Bulk Properties of a Cancer Drug API as Measured with the SSSpinTester

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1.0   Introduction

Unconfined yield strength (bulk strength) is the major principle stress that will cause material in an unconfined state to fail in shear. It is the primary flow property that governs the development of hang-ups in process equipment. It is used to compute critical arching and rathole dimensions for a given material in a hopper or bin. All hang-ups in process equipment result in the formation of a free surface. By definition, the stress acting normal to any free surface is zero. However, stresses acting along the free surface may not be zero (Figure 1). In a hang-up condition the material on a free surface is supported by stresses that act along the free surface and are equal to the unconfined yield strength of the material.
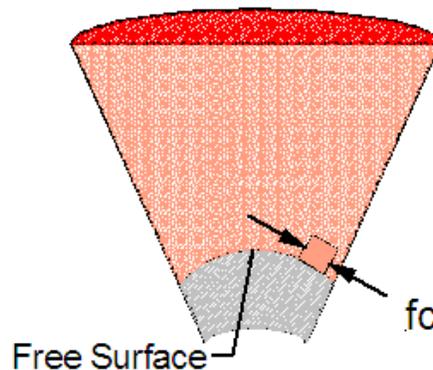

Figure 1.   Typical arch in process equipment

Critical conical arching dimension:

The critical conical arching dimension is the smallest span of a conical hopper that will prevent arching of the bulk material. It is a function of the material's unconfined yield strength and storage time in the vessel. The conical hopper must have an outlet at least this big to prevent stable arch formation from occurring. Plane flow hoppers can have hopper widths about ½ as wide and still prevent stable arch formation. The critical arching dimension is also a small function of the bin size and, hence, is usually associated with a calculation basis which represents the approximate size of a given bin geometry.

Critical rathole dimension:

The critical rathole dimension is the size of the largest flow channel that will result in stable rathole formation in a funnel flow bin design. The active flow channels in a funnel flow bin must be greater than this value to prevent stable rathole formation. It is important to note that ratholes cannot form in mass flow hoppers. The critical rathole dimension is a function of the maximum stress level in the bin and, hence, depends on the maximum diameter of the bin.

Bulk Density:

Bulk density may seem like an intrinsically simple property. It is the weight of the particles divided by the combined volume of the particles and the interstitial voids surrounding the particles. It is a function of the stress level and strain history of the material. It is used to determine the limiting rates of particulate materials. It is also used to determine the ability of a given powder to store entrained air.

2.0   Strength Testing – Background

For the process engineer, strength is the key property that determines if a bulk material will arch or form stable ratholes in process equipment. Since the goal of powder processing is to maintain reliable flow, arching and rathole tendencies are considerable problems. Strength is a far reaching flow property that controls the behavior of the bulk material in many processes. Excessive powder strength may make the bulk material difficult to fluidize, resulting in channeling and poor process control. Excessive strength may make blending impossible. Excessive strength can cause powder material to agglomerate when it is agitated. Excessive strength can cause material to arch over die cavities, making capsule filling and tablet production difficult at best. Strength can cause weight variations in filling machines. Excessive strength can also cause powder to form stagnant zones during operation.

However, sometimes bulk strength is a good thing. Just the right amount of yield strength may prevent unwanted particle segregation in powders. Strength can cause compacted material to hold together after compaction, making tableting and ceramic part production possible. And, in a serendipitous twist of fate, strength will cause a cohesive bulk material to agglomerate in roll press operations, allowing for the formation of easily handled materials and preventing many of the problems caused by bulk strength. Bulk strength measurements can provide early warning of potential process upset caused by arching and ratholing. Thus, it is an ideal measurement for quality control of powder processes.

Many current methods used to measure material strength require significant technician training to get reliable results. Many existing test methods require a significant amount of bulk solid material. Often getting this amount of material is difficult, or the material is expensive. The typical bulk solids strength test measurement process requires several hours of testing and calculation to acquire reasonable results. However, the method used in this report is a simple procedure to measure the strength of a very small quantity of sample material in just a few minutes.

3.0   Strength Testing – SSSpinTester Measurement Methodology

The test technique is to place a small quantity of material into an enclosed conical cavity; consolidate it using centrifugal force; then remove the obstructions at the bottom of the conical cavity and use centrifugal force to cause material to fail, yield or extrude from the cavity. The process is summarized in steps 1 through 4 below. The key parts of the test procedure are highlighted below:

Step 1

A guard is inserted below the smaller diameter opening of the conical orifice and material is placed into the cell by passing or vibrating the powder through a coarse sieve to break agglomerates. The gentle fill process reduces the over-compaction pressures that arise during filling.   This necessary step allows for strength to be measured at very low consolidation pressures. Over-consolidation due to handling is reduced.
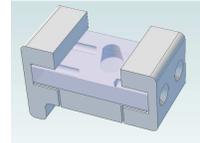
Step 2

A guard is inserted at the top of the cell and the cell is placed in the rotary cavity such that the axis of the conical cavity is 90 degrees from the direction of rotation.

Place cell in rotor
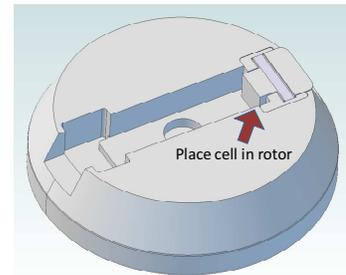
Step 3

The cell and rotor assembly are rotated to a prescribed speed and held for an allotted time. This causes centrifugal forces to act on the bulk material in the conical cell and compact the material within the cell.   The rotor speed and the weight of the material, along with the position relative to the axis of rotation, are used to compute the consolidation pressure.

Rotate to consolidate
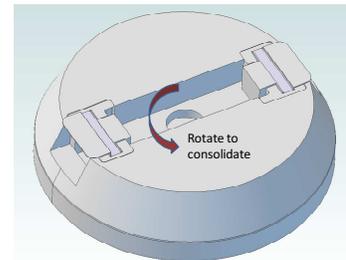
Step 4

The rotation is stopped and the guards removed. The bulk material arches over the conical cavity. The rotation speed is increased incrementally until the compacted material exits the conical cavity due to centrifugal force. The weight of the material, the position relative to the axis of rotation, and the rotation speed at the point when the material leaves the cell are used to compute the force needed to fail the compacted material in the conical arch.   This data is then used to compute the bulk unconfined yield strength.

Rotate to fail material
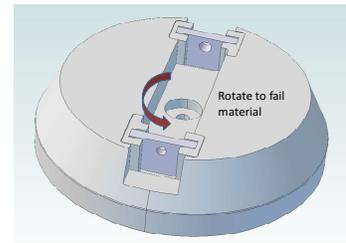
4.0   Relation of Test Results to Process

The ability to relate measured material properties to actual production parameters is essential in "getting it right the first time" from the standpoint of both development and manufacture – both product and process.

For example, in the pharmaceutical industry all drugs must be "packaged" somehow with excipients to be marketable. Material bulk properties MUST be measured at some point in the development process to quantify drug formulations for use in tablet press and tablet fill. If the bulk strength of the material is not known – all decisions regarding packaging are based on the "guess and check" method.   Real powder packaging systems operate at 40 to 200 Pa pressure. Traditional instruments measure bulk strength at pressures of 500 Pa or greater. When pressures are measured at values of 500 Pa, 1000 Pa or above, mathematical extrapolation is necessary to scale measured values to real systems.   Since strength behavior is non-linear, extrapolation results in poor deductions.

The SSSpinTester accurately quantifies the strength of bulk solids at consolidation pressures down to 30 Pa with reasonable repeatability. Since the User indicates the pressure at which the SSSpinTester will measure strength, we no longer must rely on inherently inaccurate extrapolation for answers.   The SSSpinTester is capable of directly measuring bulk strength at consolidation pressures low enough to scale to real industrial processes.

5.0   Results of SSSpinTester Analysis

We measured the unconfined yield strength and bulk density of a Cancer Drug API using the SSSpinTester. The results are found in Figures 2 and 3, and in Table I. This material is compressible, with densities between 351 kg/m3 and 499 kg/m3, depending on consolidation pressure (Figure 2). In typical feed bins, the density leaving the bin will be around 378 kg/m3.   The maximum density in a 1.2-meter diameter bin that has a vertical section that is 2.4-meters tall would be about 544 kg/m3.

We calculated the rathole and arching indices for a Cancer Drug API. The results are reported in Table II. Arching will likely be somewhat of a problem with this material. The flow properties suggest that the critical conical arching after 0-hours storage is 0.16-meter.
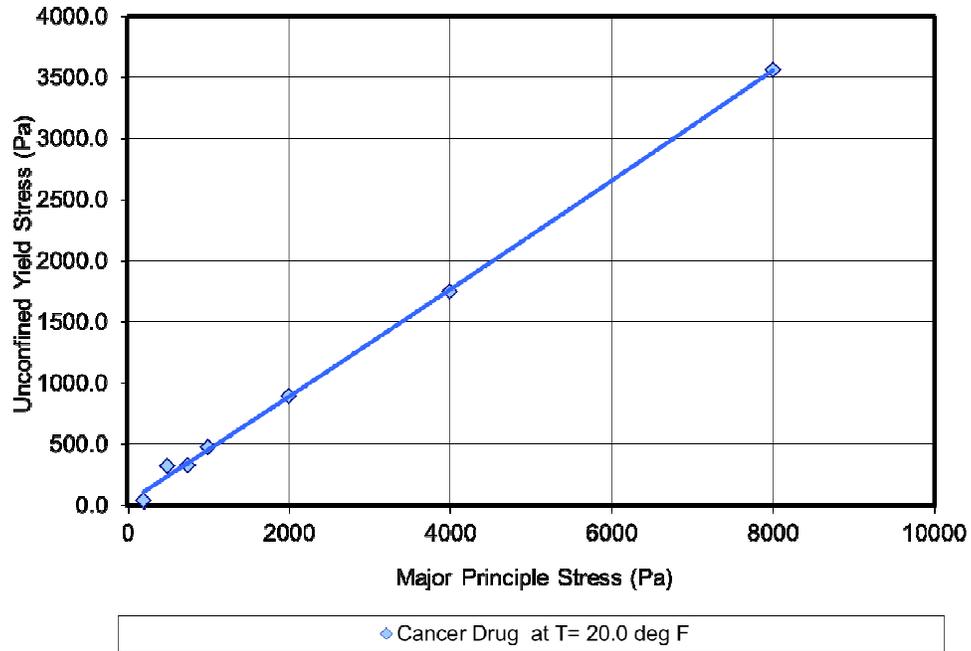
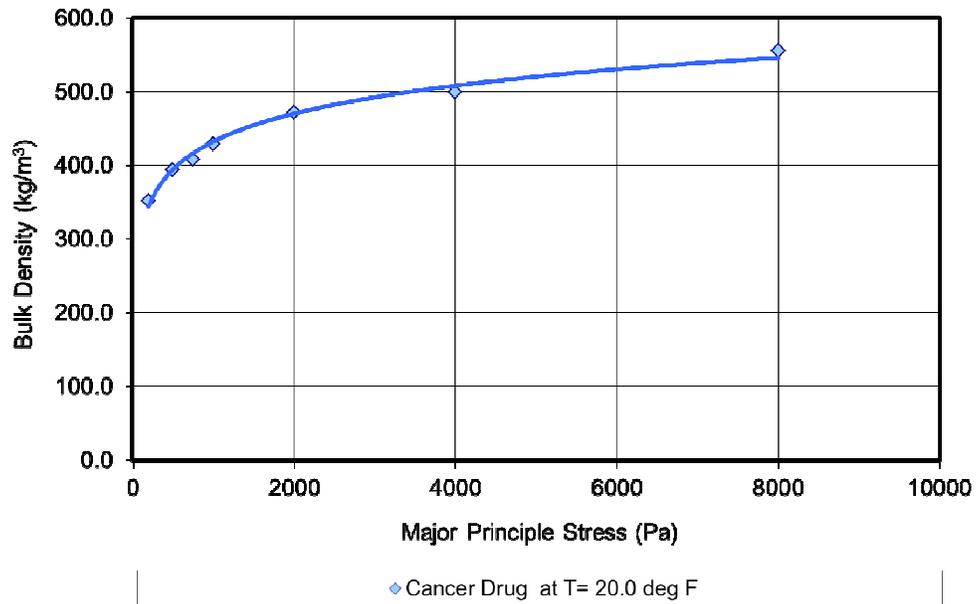**Figure 2.** **Unconfined Yield Strength of a Cancer Drug API**

Figure 3. **Density of a Cancer Drug API**

Table I: Unconfined Yield Strength and Density as a Function of Stress

Consolidation Pressure (Pa)	Bulk Unconfined Yield Strength (Pa)	Bulk Density (kg/m^3)
200	135.6	351.8
500	318.5	394.1
750	323.8	408.1
1000	474.3	429.2
2000	891.2	471.5
4000	1747.2	499.6

Table II: Summary of Flow Properties of a Cancer Drug

Flow Rate Indices			
Indices Basis : Dbin =1.20 m Dout = 0.15 m			
Bin Density Index BDI	Feed Density Index FDI	Flow Rate Index FRI	Settlement Index SI
(kg/m^3)	(kg/m^3)	(tonne/hr)	(min)
554.62	379.99	0.05	18.40
Hang-up Indices			
Indices Basis : Dbin =1.20 m Dout = 0.15 m			
Temperature in	Storage Time in	Arching Index AI	Rathole Index RI
(deg C)	(hr)	(m)	(m)
20	0.0	0.16	2.20