International Journal of Pharmaceutics, 6 (1980) 89–117

Review Article

POWDER FAILURE TESTING – PHARMACEUTICAL APPLICATIONS

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(Received June 26th, 1980)
(Accepted June 30th, 1980)

INTRODUCTION

The widespread use of powders by industry and the problems associated with their handling, flow and physical properties has highlighted the need for further understanding of the fundamental properties and behaviour of powders. In the pharmaceutical industry with the increased use of high-speed powder processing machinery and the requirement on occasion of complex drug-release characteristics from solid dosage forms, problems with powders can be particularly serious and lead to reduced efficiency for a process or may affect adversely the quality of the product. These processing and formulation requirements have also led to the need for a more critical approach to the selection of formulation excipients (Jones, 1977). A fuller understanding of the failure and other physicomechanical properties enables an improved method of material selection to be made. In practice therefore, the objective of the pharmaceutical industry in studies of powder failure properties is to provide information which can be used to minimize or eliminate powder problems and, with the knowledge gained, to improve upon the design of formulations and of equipment to handle and process these formulations, as well as to predict the performance of powder handling and processing equipment.

POWDER FAILURE THEORIES

Whilst powders are readily recognized in everyday life, the precise definition is somewhat arbitrary. According to BS2955 (1958), a material is classified as a powder if it is made up of dry, discrete particles with a maximum dimension of less than 1000 μm. It is also apparent that when powders are considered, they differ from other physical states of matter in that they are non-homogeneous in nature, consisting of discrete solid particles of different sizes and shapes interspersed with void spaces. They are similar to liquids in that they deform and flow when stressed and to solids in that they can exhibit both elastic recovery and brittle fracture. Unlike solids, however, they can expand or contract when stressed. Because of their composition, powders also contain a multitude of surfaces and it is implicit that the interactions between these surfaces lead to diverse rheological behaviour (Sutton, 1976).

Although surface parameters and interactions contribute to the flow properties of powders, the complexity of the factors involved has meant that, until relatively recently,

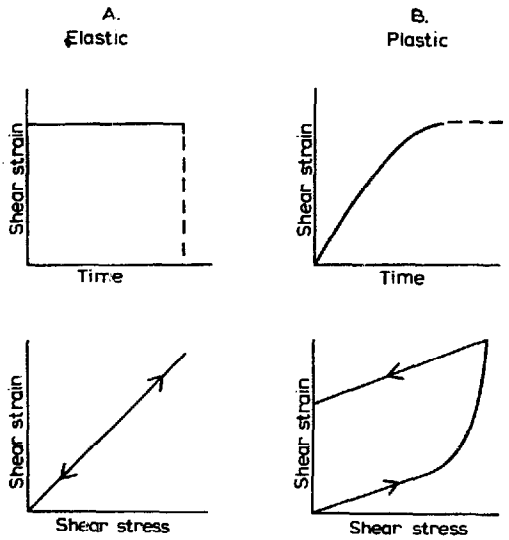


Fig. 1. Elastic and plastic deformation in solids.

powder failure studies have been carried out by regarding a powder bed as a continuum, without discrete structure. Relationships between stress and strain have been investigated using techniques similar to those employed when examining the mechanical properties of liquids and solids. This approach, developed from soil mechanics, has been termed the continuum model and has found wide application, particularly in the area of hopper design (Jenike, 1964).

Recently, however, attempts have been made to study powder failure from a particulate point of view. That is, the surface, size, shape and packing properties of particles have been recognized and information about the bulk properties obtained by summing individual interactions. Clearly this poses a complex mathematical problem.

CONTINUUM MODEL

The continuum model, where the powder bed is considered as a homogeneous body, is based on the theories and techniques of soil mechanics (Hvorslev, 1937; Roscoe et al., 1958, 1963). Jenike extended these theories to deal with dry powders as distinct from moist soils (Jenike, 1961, 1964).

The simplest kind of flow behaviour observed in solids is elastic, or Hookean, deformation (see Fig. 1A) such that when the stress is removed the material returns to its original condition. Plastic deformation (see Fig. 1B) represents the other extreme where material is permanently deformed, although not usually until a certain stress has been reached. The moist soils examined by Hvorslev (1937) and Roscoe et al. (1958, 1963) were termed rigid-plastic, or Coulomb, solids and the shear stress at failure, τ_F, could be expressed by

$$\tau_F = \mu_0 \sigma_F + \lambda e^{(k\epsilon_F)}$$

where μ_0, λ and k are constants for the material, σ_F is the normal stress at failure and ϵ_F

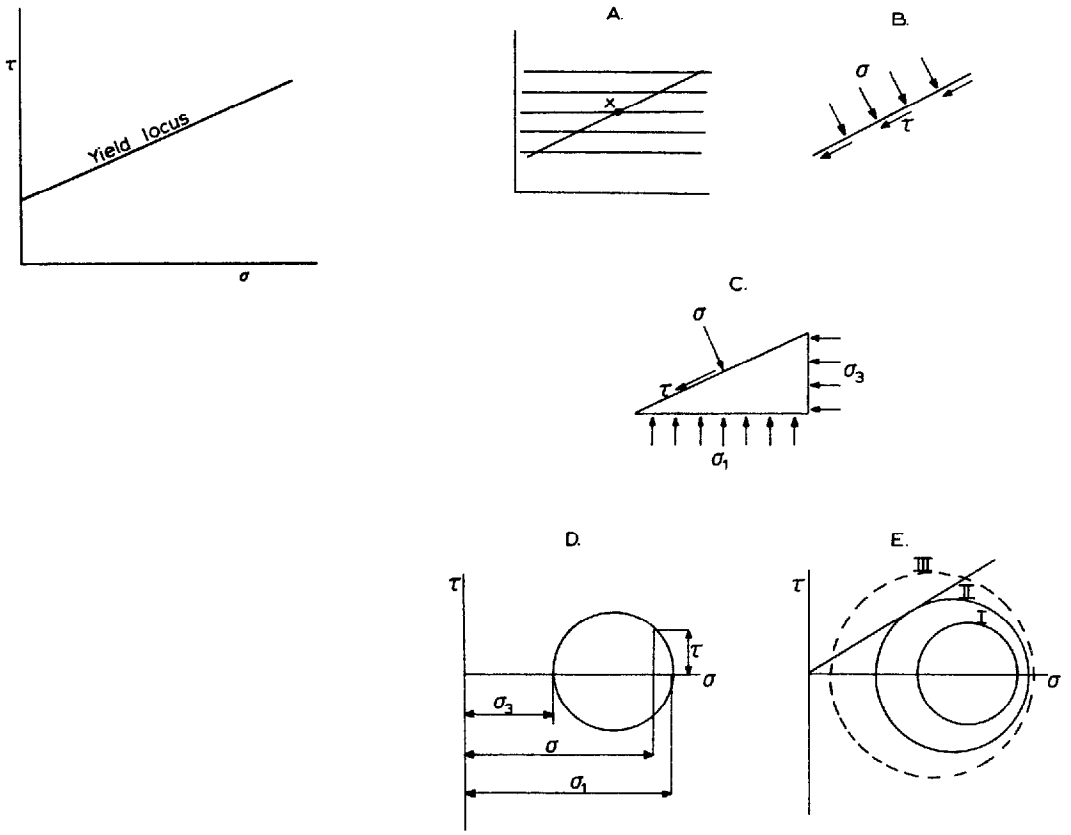


Fig. 2. Yield locus for a rigid-plastic solid. τ, shear stress at failure; σ, normal stress.

Fig. 3. Mohr circle analysis, A: location of plane and point x in powder bed. B: shear (τ) and normal (σ) stresses exerted by powder to the left of the plane on the powder lying to the right, at any point x of the plane. C: representation of τ and σ in terms of major (σ_1) and minor (σ_3) principle stresses. D: Mohr circle representation of stresses. E: yield locus with 3 Mohr circles – I, powder remains rigid to stresses represented by circle I; II, powder fails for stresses represented by circle II; III, conditions represented by circle III are not possible.

is the voidage, or porosity, at failure. The failure conditions are defined by a surface with coordinates τ, σ and ϵ. For such materials, incipient failure is governed by a limiting stress function. This can be described as a yield locus, a graphical representation of the relationship between shear stress at failure and normal stress (see Fig. 2) plotted using data obtained from shear cells. The stress conditions existing in a powder bed considered as continuum can be examined by Mohr circle analysis (Morley, 1940; Brown and Richards, 1970); Fig. 3B shows shear (τ) and normal (σ) stresses exerted by the powder to the left of the plane on the powder lying to the right, at any point x of the plane. These can be represented as in Fig. 3C by 3 principle stresses. It is generally regarded that the largest (σ_1) and smallest (σ_3) of the 3 will decide whether the powder will flow and this enables Mohr circles to be constructed in σ vs τ coordinates (Fig. 3D). Fig. 3E shows a yield locus and 3 Mohr stress circles. A rigid plastic solid remains rigid to stresses represented by

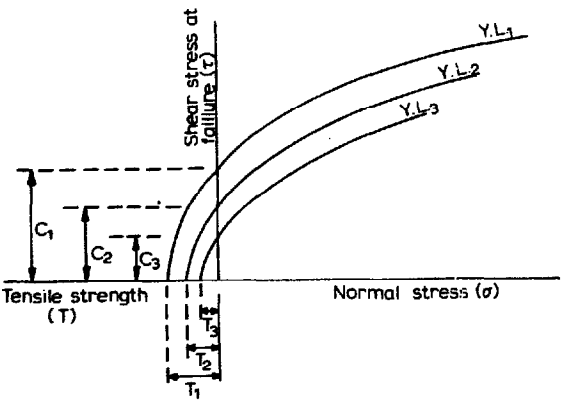


Fig. 4. Family of yield loci for a cohesive powder. c, cohesion; T, tensile strength; Y.L., yield locus; (1, 2, 3 refer to 3 different density conditions).

circle I lying below the yield locus, and deforms or fails for stresses represented by circle II. Conditions represented by circle III are not possible.

The failure behaviour of dry powders differs from that of moist soils or clays and Jenike termed them modified rigid plastic solids. Whilst the yield locus for a perfectly free-flowing powder is linear and passes through the origin on a σ vs τ plot, for cohesive powders the yield locus deviates from linearity, especially at low stresses, and has an end-point. In addition its position is not fixed but is governed by the density of the powder. In practice a family of yield loci are obtained (Fig. 4) corresponding to different consolidations, each locus terminating at the stress conditions appropriate to its consolidation. The intersection of the locus on the shear stress axis is the cohesion, C, of the material at the particular density and is defined as the resistance of a powder to normal shear at zero compressive stress (Richards, 1966). The negative intercept on the abscissa is

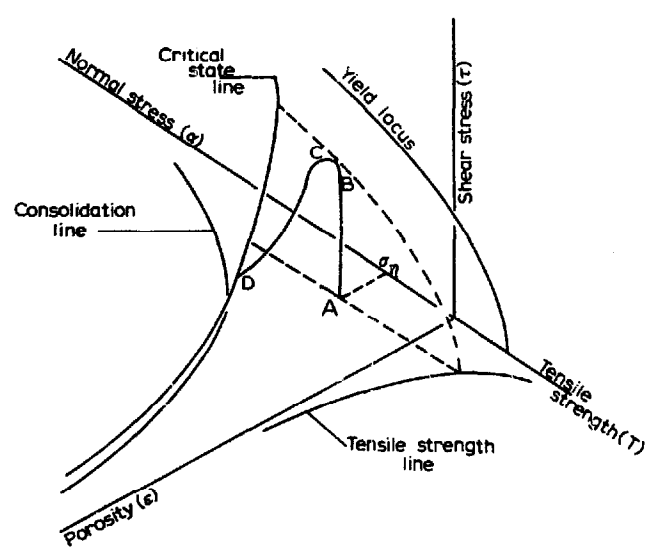


Fig. 5. Three-dimensional representation of powder failure.

the tensile strength, T, which can be estimated experimentally using tensile testers generally based on the Warren Spring Laboratory design (Ashton et al., 1964).

As mentioned previously, failure conditions can be defined by a surface with coordinates τ, σ and ϵ and this can be plotted in space 3-dimensionally (see Fig. 5). Yield loci represent projections of the failure surface onto the normal and shear stress axes. When a powder is sheared in a shear cell under a certain normal load (σ_n), at the beginning of the test the sample will be at a particular porosity (ϵ) (point A in Fig. 5). When the shearing commences, elastic deformation occurs (B) which becomes increasingly plastic up to point C. At C, the powder fails, permanent (plastic) deformation occurs after failure and the porosity in the region of the failure plane increases to point D on the critic state line.

Several authors have proposed essentially empirical equations to describe the shapes of yield loci for powders. Ashton et al. (1965), after studying more than 30 powders, proposed the following equation:

$$\left(\frac{\tau}{C}\right)^n = \frac{\sigma + T}{T}$$

where n is termed the shear index. The validity of this equation has been verified by numerous workers (Williams and Birks, 1967; Stainforth et al., 1970; Eaves and Jones, 1971; Kocova and Pilpel, 1972) and has also been given a theoretical basis (Ashton et al., 1965).

PARTICULATE MODEL

The particulate approach considers interactions between individual particles and sums them statistically in order to obtain total interaction and hence the bulk properties of the powder. However, the situation in powders is very complex since the factors associated with the nature of the particles and their surfaces – size, shape, surface morphology, packing condition and inter-particle forces – must be taken into account. These properties are difficult to define for real powder systems. At the same time inter-particle forces, which can be of a number of types – mechanical forces, surface tension, electrostatic forces, van der Waal forces, solid bridge forces or plastic welding forces – are also difficult to quantify. Consequently, progress using this model can be expected to be slow. Developments have been made, however, by considering simplified, yet realistic model systems, then verifying the derived equations with experimental data (Rumpf, 1962; Cheng, 1968). Powder tensile strength, the maximum stress required to fracture a powder bed in tension for a given density state and a term derived from the continuum model, has been related to inter-particle forces, particle size and the packing condition.

Rumpf (1962) derived an equation for the tensile strength of powders using a model consisting of unisized spheres, making 4 assumptions: (1) that the fracture section contains a large number of bonds; (2) that a random distribution in space exists of bonds in the fracture section; (3) that the particles in the test powder bed are randomly distributed; and (4) that a uniform mean attractive inter-particle force (F) exists in the surface. These assumptions enable packing conditions to be defined by porosity (ϵ) and mean coordination number (c) whilst the use of monosize spheres controls both particle size,

shape and surface rugosity.

$$T = \frac{9}{8} \cdot \frac{1-\epsilon}{\pi d^2} \cdot cF \tag{1}$$

where T is the tensile strength, d is the diameter of the monosize spherical particles. The equation was verified using narrow size ranged round limestone particles. This work has been extended by Rumpf and his co-workers to examine moist powders (Pietch and Rumpf, 1967), particle size effects (Turba and Rumpf, 1964) and the strain behaviour of test beds (Schubert et al., 1975).

Studies on the tensile strength of powders by Cheng (1968, 1970, 1973) also considered the particles in powder beds to be randomly packed. Particles are taken to have an average coordination number with the tensile strength taken as the average over a large number of particle pairs in the fracture plane. Cheng (1968) first relates the number of particle pairs per unit area on a fracture plane, N_a, to the mean coordination number, c, and the bulk density (ρ) of the powdered bed.

$$N_a = \frac{a}{\bar{v}} \frac{c}{2} \frac{\rho}{\rho_t}$$

where a is the number of particle pairs per unit area divided by the number of pairs per unit volume, $\bar{v}$ is the mean volume per particle and ρ_t is the true density of the powder.

Unlike the work of Rumpf, however, Cheng takes into account the fact that constituent particles touch only at the tips of asperities, or surface protrusions, on their surfaces (see Fig. 6). The tensile strength of a bed of powder is then considered as the product of an inter-particle attractive force per unit area, H(t) the magnitude of which is dependent upon the inter-particle separation, t, and the true area of contact between pairs of particles in the plane where the sample splits, ΣA_{ij} (see Fig. 6). Defining b as the area of contact per particle pair divided by the surface area of the smaller particle in the pair, $\bar{d}$ and $\bar{s}$ as the mean diameter and surface area per particle respectively, the following expression was obtained:

$$T = abc \frac{1}{2} \frac{\bar{s}}{\bar{v}} \frac{\rho}{\rho_t} H(t) \tag{2}$$

where

$$t = t_0 - \frac{\bar{d}}{3} \left(\frac{\rho}{\rho_0} - 1 \right)$$

with t_0 defined as the range of the attractive inter-particle forces, that is the value of t when T is zero, and ρ_0 is the value of bulk density when T equals zero. Work on dry powders has been extended to consider moist powders in the pendular state, and experimental data on a number of powders have provided support to the theory.

Both equations (1) and (2) illustrate the dependence of powder failure properties, as reflected in their tensile strength, on interparticle forces (F and H), particle size and shape ($\bar{d}$, $\bar{s}$, $\bar{v}$) and packing structure [$c(1-\epsilon)$ and t, (ρ/ρ_s)]. Whilst the particulate model is extremely complex, the fact that experimental evidence supports the theories derived

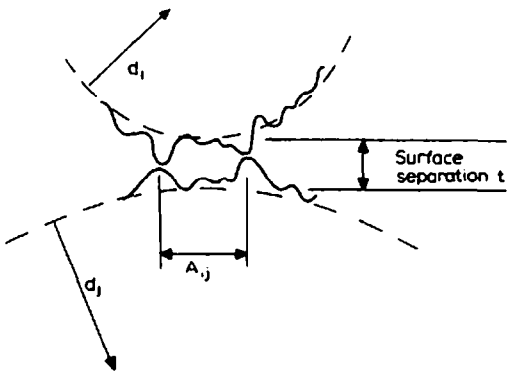


Fig. 6. Diagram showing the actual contact area between a particle pair.

from the simplified models of powder beds suggests that this approach is moving in the direction of understanding the bulk behaviour properties of powder systems.

The continuum model, nevertheless, continues to find wide application in the measurement of powder failure properties and the techniques and apparatus used in measuring these properties are now discussed.

MEASUREMENT OF POWDER FAILURE PROPERTIES

Powder beds are composed of discrete particles and present a complex state for understanding their bulk properties and pose severe problems for mathematical modelling. In addition failure, and thereby flow, of powders takes place in a complex manner and the techniques available for assessing these features are limited in that no single piece of equipment is able to take into account all component factors of the problem (Sutton, 1976).

The equipment currently available can be grouped according to the general flow nature of the powder – whether it is free-flowing, or cohesive (non-free-flowing) (see Table 1), particle size being one of the major determinants for such a classification (Harwood and Pilpel, 1968). Angular tests and flow-through orifice techniques can be applied to free-flowing powders containing particles larger than 100 μm, whilst the more scientifically based powder failure testers – shear cells and tensile testers – are used for cohesive powders generally regarded as powders containing particles smaller than 50 μm.

TABLE 1

FAILURE TESTING EQUIPMENT FOR FREE-FLOWING AND COHESIVE POWDERS

Free-flowing powders	Cohesive powders
Angular and packing characteristics	Tensile testers
Flow through orifice	Shear cell – plate type
Flow meters	– Jenike type
	– annular type

FREE-FLOWING POWDERS

The available techniques in this section have been, and remain, essentially empirical tests.

ANGULAR AND PACKING CHARACTERISTICS

Tests included in this group include the angle of repose and angles of friction (Train, 1958; Pilpel, 1966). However, published work suggests that estimated values are dependent upon the manner in which the test was formed (Jones and Pilpel, 1966a). Jenike (1964) also pointed out that the angle of repose is not a true measure of the flowability of solids and traces its practical popularity to its ease of measurement. The changes occurring in the packing arrangement for powders subjected to a standardized tapping procedure, termed the compressibility (Neumann, 1967; Carr, 1970), have also been used in flow assessment.

$$\text{Compressibility} = \frac{\text{tapped density} - \text{initial density}}{\text{tapped density}} \times 100\%$$

The percentage compressibility can be related to a qualitative descriptive assessment of the flowability of the powder (see Table 2).

Whilst recognizing the qualitative nature of these measurements, angular and packing characteristics derived from the shapes of heaps and cones of powders and changes in density resulting from particle rearrangement do provide some information about likely flow behaviour in hoppers, chutes and tablet and capsule-filling machines.

FLOW-THROUGH ORIFICES

Many correlations have been derived by various workers describing how material behaves when allowed to fall under gravity through constrictions such as orifices of varying size and shape. The correlations have included the effect of size and shape of particle, size and shape of outlet, density of material, and other parameters depending on the system (Wieghardt, 1952; Brown and Richards, 1959; Jones and Pilpel, 1966b; Harwood and

TABLE 2

RELATIONSHIP BETWEEN COMPRESSIBILITY AND FLOWABILITY (Carr, 1970)

Compressibility (%)	Flowability
5–15	Excellent
12–16	Good
18–21	Fair–passable
23–35	Poor
33–38	Very poor
>40	Very, very poor

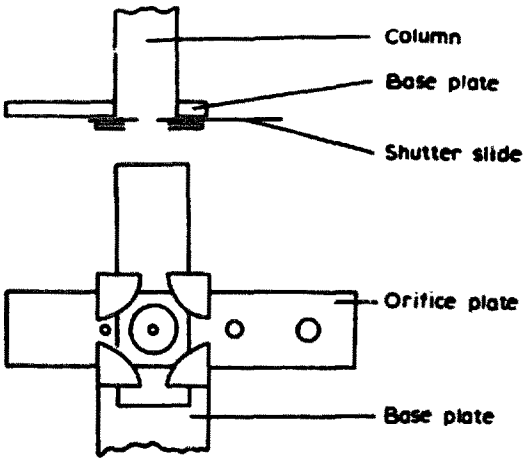


Fig. 7. Simple flow-rate apparatus.

Pilpel, 1969). Early work (Bingham and Wikoff, 1931) demonstrated that flow-rates are approximately in proportion to a power of 2.65 of the diameter of the exit orifice and are independent of head height, except when the hopper is almost empty. The complex velocity pattern of granules discharged from an orifice under a two-dimensional hopper was demonstrated by Brown and Hawksley (1947). After an initial period, a steady flow pattern develops with a trumpet-shaped zone in which particles in different regions move at different velocities.

Using a simple flow-rate apparatus (see Fig. 7) Jones and Pilpel (1966a) found the following equation to hold:

$$D_0 = A\left(\frac{4W}{60\pi\rho_t\sqrt{g}}\right)^{1/n}$$

where D_0 is the orifice diameter, ρ_t is the particle density and W is the flow-rate. Both A and n depend on the material and on particle size.

In practice, measuring the time it takes a certain amount of powder or granulation to flow through a hopper is a good qualitative or semi-quantitative measure. A funnel can be used but the difference between materials is a significant variable. Flow meters described by Gold et al., (1966, 1968a, 1968b) (see Fig. 8) are examples of more elaborate approaches to flow measurement. These workers also stress the fact that measured angles of repose did not correlate with flow-rate evaluation (Gold et al., 1966) and that flow-rates are a function of particle size and product uniformity (Gold et al., 1968a, 1968b). The greater the standard deviation of flow-rates on replicate determinations, the larger the weight variation of tablets made from the powder.

COHESIVE POWDERS

As with the free-flowing powders, many of the early attempts to assess the failure properties of cohesive powders were based on empiricism. The split-plate method (s e

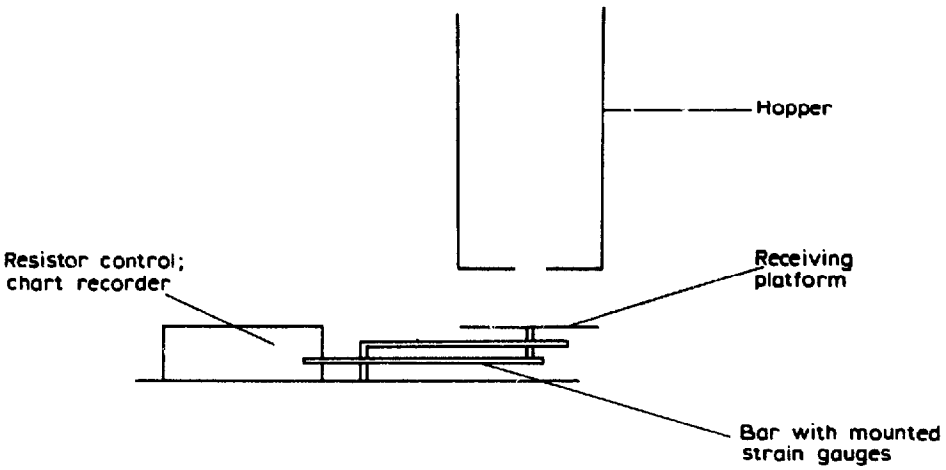


Fig. 8. Recording powder flow meter.

Fig. 9) has been used to study several pharmaceutical powders (Shotton and Harb, 1966). A bed of powder is formed on a horizontal plate, half of which is moveable, the other half fixed. A limiting angle is reached on tilting at which the bed bisects. From the bed dimensions and the measured angle, an estimate of cohesion is made.

A similar device is the tilting table (Zimon, 1962) where beds of powder are prepared on a platform which is tiled until the powder slides. The disadvantages of these techniques lie in the dredging required to prepare the bed (Jones, 1968) and the fact that true area of contact is not equivalent to apparent area of contact for a powder, and is difficult to estimate (Bowden and Tabor, 1950).

TENSILE TESTERS

An improved version of a split-plate tester is the Warren Spring Tensile Tester (Ashton et al., 1964) (see Fig. 10) which shows the original version. The powder is consolidated

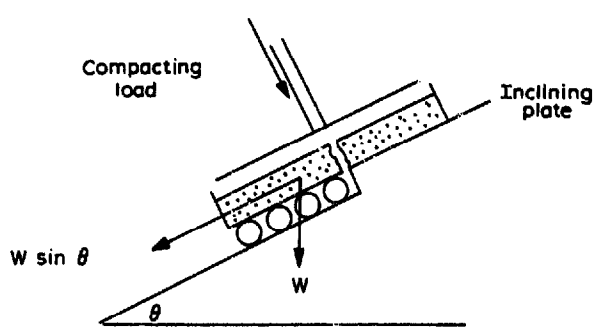


Fig. 9. Diagram of split plate apparatus.

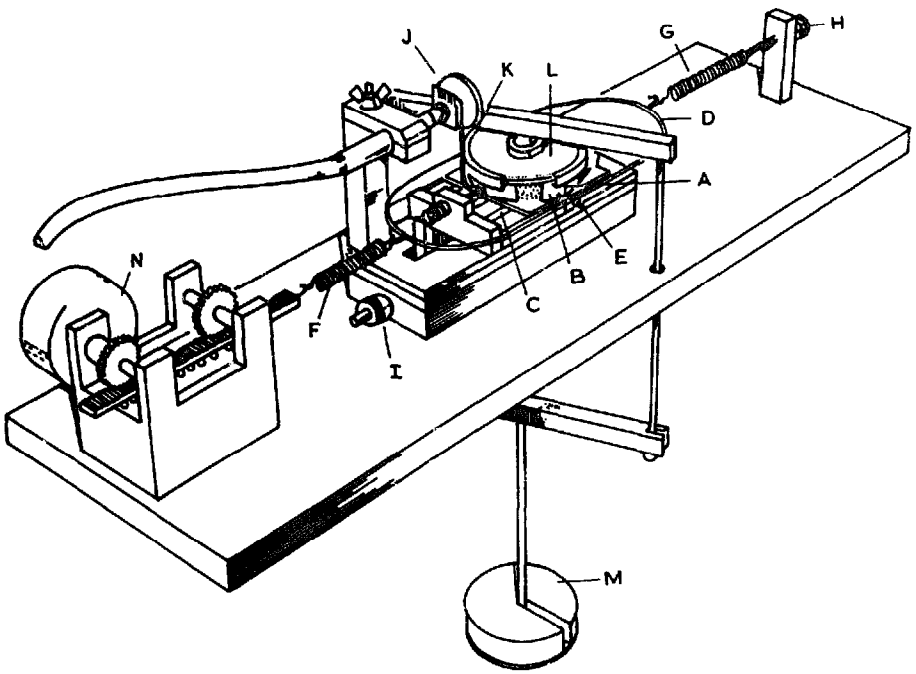


Fig. 10. Warren spring tensile tester apparatus (Sutton, 1976).

into a cylindrical cell which is split diametrically. One half of the cell is fixed and the other half moves on steel ball-bearings. A horizontal wire loop encircles the cell and is attached to it via pins. Two springs are hooked to this loop to act in opposition at right angles to the line of separation of the two half cells. By measuring the time taken for the two halves of the cell to separate, the tensile strength of the powder bed can be calculated from the calibration characteristics of the spring and the movement of the pinion. The bulk density of the bed is determined from the dimensions of the cell and the weight of powder filling it. Repeat measurements are made with the powder bed at different bulk density conditions, achieved by applying different consolidating loads during bed prepara-

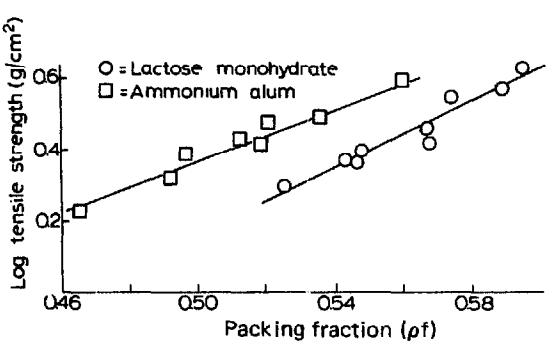


Fig. 11. Representative graphs of logarithm of tensile strength vs packing fraction. ○, lactose monohydrate; □, Ammonium alum.

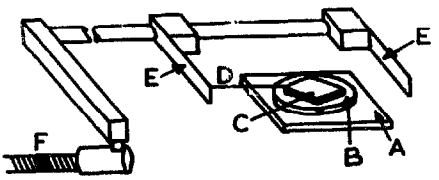


Fig. 12. Plate-type shear cell.

tion. In general, straight line relationships between logarithm of tensile strength and packing fraction (where $\rho_f = \rho/\rho_t$) are obtained; specimen data for lactose and alum powders are shown in Fig. 11. The scatter of results is attributed to minor variations in filling, consolidation and operation of the tensile tester (York and Pilpel, 1972a).

The design of this tester has been improved by modifying the mode of application of tensile stress to use an elastic steel spring (Sutton, 1976) and the use of sapphire bearings on a hard steel base plate (Schubert and Wibowo, 1970). Schubert and Wibowo (1970) also found that the height of samples in the cell affected results and extrapolated all data to zero height. A smaller and more rugged version of the tensile tester is now available (Ajax-W.S.L. Tensile Test Machine) in which the diametrically split cell is subjected to an increased separating force applied by means of springs tensioned by a lead screw. The tension spring is adjusted for initial null-balance by means of an adjusting screw balance. The stress at tensile failure is obtained from a counting device on the loading screw in conjunction with a calibration graph.

SHEAR CELLS

Plate-type shear cell

Perhaps the simplest type of shear cell is that in which a powder bed is sandwiched between two plates (see Fig. 12) (Hiestand and Wilcox, 1968; 1969). The bed is prepared by sifting powder onto the lower plate by sifting through a hole in a template and after scraping the bed level the template is removed. The upper plate, positioned on top of the powder bed with the normal load applied, is connected to a cantilever strain gauge (E) via a tow line (D). The output from the gauge, connected to a screw jack (F) driven by a constant-speed motor, is fed into a chart recorder. To make a measurement, the jack is operated until the top plate just moves. This is repeated by reversing the jack until the tow line becomes slack, then the operation re-started. When the same shear force is observed for a number of sequential pulls, the limiting 'plateau condition' is obtained.

Results appear to be dependent on a range of experimental variables, and it is essential to standardize equipment and mode of operation. The results obtained are not fundamental and unique properties of the powders, but can be used for quality control purposes and for examining materials on a comparative basis.

Jenike-type shear cell

The Jenike-type shear cell (Jenike, 1961; 1964) (see Fig. 13) was based on designs used in soil testing and was invented primarily for making measurements on powder beds for hopper design. The cell is split horizontally, with the lower half of the cell fixed and

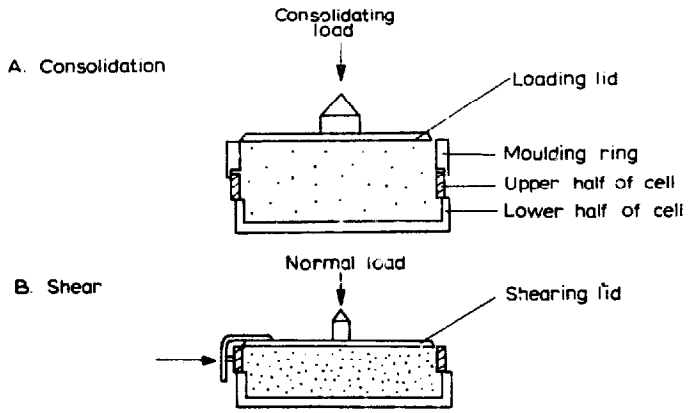
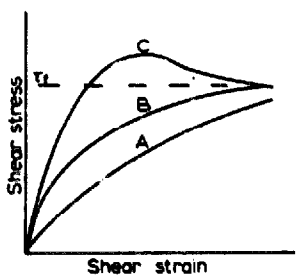


Fig. 13. Jenike shear cell.

the upper half moveable at a constant low rate. The lower section during testing is made to bear against a calibrated strain gauge. To prepare a sample of powder for test, the two halves of the cell together with a moulding ring are locked together and the powder carefully layered into the cell until level with the top of the moulding ring. Consolidation is then carried out using a loading lid, with a consolidating load applied via the lid, rotating the lid backwards and forwards through a small angle. The load, lid and moulding ring are removed and the powder scraped level with the top of the upper half of the cell. The shearing lid is placed in position and the cell sheared under a normal load, which is less than the consolidating load. The test is repeated using the same consolidating conditions (to achieve a constant bulk density of sample) with different normal loads to obtain a relationship between shear stress and normal load (i.e. a yield locus). In practice a series of yield loci are obtained at different values of bulk density.

Correct consolidation of the sample is critical and this is generally established by preliminary experiments which examine the shape of the stress/strain curve obtained during



A = under consolidated sample
B = correctly consolidated sample
C = overconsolidated sample
τ_f = shear stress at failure

Fig. 14. Typical stress/strain curves for powders A: underconsolidated sample. B: correctly consolidated sample. C: overconsolidated sample; τ_F, shear stress at failure.

shearing (Williams and Birk, 1965) (see Fig. 14). Other difficulties have been pointed out regarding the Jenike-type shear cell. The cell is time consuming to use, requires considerable quantities of test powder and necessitates operator expertise to obtain reproducible results. The question of the position of the failure plane has also been raised (Schwedes, 1975). It has been demonstrated that the failure plane can rotate from the horizontal during shear, modifying the values of shear stress (Sutton, 1976). Nevertheless, results from this type of shear cell have been successfully and widely used in the characterization of powder failure properties and in particular in the design of mass flow hoppers.

Annular shear cell

The annular type of cell (Carr and Walker, 1967; Kocova and Pilpel, 1972) overcomes a number of the practical disadvantages of the Jenike-type shear cell, in particular the reduced quantities of material required and more rapid carrying out of measurements although interpretive difficulties remain (Macmillan, 1975). A typical apparatus is shown in Fig. 15. It consists of an annular trough containing the test material, covered by an annular shoe to which normal loads are applied. The underside of the shoe has 20 recessed vanes to grip the sample. The trough is rotated slowly (about 1 rev/h) with the shoe prevented from rotating by a restraining bracket which induces a torque in a hardened steel bar fitted with strain gauges and attached to the shoe. The material is thus sheared under a known normal load, and the shear stress can be measured.

As with the Jenike cell, the material is initially consolidated by continuously shearing it under the chosen compacting load. The sample is then sheared to failure under a reduced normal load and this process is repeated with increasing normal loads until a complete locus can be plotted. The same powder sample is used for each individual locus determination since, unlike the Jenike cell, an unlimited distance of travel for the trough is possible.

A disadvantage of the cell lies in the development of the shear stress since, at any particular angular deflection, powder at the outer wall of the cell's annulus is strained more than at the inner wall. As a result there is a variation of the shear stress across the

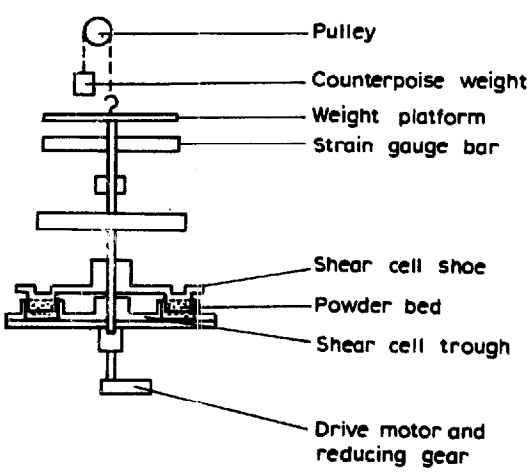


Fig. 15. Annular shear cell.

width of the annulus. The maximum strain then moves progressively towards the inner wall on continued shearing.

A correction for values of shear stress, due to the strain differential, was derived by Hvorslev (1939) and applied by MacMillan (1970). However, MacMillan found that the non-uniformity of the strain was small if the stress/strain curve reached a maximum after a long period of strain. Farley and Sutton (1972) have subsequently shown that one of the assumptions made by Hvorslev, in that in the failure zone the planes perpendicular to axis of the cell remain plane, is not valid. As with the Jenike cell, it is likely that planes of shear failure rotate to relieve the strain. Other workers have discussed the effect of wall friction (Scarlett and Todd, 1968; Scarlett et al., 1969) which can be reduced using split-ring cells. Thus, before corrections can meaningfully be applied to measured shear stresses the exact position and orientation of failure planes must be determined.

In current work on powder failure evaluation, the completely empirical tests, (e.g. angle of repose) are being superceded by the more scientifically based shear and tensile testing apparatus. However, as has been illustrated, these test methods are not fully understood even on the simpler continuum basis, quite apart from the particulate model. Nevertheless, such tests have been widely used to assess powder failure properties and have been successfully applied in a number of important pharmaceutical areas, such as powder characterization, lubricant and glidant effects in powder formulations, hopper design and powder handling situations. These applications are now considered.

PHARMACEUTICAL APPLICATIONS OF POWDER FAILURE TESTING

Whilst the understanding of several areas of powder science remains somewhat qualitative, such as powder flow-rates (Gold et al., 1968), other aspects have been treated more quantitatively, as in hopper design (Sutton, 1972). However, the different levels of interpretation have been successfully applied to several areas of pharmaceutical importance including the characterization of pharmaceutical powders, formulation, processing, and processing equipment.

CHARACTERIZATION OF PHARMACEUTICAL POWDERS

Several of the tests which qualitatively assess powder failure and flow properties have been criticized as reliable indicators of powder flow (Jenike, 1961; Gold et al., 1968; York, 1975a). The percentage compressibility, however, has recently been cited by Jones (1977) to demonstrate how powder compressibility reflects practical experience with some commonly used tablet and capsule excipients (see Table 3). Such data are a useful guide, for example, during formulation of capsules and in process control for capsule filling operations (Jones, 1977). During processing good flowability is required to deliver material from hoppers to the dosator nozzles as well as low compressibility to avoid weight variation.

The more scientifically based data from tensile and shear tests can be manipulated in a number of ways to derive parameters such as angle of effective friction, δ (Jenike, 1961), angle of internal friction, Δ (Williams and Birks, 1967), and flow factor, FF (Jenike, 1961). Jenike (1961) and others (Williams and Birks, 1967) have found that the end-

TABLE 3

COMPRESSIBILITY AND FLOWABILITY OF SOME SOLID DOSE EXCIPIENTS (Jones, 1977)

Material	Compressibility (%)	Flowability
Celutab	11	Excellent
Emcompress	15	Excellent
Star X-1500	19	Fair–passable
Lactose monohydrate	19	Fair–passable
Maize starch	26–27	Poor
Dicalcium phosphate, dihydrate (coarse)	27	Poor
Magnesium stearate	31	Poor
Titanium dioxide	34	Very poor
Dicalcium phosphate, dihydrate (fine)	41	Very, very poor
Talc	49	Very, very, poor

points of yield loci lie on a straight line through the origin (see Fig. 16). As an approximation, the angle made by this line has been termed the angle of effective friction. However, a more correct angle of internal friction, Δ, can be derived by plotting the tensile and shear data on shear stress (τ) and compound normal stress ($\sigma + T$) axes (see Fig. 17) (Williams and Birks, 1967). It has been proposed that this parameter is more useful for assessing the dynamic frictional properties than δ since Δ does not include a term for the work done against expansion of the sample during shearing. In addition, unlike cohesion (C) and tensile strength (T), the angle of internal friction often remains independent of the bulk density of the sample. Williams and Birks (1967) also demonstrated that the yield locus can be effectively linearized by the use of reduced shear and normal stresses.

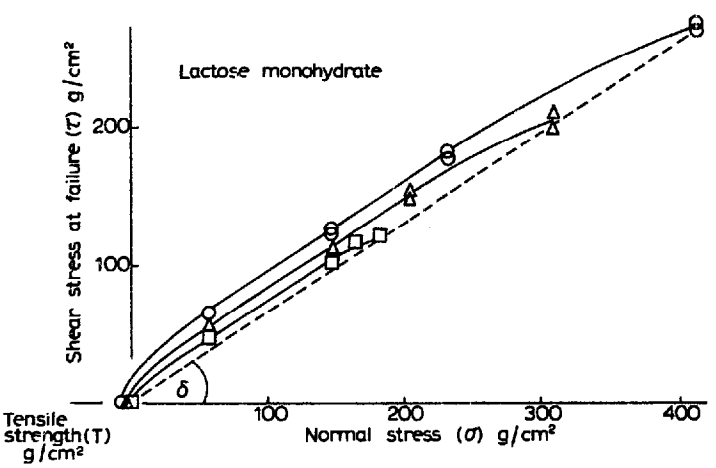


Fig. 16. Family of yield loci showing derivation of angle of effective friction, σ. Packing fraction: ○, 0.579; △, 0.553; □, 0.524.

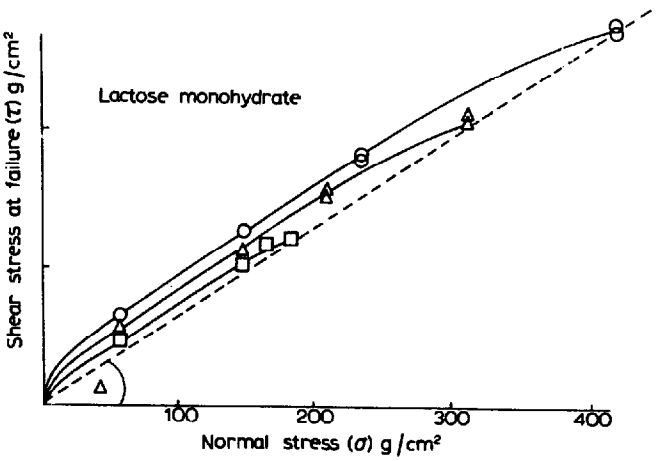


Fig. 17. Family of yield loci showing derivation of angle of internal friction, Δ. Packing fraction: ○, 0.579; △, 0.553; □, 0.524.

The tangent angle of the internal friction then becomes

$$\frac{\tau_E}{(\sigma_E + T)} = \tan \Delta$$

where τ_E and σ_E are the shear stress and normal stress respectively at the end point of a yield locus and T is the corresponding tensile strength for the density conditions of the locus. In the same way specific cohesion (p) and specific tensile strength (q) can be defined as:

$$p = \frac{C}{\sigma_E + T} \quad \text{and} \quad q = \frac{T}{\sigma_E + T}$$

These 3 parameters are now thought to provide realistic criteria for categorizing the mechanical properties of cohesive powders. Simple powders are defined as those for which p, q and tan Δ are independent of the consolidating stress and complex powders show dependence of one or more terms on this stress. Lactose and calcium carbonate (Kocova and Pilpel, 1973) and chloroquine diphosphate and ammonium alum (York, unpublished data) have been shown to behave as simple powders. Another report (Crooks et al., 1977) examining direct compression excipients found a grade of microcrystalline cellulose (Avicel pH 102) to behave as a simple powder whereas a direct compression starch (Star X 1500) and Celutab exhibited complex behaviour. Complex behaviour in powders may create problems during processing. If such powders are exposed to varying consolidating loads during processing, differing failure and flow behaviour is likely to occur.

Workers have also used cohesion (C) and tensile strength (T) as parameters for assessing the failure and mechanical properties of pharmaceutical powders and have studied

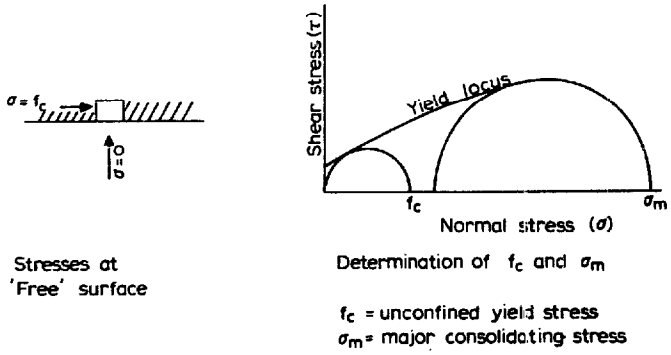


Fig. 18. Definition of unconfined yield stress, f_c, and method of obtaining f_c and σ_m from a yield locus.

the effect of moisture (Eaves and Jones, 1970, 1972a, 1972b), particle size and shape (Farley and Valentin, 1967; Pilpel and Walton, 1974). packing (Eaves and Jones, 1973), particle coating (York and Pilpel, 1973, Pilpel and Hepher, 1977) and temperature (York and Pilpel, 1972a, 1972b; Britten and Pilpel, 1978; Pilpel and Britten, 1979). These studies, as well as providing a 'data-bank' of the failure and mechanical properties of drugs and excipients examined, also give an insight into aspects of powder storage, flow, granulation and particle bonding mechanisms (York and Pilpel, 1972a, 1973; Eaves and Jones, 1973).

Several studies (York, 1975a, 1975b; Crooks et al., 1977; Ho et al. 1977) using pharmaceutical powders have utilized the flow factor (FF), a flowability term derived from yield loci data. This is obtained by drawing two Mohr's semicircles tangential to the yield locus (see Fig. 18). The first semicircle passes through the origin and defines the unconfined yield stress, f_c. This term represents, at a free surface of a mass of solid (see Fig. 18), the largest pressure which the solid is able to support in the direction tangential to the surface, and is a major pressure. The minor pressure is normal to the surface and zero. The construction to find the major consolidating stress, σ_m, requires a Mohr's semicircle to be drawn through the end point, and tangential to, the yield locus. (Some workers select a point 95% along the locus (Williams and Birks, 1965)). This stress represents the maximum consolidating stress the powder has been subjected to during

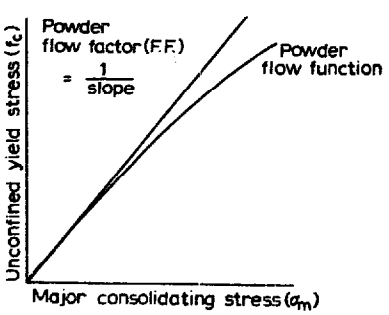


Fig. 19. Derivation of powder flow factor for powder flow function.

TABLE 4

POWDER FLOW CLASSIFICATION BY FLOW FACTOR VALUES (Jenike, 1961)

Powder flow classification	F.F.
Free-flowing	>10
Easy flowing	4 –10
Cohesive	1.6– 4
Very cohesive	<1.6

consolidation when testing. A pair of values is taken from each yield locus and the results are plotted on a graph with ordinates f_c and σ_m. The flow factor (FF) of the material is defined as the reciprocal slope of the resulting graph which is often rectilinear. (See Fig. 19). Jenike (1961) drew up a classification of powder flowability according to FF values (see Table 4). Increasing values are indicative of a powder becoming more free-flowing under gravity. Flow factors obtained for a range of pharmaceutical powders are listed in Table 5. Such data is of value when selecting appropriate formulation components, particularly for tablet formulations for direct compression and capsule formulations, as well as predicting powder failure and flow properties under gravity. Relevance of the flow factor in assessing the tabletting process has also been recently demonstrated by the finding of a direct relationship between the reciprocal of the flow factor and the coefficient of variation of tablet weight (Ho et al., 1977) (see Fig. 20).

A range of parameters are thus available to describe powder failure properties based on

TABLE 5

FLOW FACTORS OF SOME REPRESENTATIVE PHARMACEUTICAL POWDERS (Pilpel, 1971; York, 1975a; Crooks et al., 1977)

	Flow factor	Flow classification
α-lactose monohydrate (220 μm)	18.5	Free-flowing
Emcompress (191 μm)	14.8	
Celutab (282 μm)	9.7	Easy flowing
Spray-dried lactose (116 μm)	6.8	
Star X-1500 (32 μm)	4.8	
Avicel pH 101 (35 μm)	3.8	Cohesive
Calcium hydrogen phosphate (6 μm)	3.8	
Griseofulvin (12 μm)	2.4	
α-lactose monohydrate (10 μm)	1.9	
Paracetamol (2 μm)	1.6	Very cohesive
Agglomerated anhydrous cephaloridine (batch 1)	10.6	Free-flowing
(batch 2)	12.3	
Finely powdered cephaloridine	4.7	Cohesive

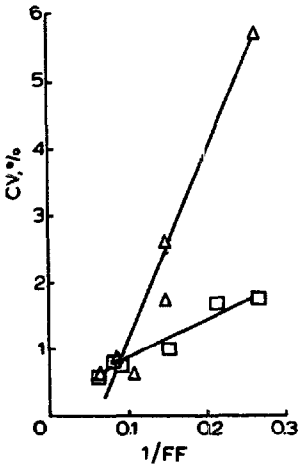


Fig. 20. Relationship between reciprocal of the flow factor and coefficient of variation of tablet weight (Ho et al., 1977).

either empirical tests or powder yield loci and the continuum model. An additional factor, the general index of flowability, ζ, has been proposed (Stainforth and Berry, 1973) and found useful for a range of plastic powders. However, this index has not yet been applied to pharmaceutical powder systems.

FORMULATION

Solid dosage formulations generally consist of mixtures of powders. Pharmaceutical powder mixtures have been examined using free-flowing (Jones and Pilpel, 1966a) and cohesive powders (Kocova and Pilpel, 1973a, 1973b; Kurup and Pilpel, 1976) and the effect of second and third components evaluated. In an interesting study of pharmaceutical powders (Kocova and Pilpel, 1973a, 1973b) the Cheng equation (Cheng, 1968) for the tensile strength of powders based on the particulate approach was extended to consider binary and tertiary mixtures. Using the modified Cheng equations, the authors were able to predict the tensile strength of these mixtures with an accuracy of ±20%. It is suggested (Kocova el Arini and Pilpel, 1974) that the parameters H(t) and t_0, the mean inter-particle force and its range respectively, might be expected to relate to the compressional properties of powders and to the strengths of compacts during tabletting. The angle of internal friction, Δ, was thought to relate more to the flow properties of powders and might be useful for predicting behaviour in mixing, handling and transportation.

A study by Esezobo and Pilpel (1974) measured the shearing and tensile properties of a typical oxytetracycline formulation to examine changes in formulation variables, in particular moisture content and gelatin used as a binding agent. The presence of microcrystalline cellulose (Avicel PH 101), alginic acid and increasing quantities of gelatin raised the mechanical strength of the formulation. Increases in strength due to moisture were found to be a function of gelatin content, illustrating the importance of moisture in formulated granules. A griseofulvin formulation has also been examined in this way

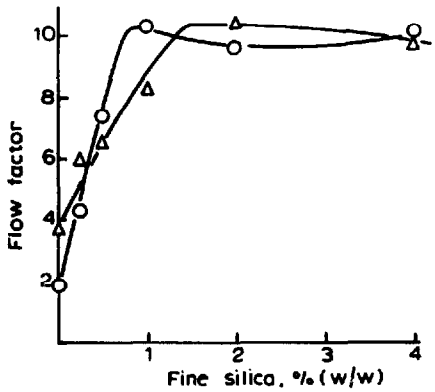


Fig. 21. Representative data illustrating determination of optimal glidant concentration (York, 1975a). ○, lactose–fine silica mixtures; △, calcium hydrogen phosphate–fine silica mixtures.

(Kurup and Pilpel, 1976). Further studies in this area are indicated, in particular studies attempting to relate the properties of typical formulations in powder form to those of compressed tablets prepared from the formulation.

The successful application of shear and tensile testing has also been demonstrated in the selection of suitable glidant concentrations for formulations (Peleg and Mannheim, 1973; York, 1975a, 1975b; Verthalis and Pilpel, 1976, 1977; Schickling et al., 1977). Both the angle of internal friction, Δ, and the flow factor, FF, were found to be useful parameters for assessing flowability. In general, optimal concentrations of glidants for improving the flowability of mixtures and formulations are demonstrated (see Fig. 21). Flow-meters have also been used to demonstrate this effect (Gold et al., 1966, 1968a). Knowledge of the optimal glidant concentration is important since the minimum concentration of glidant which optimizes flowability should be used in pharmaceutical powder systems so that there is no excess which may retard drug release and decrease bioavailability and the therapeutic efficiency of the final dosage form.

PROCESSING AND PROCESSING EQUIPMENT

One of the major applications of the failure properties of powders has been in the design of mass flow hoppers (Jenike, 1961, 1964). This type of flow pattern is essential in pharmaceutical processing (see Fig. 22). Prior to this scientifically based technique, hopper design was essentially based on empiricism and experience.

To obtain a design for a hopper, the flow function of the powder (f_c vs σ_m), the angle of friction of the powder against hopper material ϕ_w (obtained by placing the upper half of a shear cell against a specimen of wall material and determining the relationship between shear and normal stress), and the hopper flow factor (obtained from Jenike's charts (Jenike, 1961, 1964)) (see Fig. 23) are required. Graphs are then drawn of f_c vs σ_m for the hopper flow factor and the powder flow function (see Fig. 24) from which a critical value of f_c can be obtained.

When the stress acting on an arch, or bridge, created at the outlet of a hopper is less than that needed to break the arch, failure and subsequent flow will not occur. If the

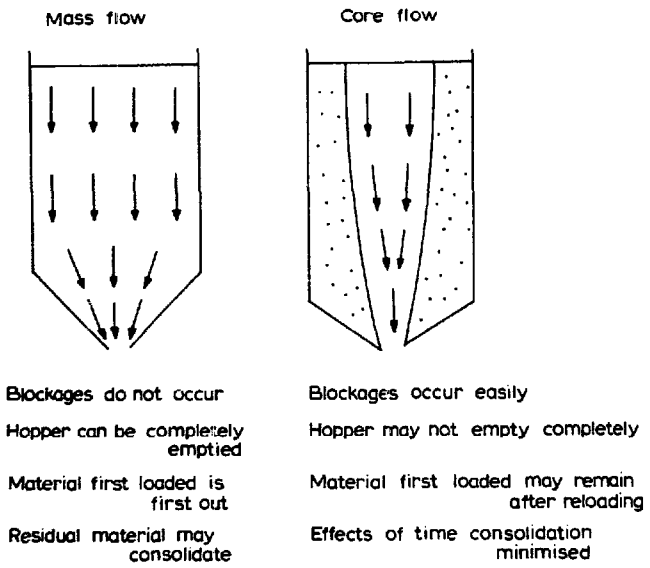


Fig. 22. Core flow and mass flow hoppers.

applied stress is greater than the strength of the arch, the arch will collapse. At the intersection, therefore, a critical value, $f_{c_{crit.}}$, is obtained. From $f_{c_{crit.}}$ the critical size of the hopper outlet (B) can be calculated from:

$$B = \frac{f_{c_{crit.}} H(\theta)}{\rho}$$

$$H(\theta) = 2 + \frac{\theta}{70} \text{ , for circular outlets}$$

$$H(\theta) = 1 + \frac{\theta}{200} \text{ , for slot outlet } (L \geqslant 3B) .$$

This technique has been widely used in the U.S.A. and the U.K. and these principles have been used by several pharmaceutical companies when setting up powder handling processes.

A recent report (Jordan and Rhodes, 1979) using a recording powder flow-meter, fitted with an electrobalance to replace the strain gauges of the original design (Gold et al., 1966), has indicated its application in areas of pharmaceutical processing. Whilst the understanding of powder flow discharge rates from flow tubes remains qualitative, the flow-meter is shown to be sensitive to both process and formulation variables (see Figs. 25 and 26) and a correlation between tablet weight and flow-rate has been demonstrated. The role of powder failure properties during the mixing process has also been referred to by Orr and Sallam (1978) when examining the content uniformity of low-dose tablets. Uniform mixing of cohesive pharmaceutical powders is difficult if powder agglomerates remain and the mixing process can be related to the rate at which component particles

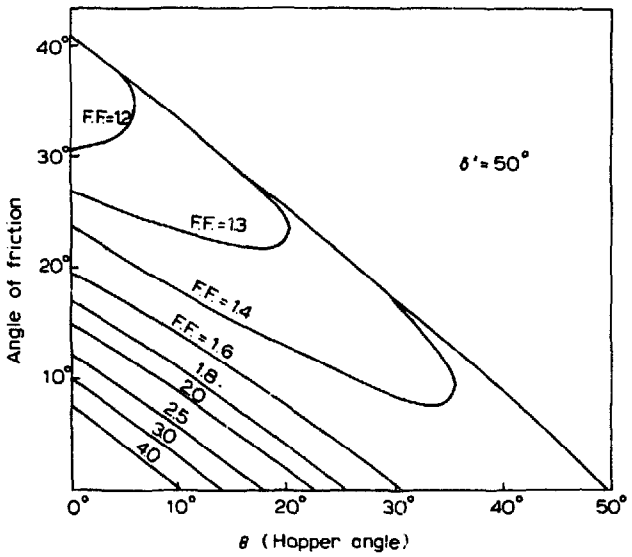


Fig. 23. Specimen chart showing derivation of hopper function for a conical tube (Jenike, 1961, 1964).

detach themselves from agglomerates (Orr and Sallam, 1978). The failure properties of both powdered drug and formulation excipients are factors associated with the breakdown of agglomerates and therefore the rate of mixing. Further work examining these relationships is indicated.

Carstensen and co-workers (1979a, 1979b) have reported on a dynamic flow measuring device which, unlike the static powder flow-meters, simulates the true powder feed situation in tablet machines (see Fig. 27). Initial work has identified two powder flow-rates as powder enters a moving die from a feed frame – an initial rate from the fairly rigid bed in the base of the hopper and a second rate from the loosened bed created after the initial flow. Studies of dynamic flow-rates may prove of practical significance particularly in reducing problems during scale up to high speed tablet machines.

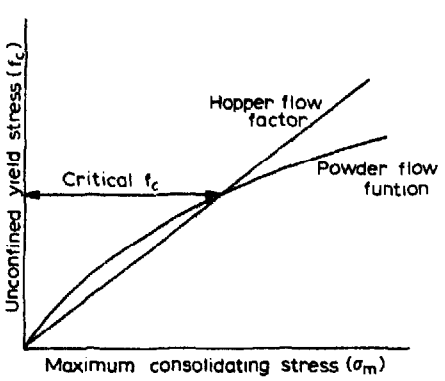
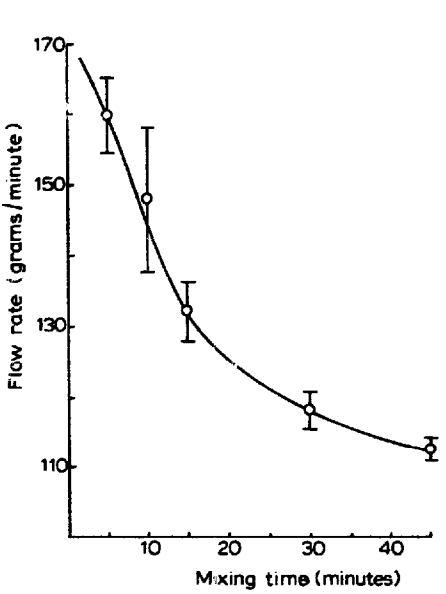


Fig. 24. Estimation of critical unconfined yield stress ($f_{c_{crit.}}$) using powder flow function and hopper flow factor.



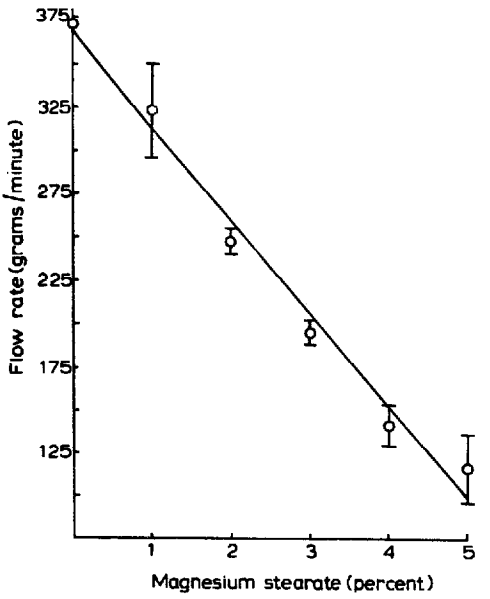


Fig. 25. Flow-rate as a function of mixing time (Jordan and Rhodes, 1979).

Fig. 26. Flow-rate as a function of percentage magnesium stearate (Jordan and Rhodes, 1979).

When designing equipment for powder processing, it is important to consider and apply the most appropriate flow index from the many available as well as considering the properties of the powders. In one equipment design study (Pilpel and Walton, 1974), the various forces associated with a storage hopper above an auger feed device (see Fig. 28), a system suitable for dispensing powders into unit dose containers were considered. The failure properties of the powder under gravity will control the porosity of the powder in the hopper and the rate of feed to the auger. The auger applies both compressive and

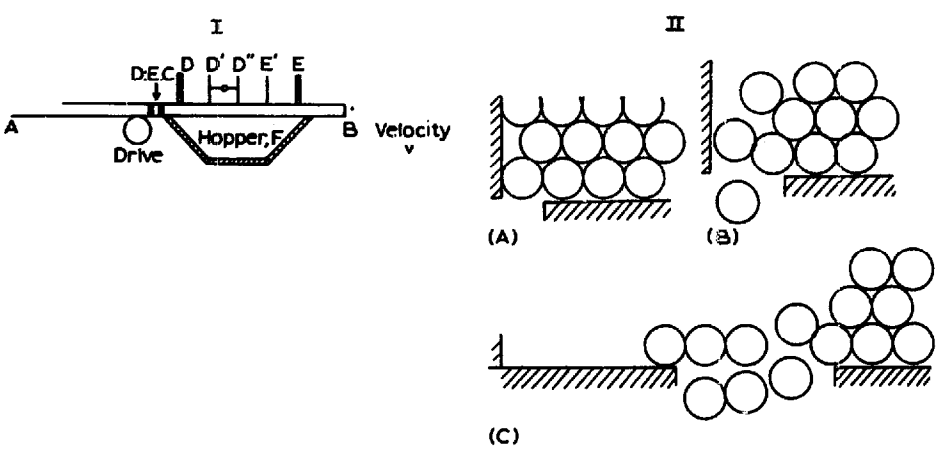


Fig. 27. Diagrams of dynamic flow apparatus and flow-rate model (Carstensen and Laughlin, 1979). I, apparatus; II, proposed model to distinguish two flow-rates.

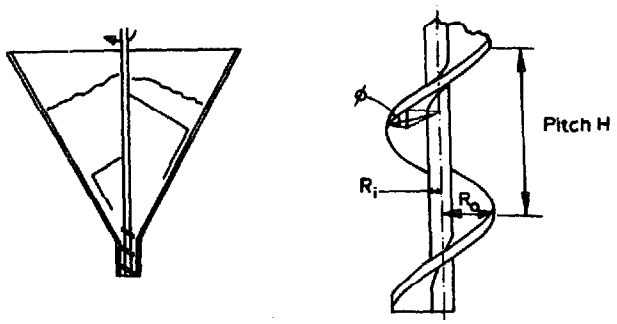


Fig. 28. Hopper and Auger feed (Pilpel and Walton, 1974). ϕ, angle of auger; R_i, radius of auger stem; R_0, radius of auger face.

shearing forces, decreasing the porosity of the powder. Powder flow from the hopper will depend on the flow factor, which can be modified by changing particle size and shape (Pilpel and Walton, 1974). But the auger increases the bulk density of the powder, which is generally disadvantageous since the mechanical strength of the powder is often particularly sensitive to changes in bulk density and will modify flow behaviour. The compressive effect can be minimized by making the auger as short as possible, whilst consistent with its metering function. Other design changes considered were modification to the auger flight, which would modify consolidation of powder at the outer constraining wall, and reduction in pitch, H, to maximize the vertical stress component to move downwards rather than horizontally (Pilpel and Walton, 1974). From this discussion, it can be seen that by combining changes in equipment design, after considering powder behaviour, with control of particle failure behaviour by modifying particle size and shape, a system providing maximum uniformity of dose in each container might be achieved.

CONCLUDING REMARKS

Undoubtedly as the understanding of powder behaviour increases, particularly at the particulate level by extending the simple models taken by Rumpf (1962) and Cheng (1968) to consider more advanced concepts, the prediction of the failure properties of powder systems and formulations and their behaviour during handling and processing will become possible. Whilst this must be regarded as a long-term objective because of the complexity of real powder systems, both comparative techniques and methods based on the continuum model can be applied to consider pharmaceutical powders and systems and associated problems. This has been successfully demonstrated in a number of areas including powder characterization, formulation, powder processing and processing equipment.

SUMMARY

The review traces the development of the continuum and particulate models which are used for analyzing powder failure behaviour. Currently available equipment used for mea-

suring failure properties is critically assessed and the applications and relevance of these measurements to 3 broad areas of pharmaceutical interest – characterization of pharmaceutical powders, formulation, processing and processing equipment – is discussed.

ACKNOWLEDGEMENTS

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