

FLODEX Technical Bulletin

Intrinsic flowability: a new technology for powder-flowability classification

ALBERTO GIOIA

THE FLOWABILITY of the powdered materials used in a tablet formulation is a major consideration in the production of this popular dosage form. **Flowability** may be defined as the powder's ability to flow evenly, by means of gravity and other forces, from the top to the bottom of the hopper and then on to the dosage, compaction, and crushing chambers.

In tableting applications, powder with a high degree of flowability offers several advantages. (1) A smooth downward flow of the material will minimize air-pocket formation. (2) The dosage chamber may be filled very accurately, which not only increases average weight and decreases variation in average-weight coefficient but also creates even pressure during compression, thereby lessening wear on machine parts. (3) **Flowable** powder increases the reproducibility of feed parameters, which results in consistent tablet hardness, friability, dissolution rates, and blood levels. (4) During compression, air is expelled well because of the powder's high degree of permeability, a quality which helps eliminate such tablet flaws as capping and splitting. (5) Finally, high production speeds may be maintained.

If flowability of the powder has been obtained by minimizing the percentage of fine powders, two additional advantages result: the limited surface area of the powder particles makes lubrication easy; and the reduced electrostatic and pneumatic dust sprays of fine powders help to increase yields and to keep rooms and machines clean.

Weight Uniformity

Attainment of weight uniformity is the prime objective in powder fractionation, but it is also something of a problem. First, although many pharmacopeias indicate the weight-variation limits acceptable in monodose forms, they do not

delineate procedures for fractionating the bulk material in such a way that these limits are met. Moreover, the pharmaceutical industry's practice of using volumetric dosage in bulk fractionation ensures satisfactory uniformity only when the bulk material is liquid and nonthixotropic. For liquid materials, standard laboratory methodologies do exist for quantitative viscosity control under both virtually static and more or less dynamic conditions.

Powders to be fractionated should also have good **flowability**, but until now no laboratory methodology has been suitable for determining flowability indexes that were applicable to actual production. Augsburg and Shangraw perhaps came closest when, emphasizing that the main objective should be to attain a uniform weight, they experimented with some mixtures in tableting machines and considered the variation coefficient of the average weight as the flowability index.⁷ Unfortunately, this evaluation system is flawed in that it is not absolute — it depends on working conditions and machinery used. Furthermore, the method requires that mixtures have reasonable flowability and lubrication. The average weight (CV) obtained in the production equipment, however, may be used as the point of comparison in laboratory tests, just as blood levels are used as points of comparison in dissolution tests.

Parameters Affecting Flowability

Many researchers have identified powder flowability with interparticle friction, which can be measured by various techniques — the flowability cone **angle**,² the tilting-table **angle**,³ and the flow time under standard **conditions**,⁴ to name a few. Gold et al. obtained a weight/time-variation layout under standard vibration conditions by sacrificing the clarity of data on a single **variable**.⁵

The data obtained by the aforementioned laboratory methods, however, do not represent a dependable estimate of the powder's behavior in the machine. I believe that these tests are unsuccessful because they are not directed at the true crux of the problem. In particular, it is incorrect to identify flowability with interparticle friction, as though powder particles were like glass or sand spheres.

The truth is that the parameters determining powder flowability are numerous — particle size, fines, unit surface, particle shape, actual density, bulk density, porosity, air permeability through the powder, electrostatic charge, humidity, settling effects, and cohesion forces (e.g., London and hydrogen) — and they have contrasting and interdependent influence. Flocculation alone — which is caused by cohesion forces, all other parameters permitting — can impair flowability, while very good flowability can be obtained with high-bulk-density powders consisting of almost spherical granules, without flocculi.

Flocculation and Its Origin

Flocculi are groups of low-cohesion fines; they cannot be isolated in a laboratory because they disintegrate easily in sieves. In production equipment, powder containing flocculi tends to adapt to the container (the hopper), a behavior similar to that of a liquid gelatinizing in its container.

Flocculation occurs when the large surface area — and therefore large contact area -- of fines favors cohesion forces. These are the same cohesion forces that greatly increase during compression to produce hard tablets; in powder bulk, however, these forces are too weak to force out the air created by the well-known embolic property of capillaries. Distances between granules therefore remain at $100 \text{ \AA} = 0.01 \text{ \mu m}$. Lactose, starches, and calcium carbonate provide classic examples of flocculation.

Humidity favors the occurrence of flocculation by increasing the contact surface among powder particles, by reducing electrostatic repulsion force since the dielectric constant of water is 80, and by favoring the leakage of electrostatic charge. On the other hand, a light electrostatic charge — obtained, for example, through sifting or by the addition of Cabosil — might contribute to the elimination of flocculi.

An Experimental Method

Principle behind the Method

The basis for this method is the powder's ability to fall freely through a hole in a plate. The diameter of the smallest hole through which the powder passes three times out of three is taken as the flowability index. This method has proved easily reproducible. Each trial is considered valid when the powder that falls involves the entire height of the powder (not to be less than 60mm).

Description of the Equipment

Very simply, the Dow-Lepetit device for testing intrinsic powder flowability (Hanson Research Corp., Northridge,

California) consists of a cylinder with a series of replaceable disks — of different diameters — in the bottom; the hole is closed by a mobile shutter (Figure 1). The actual components of the system are as follows:

1. A stainless steel cylinder with an approximate capacity of 200 ml.
2. A series of stainless steel disks. Each disk has a precise hole in the center in graduated sizes differing 1-2 ml in diameter and is easily attached to form a bottom for the cylinder.
3. A shutter that covers the hole and that may be quickly removed without vibration to allow the powder to flow through the selected hole.
4. An adjustable funnel for loading the sample cylinder with a free fall of the test powder.
5. A suitable container to collect the powder that flows through the unit.

The Procedure

The ring is secured to the bearing to allow the bottom of the funnel to be near *but not touching* the powder surface. A powder load of 50 g is then poured through the funnel into the middle of the cylinder. When loading is completed, 30 sec must be allowed for possible formation of individual flocculi or mass flocculation of the whole load (Figure 2).

Now the lever device is operated to open the hole in the disk quickly and without vibration. A very flowable powder will slowly flow through the small-diameter holes, leaving a cavity shaped like an upside-down, truncated cone (Figure 3). A powder that flocculates in bulk, on the other hand, will fall abruptly, forming a cylindrical cavity. If the experiment is negative — i.e., if the powder falls as just

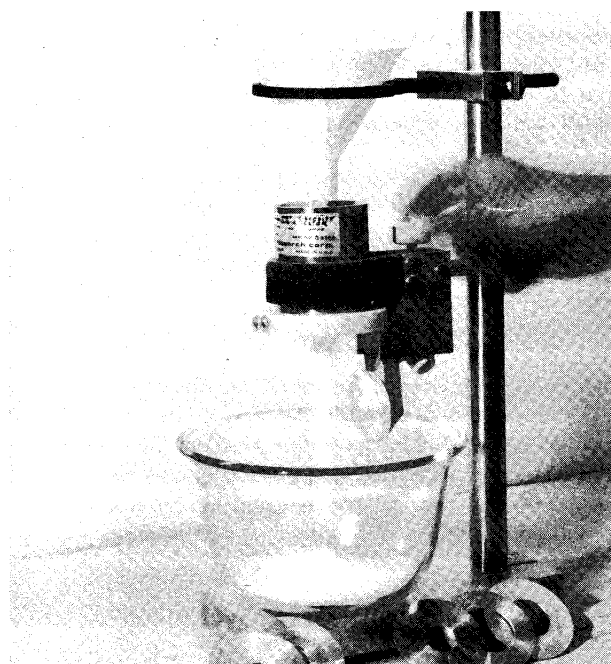


Figure 1: The equipment for testing powder flowability consists of a cylinder with a series of replaceable disks of different diameters — in the bottom; the hole is closed by a mobile shutter.

described — the powder must be tested again with a disk having a larger hole.

Physicomathematical Interpretation

It is simple to demonstrate the direct relation between the radius of the hole and the internal-friction coefficient -i.e., the viscosity — of the powder. Using K as the internal-friction coefficient, r as the radius in centimeters of the smallest hole that allows the powder to flow freely, and d as the nontapped bulk density of the powder in grams per milliliter, we can easily obtain

$$K \leq 490 \cdot r \cdot d$$

Here, K is expressed in dynes per square centimeter, or poises; and 490 is equal to one-half the acceleration of gravity, or $\frac{1}{2}g$.

The weight of the cylinder of powder that is compelled to fall must be greater than the friction on the side surface of the cylinder itself:

$$\pi r^2 h \cdot d \cdot g \geq 2 \cdot \pi \cdot r \cdot h \cdot K$$

where

- h = height of cylinder of powder
- $\pi \cdot r^2 \cdot h$ = volume of cylinder of powder
- g = 980 cm/sqsec (acceleration of gravity)
- $2 \pi \cdot r \cdot h$ = side surface area of powder cylinder
- K = coefficient of friction per square centimeter

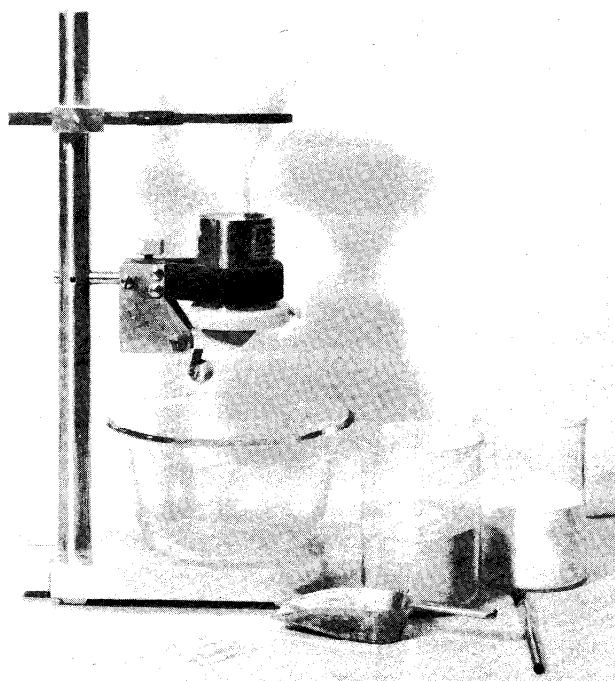


Figure 2: When loading is completed, 30 sec should be allowed for possible formation of individual flocculi or mass flocculation of the whole load.

Simplified, the equation reads:

$$\begin{aligned} r \cdot d \cdot g &\geq 2 \cdot K \\ K &\leq \frac{1}{2} \cdot r \cdot d \cdot g \\ K &\leq 490 \cdot r \cdot d \end{aligned}$$

It can also be said that a powder having viscosity K and nontapped bulk density d is sure to fall freely if

$$r \geq \frac{K}{490 \cdot d}$$

For example, a powder with a density of 0.5 g/ml passing through a hole with a diameter not smaller than 24 mm (i.e., $r = 1.2$ cm) has a viscosity (or shearing strength) of $K \leq 294$ poise = 29,400 cp.

The force initiating flow for powders having good flowability is the weight of the powder cylinder. Such powders flow from the top until the plane is inclined in such a way as to stop the flow.

Test Acceptability Limits

The limits that ensure good fractionation or granulation of the powder — that is to say, that ensure a low average weight — depend on machine type, working conditions, and powder composition. Our experience, however, allows us to make the following generalizations:

1. With Zanasi (Fratelli Zanasi SpA, Bologna, Italy) and MG 2 (MG2 Macchine Automatiche SpA, Bologna, Italy) capsulating machines, a good range is within disk-hole diameter limits of 10–24 mm.
2. With tableting machines, limits of the disk-hole size are 50%–120% of the diameter of the punch used.

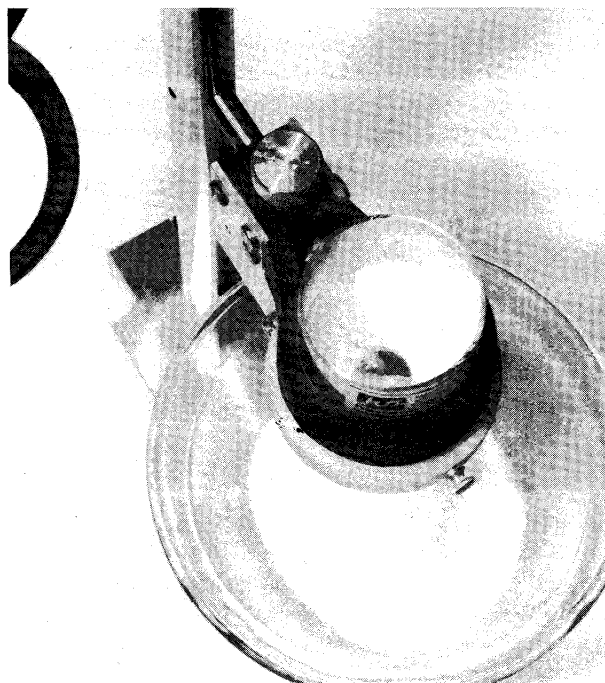


Figure 3: A very flowable powder will slowly flow through the small-diameter holes, leaving a cavity shaped like an upside-down, truncated cone.

Table I: A comparison of the flowability index and the coefficient of variation of typical pharmaceutical dosage forms.

Coefficient of Variation of Average Weight*											
Flowability Index (mm)	Capsule Size 3600 Prod/Hr		Tablet Size								
	No. 1†	No. 0†	13,000 Prod/Hr				90,000 Prod/Hr				
			Dia. 6‡	Dia. 10‡	Dia. 13‡	Dia. 20‡	Dia. 8.5§	Dia. 11§	Dia. 11.5§	17.5 X 7.15	19.5 X 8.55
4								1.09			
5						0.93					
6			1.10	1.17							
7				1.28					1.17		
8											1.32
10				1.32			0.60				
12					0.98						
20	0.52										
22	1.20						1.30				
24	1.76									0.87	
26	2.24	1.56									
30	3.33										
32										3.69	

* Capsules are calculated on the basis of contents without enclosure.
† Machine used: Zanasi-Lz-6 (2 punches).
‡ Machine used: Ronchi Rotary (8 punches).
§ Machine used: Manesty Express Rotary (20 punches).

The latter limits are much more restrictive than the former; this means that blends for tablets must frequently be granulated.

Conclusions

We have defined *powder flowability* and outlined the parameters affecting its quality. Of particular importance are powder bulk density, which can be easily measured and can aid the powder's flow, and the presence of flocculi, which can obstruct powder flow.

In addition, we have defined the formulas for determining flowability. These formulas can be expressed as follows: flowability = 1/diameter (in centimeters) determined by the test to be

$$\cong \frac{d \cdot g}{4 \cdot K}$$

The denominator is the viscosity coefficient and includes all the factors that oppose the powder flow. The numerator includes two parameters that aid the powder flow: bulk density and gravity acceleration. The electrostatic charge does not appear in this equation, although it may interfere indirectly. In fact, as mentioned earlier, a weak electrostatic charge can help eliminate flocculi, which reduces the K value. A strong electrostatic charge, you will recall, turns the fines away from each other, provoking a reduction in the nontapped bulk density of the powder and thus a reduction in flowability.

Low bulk density has two consequences: low weight and low flowability. During wet or dry granulation, therefore,

both bulk density and flowability should be maximized. Moreover, prior to either capsule or tablet manufacturing, one should test both nontapped bulk density and flowability since these two parameters allow one to calculate the value of K.

In our laboratories at Gruppo Lepetit SpA (Milan, Italy), we have adopted flowability-index numbers that were obtained with the simple apparatus described herein as receiving and quality control specifications for all powders. The flowability index is now specified on all materials purchased from our suppliers.

Since these procedures were inaugurated, incidences of downtime and of failure of products to pass necessary tests (e.g., dissolution and product uniformity) have been reduced to zero. The value of establishing a limits of flowability index of feed powders to ensure product uniformity is suggested by the data in Table 1. The savings in production time and labor and the decrease in recalls have more than offset the investment made in adapting this uncomplicated test to purchasing, quality assurance, and manufacturing protocols.

References

1. Augsberger, L.L, and Shangraw, R.F., *J. Pharm. Sci.*, Vol. 55, No. 4, 1966, p. 418.
2. Nelson, E., *J. Am. Pharm. Assoc., Sci. Ed.*, Vol. 44, No. 7, 1955, p. 435.
3. Train, D., *J. Pharm. Pharmacol.* Vol. 10, 1958, p. 127T.
4. Hammerness, F.C., and Thompson, H.O., *J. Am. Pharm. Assoc., Sci. Ed.*, Vol. 47, 1958, p. 58.
5. Gold, G., et al., *J. Pharm. Sci.*, Vol. 55, No. 11, 1966, p. 1291.