing disc and tamping pin; dosator and pin; and vacuum drum. The mechanics of equipment operation are different in each case but in terms of process steps there are many similarities. In basic terms, capsule filling involves the extraction of powder from a bulk supply into a confined space of known volume, compaction of the dose to ensure a complete fill at consistent bulk density, and transfer of the compacted plug to an appropriate receptacle, often directly into the capsule.

Defining Relevant Powder Properties

Dynamic measurements directly quantify the ease with which a powder flows. Basic Flowability Energy (BFE) characterises flow under confined flow conditions while specific energy (SE) measures how easily the powder flows when unconfined. Studies have shown that both parameters are relevant to capsule filling processes, during which powders initially flow under low stress into an empty die, but are then subject to compaction, as more powder is compressed into the die to achieve the desired fill. Direct correlation has been observed between BFE and SE, and dose weight consistency, a key indicator of process performance.

During compaction, the compressibility of the powder is also important. Compressibility is a bulk parameter that defines how the volume of a powder sample changes with applied consolidation stress. With a highly compressible powder a compacting force tends to act locally, consolidating the powder most densely in the region directly beneath the point of application of the stress. This can lead to inconsistency in dose density. Less compressible powders, in contrast, undergo more homogeneous compression as the applied stress is more efficiently transmitted through the dose. Such powders are therefore easier to compact to consistent bulk density during the filling process, which assists in the attainment of uniform dose weight during the filling process.

Finally, shear testing offers insight into the strength of the powder plug, and of likely interactions between the powder and processing equipment surfaces. Conventional shear test data quantify the cohesivity of the sample, while wall friction data, which are derived using a similar technique, allow the comparative investigation of the likelihood of powder adhesion to the process equipment surfaces. An ideal formulation exhibits sufficient cohesivity to form a stable powder plug for transfer but has sufficiently low interaction with the processing equipment to avoid contamination of the equipment surfaces.

This last point illustrates the importance of balancing powder properties to achieve optimal process performance. For capsule filling, powder testers that deliver shear, bulk and dynamic properties provide the comprehensive data set needed to formulate and design towards this balance and can therefore be a cost- and time-efficient choice for formulation scientists and process engineers.

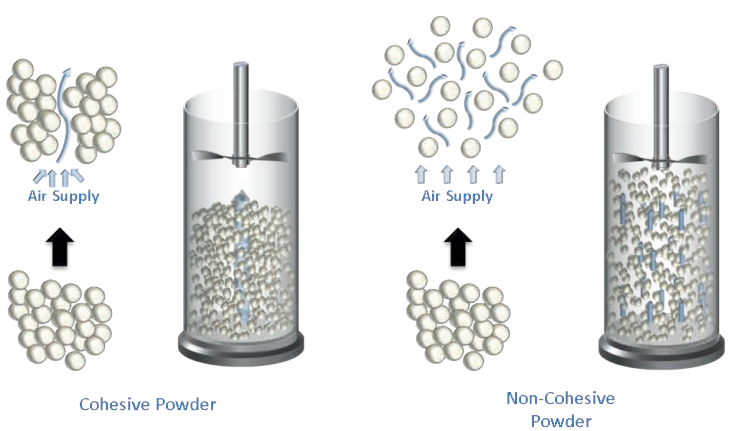
4.3 | Powder Characterisation Techniques for Dry Powder Inhaler Applications

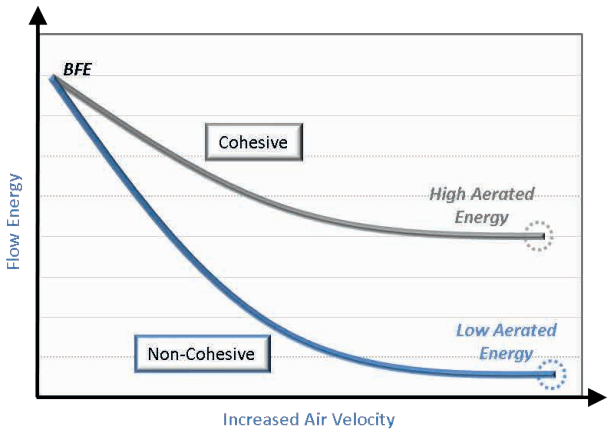
At the heart of DPI technology lies a demanding powder engineering challenge. Particles in the sub-5 microns range required for deposition in the lung tend to be cohesive, making them difficult to handle and disperse. Efficient aerosolisation of the dose is a primary goal of formulators but it is vital that a developed formulation can be successfully manufactured into a finished product, a critical step being the extraction of a small, representative dose into a capsule or blister. Developing formulations that disperse efficiently and process well is a significant task, with product manufacture normally considered later in the product life cycle. A Powder Rheometer combines bulk, shear and dynamic powder testing to give detailed insight into the nature of a DPI formulation and can directly assist with this challenge.

Controlling Dispersion

Fine particle dose (FPD) is the amount of active that will tend to deposit at the target site within the lung and is a commonly utilised in vitro measure of drug delivery efficiency. Developing a formulation that disperses readily under the conditions applied during product use is the key to achieving a high FPD, with the energy available for aerosolisation typically provided solely by the inhalation action of the patient. As many DPI formulations use a carrier to improve flowability characteristics, dispersion is complex and involves stripping the active from the larger excipient particle.

Since DPI dose dispersion proceeds via a process of fluidisation, the response of a formulation to air is highly relevant. One of the unique features of dynamic powder characterisation - measurement of the powder flow properties whilst in motion - is that it enables the testing of powders in an aerated or fluidised state to directly quantify this response. With non-cohesive powders, air flowing through a powder bed separates the individual particles because inter-particulate tensile forces are weak or negligible. As a result, the aerated flow energy of such powders, a dynamic parameter, decreases rapidly with increasing air flow rate, to the point of uniform fluidisation of the bed. In contrast, for cohesive powders, higher inter-particulate forces between particles make them resistant to separation, limiting fluidisation of the bed, with air tending to channel through the powder rather than exerting a uniform effect.





Research has demonstrated a direct correlation between aerated flow energy and FPD for DPI formulations. Formulations with an appreciable degree of cohesion, and consequently a relatively high aerated flow energy, produce a higher FPD than less cohesive materials with lower aerated flow energy. Visualisation studies suggest that this is because the low permeability and greater resistance to flow associated with more cohesive powders results in the development of a significant pressure drop across the powder dose as air is drawn through it. Aerosolisation consequently occurs via a single highly energetic event. In contrast, less cohesive formulations with higher permeability disperse less effectively via a more gradual process of erosion.

Controlling Dispersion

While aerated flow energy is a good powder descriptor for studying dispersion behaviour, other studies have shown that for DPI manufacture, and more specifically dosing, flowability and compressibility are more relevant to in-process performance. Accurate dosing relies on consistently filling a known volume - a die or dosator, for example - with powder of constant bulk density. Poorly flowing powders result in variable fill weight while those that are relatively compressible tend to form non-uniform powder plugs that lack the stability required for robust transfer to packaging.

This analysis highlights the benefit of multi-faceted powder measurement in the development of DPI formulations. Powders can be quantified via a range of different properties and these vary in terms of their relevance to aerosolisation performance and to manufacturing efficiency. Testing with a universal powder tester that offers dynamic, shear and bulk property measurement generates the data to optimise powder behaviour to meet performance goals and manufacturing constraints in a reproducible, cost and time efficient manner. Such instruments are therefore a productive solution for this especially demanding application.

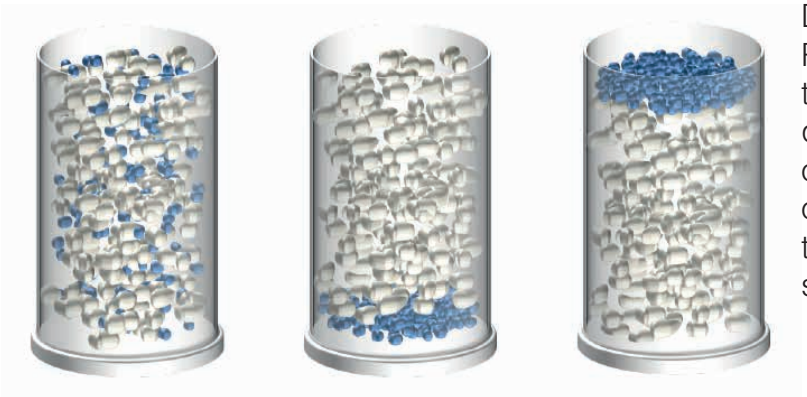
4.4 | Powder Characterisation Techniques for Predicting Segregation

Segregation tends to be unplanned and/or undesirable - or indeed both! Segregation is particularly problematic in situations where a small amount of an active ingredient is distributed within a powder blend, with pharmaceutical formulations being the obvious example. In the manufacture of pharmaceuticals, segregation in a hopper or feed frame, or during conveying and transport can have a catastrophic effect on content uniformity. It may also impact processability, although this would be considered a relatively low priority in light of content uniformity issues.

Segregation generally means the separation of one group from another. In powder processing it usually refers to the physical reorganisation of a previously homogeneous blend, most commonly on the basis of size, although other properties such as particle density and shape can also be influential. Segregation proceeds via different mechanisms depending on whether it is promoted by vibration, shear and flow, or aeration of the sample. Understanding these effects is important for the successful identification and resolution of a problem.

Gentle vibration of a sample may encourage smaller particles to move downward, and larger particles to rise to the surface. As the powder is agitated, finer material is able to travel downward filling inter-particulate gaps and forcing larger particles upwards. Segregation of this type is often driven by differences in particle size.

On the other hand, with an aerated sample, especially one close to the point of fluidisation, larger and/or heavier particles tend to sink to the bottom of the sample leaving fines disproportionately distributed in the upper layers. Here, the bulk of the powder behaves like a fluid through which heavier particles fall in the same way as they would through a low viscosity, lower density liquid. With samples containing similarly sized particles of different density it will be those that are denser that concentrate in lower regions of the sample via this sedimentation process.



Dynamic powder testing, using a Powder Rheometer, is one way to evaluate the tendency of a material to segregate and quantifies the impact of segregation on flow behaviour, a key determinant of processability. Two features of the technique are particularly beneficial for segregation studies.

Firstly, it is possible to submit the sample to controlled segregation cycles, well-defined low stress agitation for a set period of time. Determining the extent and rate of change of flow energy as a function of number of segregation cycles assesses the tendency of the sample to segregate. Generally speaking, with samples that segregate easily, flow energy will change significantly and quickly as the number of segregation cycles increases. Secondly, dynamic measurements can be carried out after the sample has been aerated or fluidised. This makes it possible to apply a test methodology that measures if and how the powder tends to segregate as a function of aeration, meaning that alternative segregation mechanisms can be investigated.

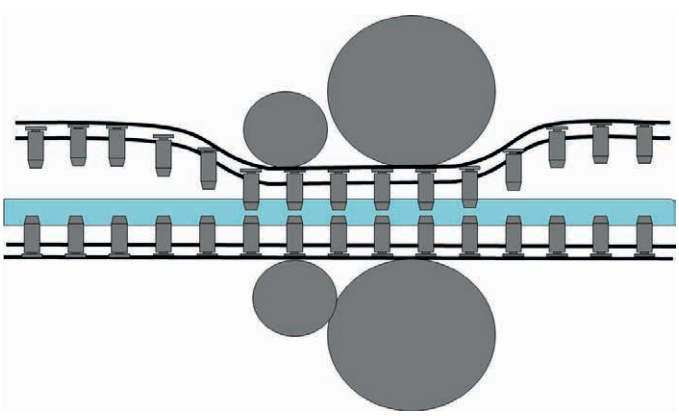
Segregation is a major issue, particularly for pharmaceutical manufacturers, with non-uniform distribution of an active ingredient the most pressing driver for its avoidance. Dynamic powder characterisation enables the investigation of both the tendency towards, and the mechanisms of, segregation providing useful information to enable formulators and process engineers to mitigate its effects.

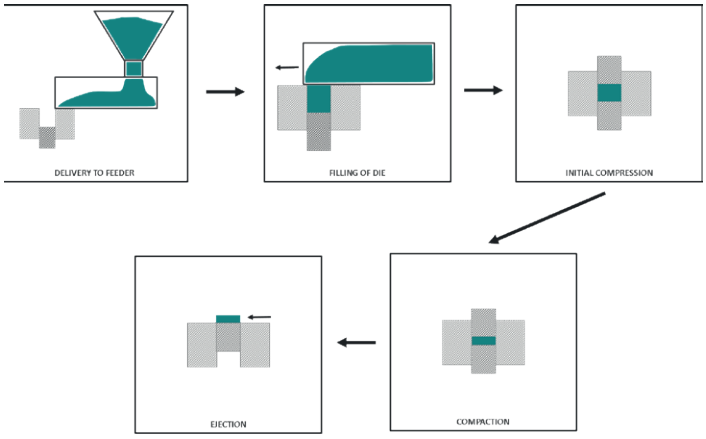
4.5 | Powder Characterisation Techniques for Tableting Applications

Highly stable, simple to administer, and cost-effective, tablets remain the most popular drug delivery vehicle. Tablet production has a long history but continues to evolve as the industry innovates increasingly sophisticated products and works towards greater efficiency. The drive towards continuous manufacture, faster production speeds, increasingly potent actives and the adoption of complex multi-layer tablets present modern-day tablet manufacturers with significant challenges. Understanding how to manipulate the properties of the blend towards better processing performance and products with defined critical quality attributes is essential.

The Basics of Tableting

The sequential stages of a tablet manufacturing process subject the powder blend to a range of different conditions. Initially, the blend is transferred from the hopper into the feedframe, from where it circulates on to the table, flowing into each die. Consecutive passes of the feedframe blades encourage complete die filling. The following “micro-process” is compression, where punches compress the prescribed volume to a defined compression force within the die to form a stable tablet. Ejection of the tablet from the die completes the process.





Moving on from Traditional Test Methods

Historically, tablet producers have relied on powder characterisation techniques that describe a blend with just a single figure, or in terms of only one aspect of its behaviour. Carr’s Index for example, angle of repose, or even shear cell techniques have pronounced limitations when it comes to the rigorous optimisation of tableting processes and powder testing methodology has developed considerably since their introduction. Modern instruments complement automated and precise shear and bulk property measurement with dynamic testing. Dynamic analysis, of a powder in motion, is especially useful for process-related studies and for quantifying cohesion and the response of a blend to air.

Defining Relevant Powder Properties

For tableting applications, dynamic flow properties quantify the ease with which a blend will flow into an empty or partially filled die. Furthermore, dynamic testing can detect a tendency towards segregation, of a fine, sparsely dispersed active, from the excipient bulk. Permeability can also be studied directly. Ideally, once in the die the powder blend should release air quickly to ensure a complete fill. Unreleased, entrained air may be compressed, potentially resulting in lamination or capping of the tablet, post-compaction.

Compressibility is another bulk property of relevance to the compaction step. With a highly compressible blend, tablet thickness, hardness and mechanical integrity will be compromised, whilst, for a less compressible powder the applied force from the punches will be transmitted more uniformly, giving a more homogeneous, stable tablet.

Shear cell testing does have complementary value for tableting applications and can be informative with respect to hopper discharge behaviour. Wall friction data are also helpful in predicting whether a blend is prone to 'picking' or adhesion of the powder to the processing equipment.

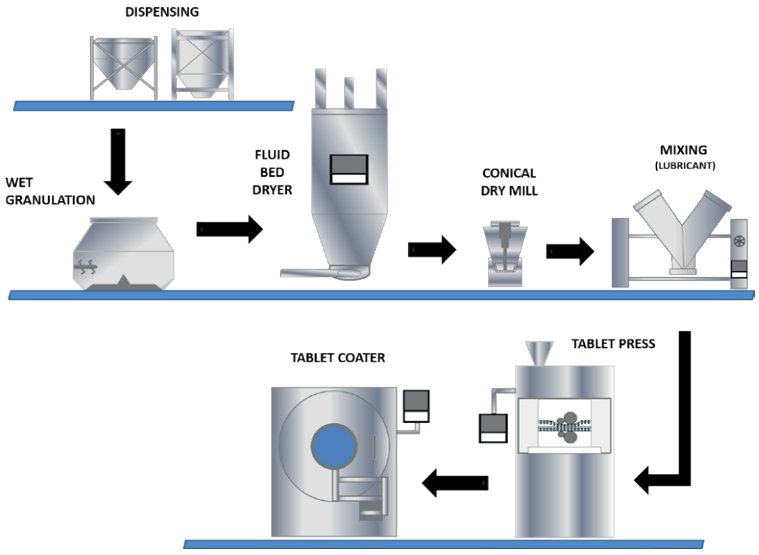
This brief analysis highlights how different powder parameters are pertinent at different stages of the process. Tools that quantify a range of behaviour characteristics for the blend, rather than measuring a single figure result, make it easier to see this 'bigger picture'. During formulation such information promotes a more holistic approach that includes good processability as one of the criteria for success. Later, at the process design stage, these same data produce more secure understanding that can reduce the need for post-commissioning changes. And finally, during day-to-day manufacture, detailed and sensitive powder specification minimises problems surrounding batch-to-batch variability – in either the raw material or intermediate product – and supports effective troubleshooting. In all these ways an investment in the most suitable analytical instrumentation returns value at every stage in the production of a tablet.

4.6 | Powder Characterisation Techniques for Wet Granulation Applications

Wet granulation is a widely applied unit operation, especially within the pharmaceutical industry where it is a common precursor to tableting. It is often carried out as a batch process, with endpoint detection an important issue. Here, dynamic powder testing offers proven benefit. By providing sensitive detection of the transition from wet mass to granulate, using a property that is independent of scale, this powerful analytical technique can accelerate scale-up and process optimisation.

The Challenge of Developing Wet Granulation Processes

High shear mixers are traditionally the preferred choice for wet granulation. After initial blending of the dry components, a binder solution is added, whilst mixing continues, to wet the blend and promote granulation to a desirable endpoint. Control parameters include the amount of binder added, the rate of addition, processing time and impeller speed.



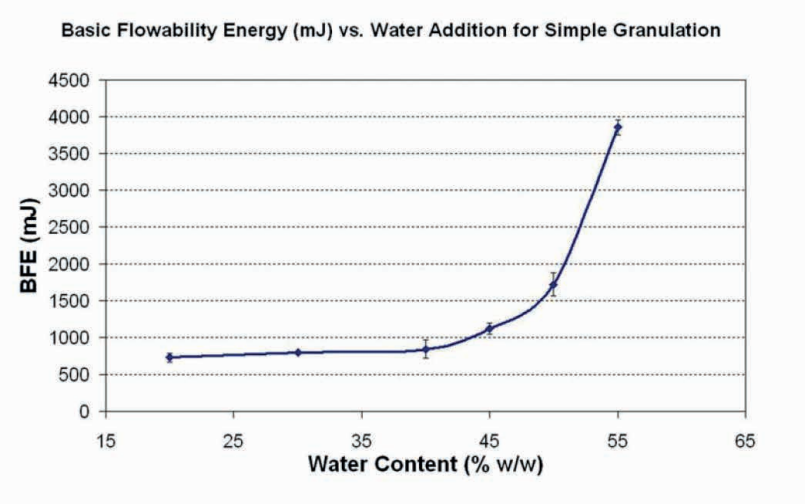
Two major issues complicate process development. Firstly, wet granulation is often an intermediate step so determining an optimal endpoint frequently involves working-up a number of batches at small scale, through to a final end product, such as a tablet. This can be a lengthy process but is essential if the properties of this intermediate material cannot be used to predict attributes of the finished tablet.

Secondly, the process variables used to control wet granulation do not scale in a linear manner. For example, a large-scale unit may need a water addition of 27% instead of the 24% required by a pilot scale process, to reach the same endpoint.

Identifying a property that can be used to accurately detect granulation endpoint throughout the development cycle is advantageous.

The Value of Dynamic Powder Properties

Basic Flowability Energy (BFE), a dynamic powder property measured using a Powder Rheometer, has been successfully used to track wet granulation processes to an optimal endpoint. BFE remains approximately constant in the early stages of a granulation but increases sharply as the mass becomes wetter. Image analysis confirms that this sharp rise corresponds with the processes of nucleation and granule growth. The rapidity of the rise makes BFE extremely sensitive at this most crucial part of the process, providing an opportunity for precise endpoint definition.



Tracking a Wet Granulation Process with Basic Flowability Energy Measurements

For a new wet granulation process, BFE monitoring quickly identifies the operating region of interest. Working up a number of batches made under different conditions within this region precisely sets a target BFE that exactly defines an optimal granule. For example, in pharmaceutical applications the BFE of granules has been successfully correlated with certain critical quality attributes of tablets made from them, notably hardness. A BFE specification for granules can therefore be set to ensure the manufacture of tablets with a consistent, required hardness. Associating an optimum granule with a BFE value rather than a specific set of processing conditions defines a relationship that is independent of scale.

Once established such BFE specifications can be used for all subsequent development work. As the process moves towards commercialisation, optimised processing conditions can be determined relatively quickly, at each stage or scale, to meet the target BFE. Furthermore, over the longer term, operating the process to a BFE endpoint, rather than with preset parameters, introduces the potential for adaptive control, the timely manipulation of process variables to maintain a consistent output even when excipient properties unexpectedly vary.

Process control can be further improved using inline monitoring technology. The Drag Force Flow (DFF) sensor measures the flow force associated with the movement of granules, in real-time, producing data that have been shown to correlate with BFE measurements. Going forward there may therefore be potential to define a wet granulation endpoint in terms of BFE and then transfer that specification into the process environment as a set point for real-time control, on the basis of DFF data.

Wet granulation can undoubtedly be a challenging process to develop and operate but dynamic testing can help, to accelerate process optimisation and to achieve flexible and efficient manufacture across the lifetime of the product.

CHAPTER 5

5.1 | Powder Characterisation for Formulators

Requirements in R&D are often markedly different from those in QC. In this chapter we will now look at powder testing from the perspective of where in the product lifecycle it is being applied, starting with an activity that takes place relatively early in the development of pharmaceutical products - formulation.

The Goals of Formulation

Accelerating product development through formulation into successful manufacture and on to the marketplace, is an important goal for the pharmaceutical industry. Optimising the formulation process and more efficient production are strong themes as revenues come under intense pressure. For formulators the principal focus is developing a product that delivers desirable clinical performance, but manufacturing demands are increasingly influential. Steps taken at an early stage to thoroughly scope the links between process and product variables, as advocated by Quality by Design (QbD), can pay dividends over the long term. This is particularly true for powders, where optimisation of the formulation and process, in combination, builds quality into manufacturing from the outset.

Cost-effective tools for sensitive and relevant powder characterisation are an essential part of the formulator's resources. Universal powder testers are especially useful, their value deriving from a unique combination of features which crucially includes:

- Multi-faceted powder characterization (shear, bulk and dynamic properties)
- Exemplary reproducibility
- Process relevant measurements

Relevant, Reproducible Testing

Describing a powder using an array of variables rather than a single number is now widely accepted as the optimal approach since the complexity of powder behaviour cannot be adequately captured using just one descriptor. Instruments that offer multiple measurement strategies are an efficient way of gaining maximum insight, making it easier for formulators to identify and accurately measure the unique powder properties that correlate with specific aspects of clinical performance. For example, research has shown that the aerosolisation characteristics of dry powder inhaler formulations correlate directly with aerated flow energy. This parameter is only accessible via dynamic powder testing so this correlation would be missed using conventional, single parameter tests.

Excellent reproducibility enhances the sensitivity of any analytical instrument, sharpening the quality of the data. The correlation of different variables is severely hampered by 'noisy' data that can make it impossible to tell whether differences between samples are real, or simply measurement inaccuracies. For the formulator, sensitive analysis therefore provides fine detail, enhancing understanding of the factors influencing product performance.

Finally, process relevant data means that researchers can predict the in-process behaviour of a powder with just small amounts of sample, offering the opportunity to formulate on the basis of process understanding and control, as well as clinical performance. Producing a database of reproducible powder properties helps to break down the traditional barriers between formulation, process design and operation, promoting a more holistic multidisciplinary approach to development that captures the knowledge of different disciplines. Lessons learned during

pilot and full-scale operation can inform new development if the information can be fed back upstream. For example, the manufacturing team may know that formulation A performs well in a vacuum vial filling process while formulation B is more problematic. Analysing the powders reveals that the poor performance of B can be quantified in terms of its permeability and the impact on flow properties (Basic Flowability Energy) induced by applying a vacuum. This is valuable information for formulators developing a new product that will be processed in a similar way.

In summary, comprehensive, sensitive, process-relevant powder characterisation is vital for effective formulation. Universal powder testers, such as the FT4 Powder Rheometer, cost-effectively meet this need and can significantly streamline and improve the formulation process.

5.2 | Powder Characterisation for Process Designers and Engineers

For process designers specifying new plant, the goal is to engineer equipment that will process and handle powders consistently and efficiently, as specified by the design brief. In contrast, engineers working as part of the manufacturing team rarely have the option of changing out equipment but strive to achieve acceptable operation using the existing plant. While these goals are somewhat different, the two groups share a need for detailed process understanding, knowledge of the interplay between powder properties and process equipment and how, in combination, they deliver product with the intended properties and quality. For the particulate handling industries this can be a significant challenge. To successfully design and operate powder processes, engineers need to determine the conditions to which a specific unit operation will subject the powder, and then measure the powder's response to each of these environmental conditions.

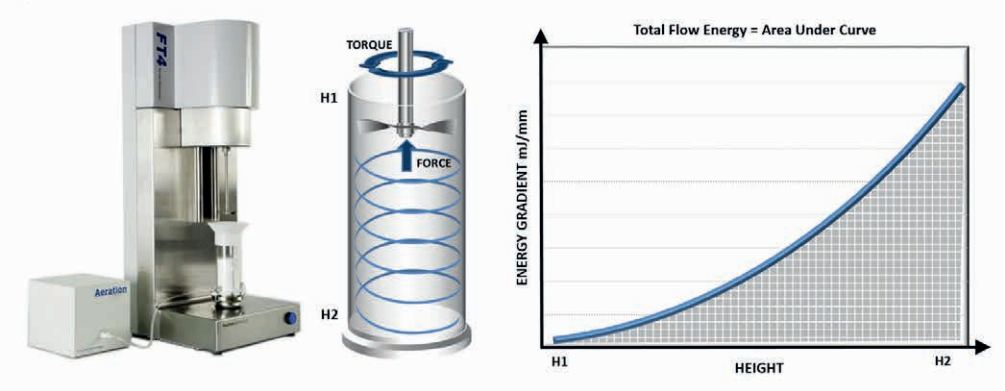
Identifying Process Problems

Consider the example of a blend flowing from a hopper into the feed shoe of a die filling process. Each time the powder level falls below a certain point, the hopper is refilled with a new batch of feed material. However, for certain blends it is noticeable that for a short time before and after this refill, discharge flow becomes erratic, triggering process problems. When the hopper level is too low, or after recharging of the hopper, the stress in the powder at the outlet of the hopper varies. This translates through to inconsistent pressure in the shoe and variation in die filling performance with some, but not all blends.

Analysis of these relatively simple process steps reveals the variable conditions imposed on the powder. As the hopper fill level decreases, the normal stress acting on the powder near the outlet reduces and a stable arch forms, causing an interruption in flow. A stable arch may also form during recharging of the hopper, as high levels of consolidation are induced by the relatively high normal stress imposed by the additional powder. Should it be necessary to stop the process for any reason, consolidation by vibration from surrounding machinery may also become an issue. Here then, the response of the powder to consolidation, by direct compression or vibration, and its cohesive strength is highly relevant. If consolidation brings about a major change in flow properties, then problems are more likely to arise.

Rationalising Powder Performance

Universal powder testers incorporate bulk, shear and dynamic measurement1 in a single instrument, and for engineers offer an intuitively sensible approach. They allow measurement of the powder in motion and permit the analysis of samples in a consolidated, moderately stressed, aerated, or fluidised state. Comparing the flow energies of conditioned samples with those of samples consolidated by compression or tapping gives a consolidation index (CI). Quantifying the response of the powder to consolidation in this way provides the insight necessary to rationalise the processing behaviour outlined above.



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Comparative studies of the die filling performance of two different powders, A and B, provide an illustration of this point. Sample A (Aluminium powder) has a CI (tapped) of 1.43 while that of sample B is 2.32 (Tungsten powder). This indicates that B, a cohesive material with very fine (4 microns) angular particles, is significantly more affected by vibration than A. Die filling trials confirm that the performance of sample B deteriorates significantly if it is consolidated, as would be expected. For example, at a shoe speed of 50 mm/s, Filling Ratio falls from over 90% to less than 50% as a result of vibrational consolidation (20 taps), where Filling Ratio is the mass of powder in the die after filling relative to the mass associated with a completely full die. In contrast, Sample A demonstrates much more robust behaviour whereby filling performance is approximately the same before and after consolidation, at an equivalent shoe speed.

In this case, a designer with access to the information provided by the powder tester has options - specify a more accommodating hopper, with more steeply angled walls or a larger outlet; pursue a policy for reducing equipment vibration; and/or install additional mechanical aides for rectifying blocked hoppers. This same information leads the manufacturing team to better operational practice with respect to hopper filling and an improved response in the event of blockage. Refilling the hopper more frequently with smaller quantities of feed is likely to be one of the best ways of reducing process upsets. For both groups it is detailed and relevant powder testing that provides the information needed to effectively manipulate either design parameters or operating practice to achieve manufacturing goals.

5.3 | Powder Characterisation for Equipment Manufacturers

Equipment manufacturers share with process engineers the task of specifying plant for optimal performance. For processes involving powders this is a challenge, with compatibility between plant and material being fundamental to success. Designing or modifying equipment to suit the characteristics of a powder provides a firm basis for reliable and successful operation, building quality and robust performance into the manufacturing process from the outset.

Understanding Powders

It is too simplistic to label powders 'good' or 'bad' when in fact the response they exhibit depends on the demands of any given process step. For example, spherical spray dried lactose with a relatively large particle size may flow freely from a hopper, but perform badly in a feeder, with the particles 'locking up' under the imposed forced flow conditions and the powder bed resisting movement with significant strength. This may subsequently result in particle attrition, with accompanying changes to particle size, morphology and flow properties.

Developing a relevant and comprehensive understanding of the nature of a powder is the first step towards achieving a good match between a formulation or process material and the plant. By combining a suite of complementary measurement techniques that allow real insight into powder behaviour, universal powder testers deliver the necessary information. Quantifying powders in terms of well-defined shear, dynamic and bulk properties allows the building of a database that can be used to learn how to design equipment that will work well with different materials. And conversely how to develop specifications for powders that will suit a particular piece of plant.

Matching Powders and Plant

In this context, Processability Index is a useful concept. Consider an equipment manufacturer developing a new tablet press or working to enhance the capabilities of an existing press design. Various tableting blends are run through a prototype, pilot scale or modified press and the results vary significantly. Formulation A processes easily at high turret speeds, giving tablets of excellent quality while with formulation C, in contrast, no acceptable tablets are produced. Formulation B lies between these two extremes - if the press is carefully operated at moderate turret speeds, successful manufacture is possible. Ranking these powders in terms of processability, creating an index, we could assign formulation A a score of nine, B five and C two.

Correlating these scores with measured powder properties identifies the optimum values for the parameters that dictate performance in the press. These would typically include, for example, aerated flow energy (cohesion), compressibility, permeability, and unconfined shear strength. If an equipment manufacturer develops a specification of this type for each unit then establishing the best option for a customer with a new formulation is straightforward. Testing the new material and comparing the results with the defined specifications identifies the best solution.

A similar approach is valuable when adapting or changing plant to accommodate a certain formulation. In this case analysis and comparison will reveal whether or not a powder will process well, and if not, which properties deviate most from the ideal. This helps to pinpoint where and why problems are likely to occur, facilitating informed equipment modification.

Robust and reliable powder processing is achieved by designing and/or specifying plant that works with, rather than against, the powder. Failure to achieve a good match results in an inherently sub-optimal plant that is likely to suffer poor operational efficiency throughout its lifetime. The insight provided by universal powder testers helps equipment manufacturers and process designers to properly understand the nature of a process material, enhancing their ability to establish an optimal manufacturing solution from the outset.

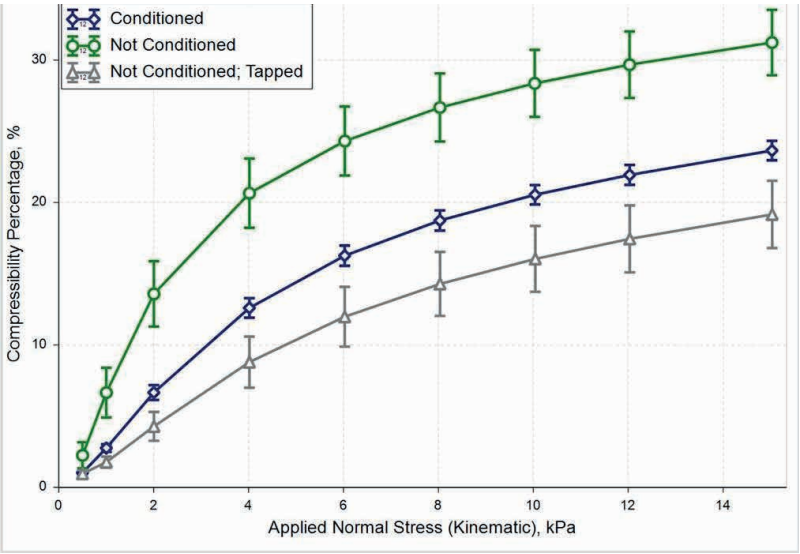
5.4 | Powder Characterisation for Quality Control

Quality control, of either an intermediate material or final blend, places a unique set of demands on an analytical tool. Sensitive differentiation between samples is essential, as is the need to measure a parameter that accurately reflects performance, during manufacture or within the customer's application. Historically for powders, both these issues have presented a challenge, but significant advances in characterisation technology have transformed this situation. Universal powder testers now measure a comprehensive set of dynamic, shear and bulk properties with exemplary reproducibility, making them a suitable choice for sensitive QC.

Reproducible Measurement…

Powder behaviour is complex and cannot yet be mathematically described using the many discrete variables that influence it. The ease with which a powder flows, for example, depends on an array of primary variables, including particle size, shape and surface texture, but also on many system parameters such as degree of consolidation stress, shear rate and moisture content. Poor control of any influential variable within the test will compromise the reproducibility of an analytical technique.

Modern powder testers reflect widespread recognition that achieving excellent reproducibility relies on employing closely defined measurement protocols and significant automation, and on 'conditioning' the sample before analysis. Conditioning involves gently agitating the powder to release excess air and/or break up agglomerates and leaves a homogeneous loosely packed bed. Ensuring that a powder is always measured in this same baseline state significantly enhances reproducibility and, consequently, sensitivity. Differences detected by instruments that employ these strategies to deliver exemplary reproducibility can be confidently attributed to real differences between samples, rather than variability in the technique.



…of a Relevant Variable

While accurate measurement is critical for effective QC it is equally important to select a variable that will best reflect performance targets. Consider a manufacturer sourcing alternative supplies of a raw material. The material has a specification defined in terms of composition and properties such as particle size and bulk density, but when an alternative supply meeting this specification is introduced into the process, production efficiency plummets. The new material causes blockages and the final product quality is inconsistent. Clearly the defined specification does not include key variables that directly impact processability and is therefore inadequate for identifying an optimal quality/cost supply.

Powder testing instruments that offer multiple methodologies make it easier to quickly identify those parameters relevant to performance. Building a database of shear, bulk and dynamic properties for a material facilitates the correlation of specific variables with aspects of processability or product performance. For the raw material, for example, a short study may reveal that the specification is more precisely defined in terms of Basic Flowability Energy (BFE), a dynamic term, and permeability, a bulk property, as well as composition and particle size. With a well-defined specification, testing alternative sources of the raw material and identifying the best supplier becomes very much easier.

Simple powder characterisation techniques such as angle of repose, Hausner Ratio and flow through an orifice, have a well-established place within the powder processing industries but typically measure just a single property, often with poor reproducibility. In contrast, modern universal powder testers deliver multi-faceted powder characterisation and exemplary precision and reproducibility. Automated, with well-defined measurement procedures these instruments enable sensitive specification setting and the highly effective QC needed to target premium product performance.

CHAPTER 6 - Conclusion

Powder Characterisation for Modern Manufacturing

It is widely acknowledged that powders exhibit complex behaviour and are not as easily characterised as gases and liquids, for example. Over the years many powder testing techniques have been devised and each offers some insight into powder behaviour. However, where improved manufacturing efficiency is concerned it is becoming clear that methods offering precision, sensitivity, and reproducibility - and which deliver process relevant data - have most value.

Developments in powder testing instrumentation have not only introduced new methods but have also improved the reproducibility and relevance of more established techniques. Dynamic testing for example, which measures the flow energy of a powder, is a more recently introduced technique that has demonstrated considerable industrial uptake largely because of its proven relevance and sensitivity. Shear testing, a well-established method, remains popular, and its implementation in more modern instrumentation has improved both precision and reproducibility. Furthermore, it is now possible to assess and rank flowability via uniaxial testing. Simple to use, cost-effective and sensitive, a uniaxial tester can directly measure unconfined yield strength and Flow Function more quickly and easily than any shear cell.

The relatively recent commercialisation of uniaxial testing provides quick, inexpensive testing, as delivered by traditional techniques such as angle of repose, but there are critical differences. Measurements are automated, the property measured is an intrinsic characteristic of the powder, and the results are highly reproducible over a range of stress conditions. These features make the data more robust and reliable, increasing its value for testing in areas such as QA and QC.

Conversely, there are also automated, comprehensive powder testers that combine the best techniques available - shear, dynamic and bulk property testing - to reliably deliver a diverse data set that correlates with performance in a wide range of processes and applications. These testers make it possible to quantify meaningful and relevant powder properties in order to achieve two important goals. Firstly, to numerically describe, rationalise and ultimately, better understand powder processing operations. This is the key to developing design algorithms that support improved equipment specification and more efficient process operation. And secondly to extend our knowledge of the different factors that influence powder behaviour. By quantifying powder behaviour we can systematically and scientifically explore the parameters that affect it – how do variations in air, moisture content, electrostatics, particle size and shape manifest for example?

In conclusion, I believe that we have made significant progress towards establishing the right powder testing toolkit for modern manufacturing, with key, complementary elements now in place. Adopting these tools will enable the move towards more efficient, productive, and knowledge-led powder processing.

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