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OVERVIEW OF COMPACTION DATA ANALYSIS TECHNIQUES

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ABSTRACT

In this review article, the techniques that have been utilized to assess the compactional behaviour of pharmaceutical materials were presented, and the advantages, limitations and modifications of some of these methods were discussed. It was concluded that despite some of these techniques, such as Heckel equation, F-D curves, energy of compaction, tensile strength and hardness measurements, have received considerable attention, none of them was found to be satisfactory for the comprehensive analysis of the mechanisms involved in the compaction of the solid particulate matter.

INTRODUCTION

The phenomena and mechanisms involved during compaction of pharmaceutical materials became an increasingly important concept in the design and development of solid dosage forms, since the systematic investigations facilitated by the use of instrumented single-station and multi-station tablet presses (1-6), universal testing machines (7,8), and integrated compaction research systems, also known as compaction simulators (9-13). Several authors reviewed the mechanisms of compaction and/or the data analysis techniques (14-19), and the application of instrumented methods to all aspects of tabletting technology (1,2,13,20-26). The parameters monitored during compaction varied widely in these studies. Data obtained from the measurements of forces on and displacements of the upper and lower punches (5,6,13,27,28), axial to radial load transmission (29-34), die wall friction (28), ejection force (4), temperature changes (35-37) and other miscellaneous parameters (4,38,39) have been used to assess the compaction behavior of a variety of pharmaceutical powders and formulations.

It has been pointed out that the number of compaction equations proposed to characterize the compressional process approximates to the number of workers in this field (13). However, many of the equations have been shown to have applicability over only a limited range of applied force and for only a few types of materials. Certainly no universal relationship has yet emerged and is unlikely to do so, as the comprehensive analysis of the mechanisms involved is difficult due to complexity of the systems being compacted.

The aim of this review article is to discuss the techniques that have been used to evaluate compaction data obtained from the measurements of several parameters during a compaction cycle and after ejection. The stress-strain phenomena (e.g., stress relaxation measurements) are excluded.

DATA ANALYSIS TECHNIQUES

It would be convenient to classify the compaction data analysis techniques in three groups, as those that utilize the data obtained from the measurements of the:

- applied pressure and punch displacements
- transmitted pressure
- miscellaneous parameters

A. Utilization of Applied Pressure and Punch Displacement Data

Measurements of the forces on and the displacements of the punches have been proven to be a valuable method to study the relationship between applied pressure and the volume of the compacts. A number of mathematical equations, many of which are empirical in nature, have been developed from this relationship in order to assess the densification and consolidation mechanisms involved during the compaction of solid materials. Kawakita and Lüdde (14), Bockstiegel (15) and Macleod (19) evaluated and compared many of these equations. Table 1 presents a simple comparison and a list of some of these compaction equations, as well.

TABLE 1

A summary of powder compaction equations based on applied pressure and compact volume relationship (After Ref. 19)

No.	*Equation*	*Authors*
1	$\ln \frac{\rho_t - \rho_i}{\rho_t - \rho_c} = KP_A$	Athy, Shapiro, Heckel, Konopicky, Seelig
2	$\ln \frac{\rho_c}{\rho_i}\left(\frac{\rho_t - \rho_i}{\rho_t - \rho_c}\right) = KP_A$	Ballhausen
3	$\ln \frac{\rho_i}{\rho_t}\left(\frac{\rho_t - \rho_i}{\rho_t - \rho_c}\right) = KP_A$	Spencer
4	$\ln \frac{\rho_c}{\rho_i} = KP_A^n$	Nishihara, Nutting
5	$\ln \frac{\rho_t - \rho_c}{\rho_t} + K\left(\frac{\rho_c}{\rho_t - \rho_c}\right)^{1/3} = aP_A$	Murray
6	$\ln \frac{\rho_t}{\rho_c}\left(\frac{\rho_c - \rho_i}{\rho_t - \rho_i}\right) = \ln Ka - (b + c)P_A$	Cooper and Eaton
7	$\frac{\rho_i}{\rho_c} = 1 - KP_A^n$	Umeya
8	$\rho_c = KP_A^n$	Jaky
9	$\rho_c = K(1 - P_A)^n$	Jenike
10	$\rho_c - \rho_i = KP_A^{1/3}$	Smith
11	$\rho_c - \rho_i = KP_A^2$	Shaler
12	$\frac{\rho_c - \rho_i}{\rho_c} = \frac{K \times aP_A}{1 + aP_A}$	Kawakita
13	$\frac{\rho_t}{\rho_c}\left(\frac{\rho_c - \rho_i}{\rho_t - \rho_i}\right) = \frac{KP_A}{1 + KP_A}$	Aketa
14	$\frac{1}{\rho_c} = K - a \ln P_A$	Walker, Bal'shin, Williams, Higuchi, Terzaghi
15	$\rho_c = K + a \ln P_A$	Gurnham
16	$\frac{1}{\rho_c} = K - a \ln P_A$	Jones
17	$\frac{1}{\rho_c} = K - a \ln (P_A - b)$	Mogami
18	$\frac{\rho_c - \rho_i}{\rho_c} = KP_A\rho_i + a\left(\frac{P_A}{P_A + b}\right)$	Tanimoto
19	$\frac{\rho_c - \rho_i}{\rho_c} = \ln (KP_A + b)$	Rieschel

[*] ρ_t, net density of powder; ρ_i, initial apparent density of powder; ρ_c, density of powder under applied pressure P_A; K, a, b and c are constants.

Walker and Bal'shin Equations:

Most of the earliest attempts to study the degree of consolidation of the powders were made in the field of powder metallurgy (40-42). As early as 1923, using materials such as lead shots, ammonium chloride, sodium chloride and potassium nitrate, Walker (40) observed a logarithmic relationship between the applied pressure (P_a) and the relative volume (V_r) of the compact as:

$$V_r = C_1 - K_1 \text{ Log } P_a \tag{1}$$

where C_1 and K_1 are constants. In this work, K_1 values were found to be greater for plastically deforming materials when compared to those for brittle fractured ones. Walker related the ratio of C_1/K_1 to the compactional behaviour of powders and reported that relatively high ratios were generally found for materials producing weak tablets. These findings were supported in a recent work by Çelik and Marshall (13) who observed higher C_1/K_1 ratios for elastically deforming materials than those for plastically deforming or brittle fracturing substances.

Bal'shin (41) also proposed a similar relationship for some metallic powders as follows:

$$\text{Log } P_a = -K_2 V_r + C_2 \tag{2}$$

where K_2 and C_2 were the two dimensionless material properties, K_2 being the 'Pressing Modulus' analogous to Young's Modulus, and C_2 the 'Coefficient of Deformability'. The metallic powders exhibited linearity at low and intermediate pressure ranges. Later, the work of

Bal'shin was confirmed by the findings of Huffine and Bonilla (43) who also defined K_2 as a single exponential function of the particle size.

Kawakita Equation:

Another equation which has received considerable attention in the field of powder compaction was developed by Kawakita (44) and is expressed as:

$$C = (V_i - V_p) / V_i = abP_a / (1+bP_a) \qquad (3)$$

where C is the degree of volume reduction, V_i is the initial apparent volume, V_p is the powder volume under applied pressure P_a, and both a and b are the constants which can be calculated from the P_a/C vs P_a plots. The 'constant a' does not correlate to any properties of the material being compacted while the 'constant b', which is termed as the coefficient of compression, is related to the plasticity of the material (45).

Yamashiro and others (46) applied Kawakita's equation to the tap density measurements of their materials by using the following formula:

$$N/C = N/a + 1/ab \qquad (4)$$

where N is tapping number. A linear relationship was observed between N/C and N even at small tapping numbers and the constants a and b were related to the powder fluidity and tapping ability, respectively.

Van der Zwen and Sisken (47) who considered the compaction of granulated materials as a four stage process (i- filling of the holes between granules, ii- fragmentation and plastic deformation of granules, iii- filling of the holes between the primary particles, iv- fragmentation and plastic deformation of primary particles) reported that the Kawakita equation can only be applied to materials in powder form. These workers adapted this equation by substituting the 'initial compaction volume' with a 'bulk volume' in order to have a better fit to the Kawakita equation for the granulated matters.

Another limitation of the Kawakita equation is that, using this method, the compaction process can be described only up to a certain pressure above which the equation is no longer linear (48).

Heckel Equation:

The most commonly used equation in the pharmaceutical compaction studies was developed by Heckel (49,50) who considered that the reduction in voidage obeys a first-order kinetics type of reaction with applied pressure. This relationship between porosity and applied pressure is similar to those proposed previously, by some other workers, such as Athy (51), Shapiro and Kolthoff (52) and Konopicky (53). Heckel's equation is expressed as:

$$\ln [1/(1-\rho_r)] = KP_a + A \qquad (5)$$

where ρ_r is the relative density of the compact, K and A are constants which can be determined from the slope and intercept of the extrapolated linear region of the plot, respectively, as shown diagrammatically in Figure 1-a.

In his second paper (50), Heckel proposed a relationship between the constant K, and the yield strength of the material, Y, as expressed by the following equation:

$$K = 1/3Y \tag{6}$$

Later, Hersey and Rees (54) related the constant K to the mean yield pressure (P_y) as:

$$K = 1/P_y \tag{7}$$

Hence, K is inversely related to the ability of material to deform plastically under pressure.

The constant A is a function of the initial compact volume and can be related to the densification during die filling and particle rearrangement prior to the bonding.

The Heckel equation was found to be similar to several other compaction equations (15, 55). These equations differ only in the nature of the constant A which was considered by Heckel (50) to be the sum of two terms as defined in the following equation, rather than a true constant.

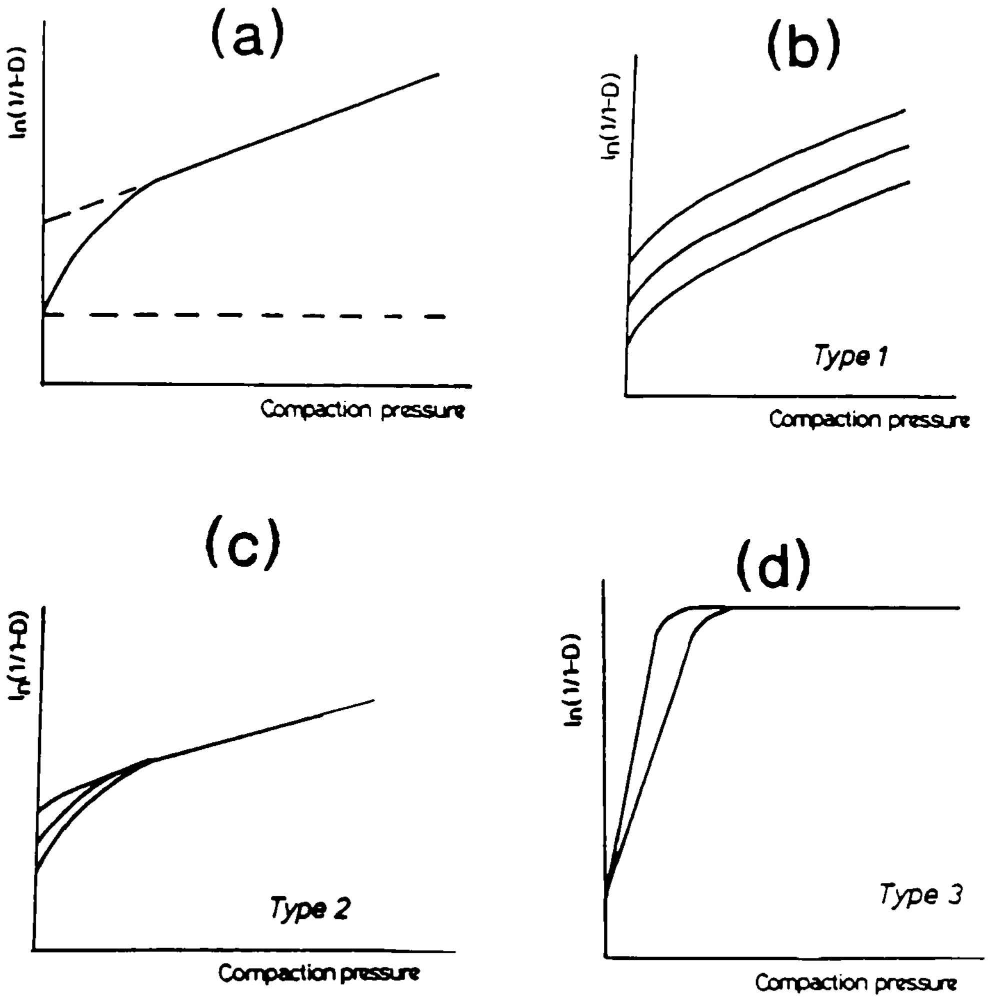


Figure 1

Heckel Plots:

(a) A diagrammatic representation

(b) Type 1 (After Reference 54)

(c) Type 2 (After Reference 54)

(d) Type 3 (After Reference 57)

$$A = \ln [1 / (1 - \rho_a)] + B \qquad (8)$$

where ρ_a is the apparent density of the powder and B is the densification which takes place by individual particle motion at low pressures before appreciable interparticle bonding takes place.

A typical Heckel plot, as can be seen in Figure 1-a is linear only at high pressures. Heckel (50) suggested that the initial curved region of the plots can be attributed to the particle movement and rearrangement in the absence of inter-particulate bonding. Therefore, he proposed that this stage corresponds to the packing process discussed by Seelig and Wulff (42). The linear portion of a $\ln[1/(1-\rho_r)]$ vs P_a plot was attributed by Heckel to both plastic deformation and cold-welding.

The application of Heckel plots to the compaction of pharmaceutical powders permits an interpretation of the consolidation mechanisms and a measure of the yield pressure of the powder under examination. Heckel plots have been classified into three types. The Type 1 (Figure 1-b) and the Type 2 (Figure 1-c) were suggested by Hersey and Rees (54, 56), and the Type 3 (Figure 1-d) was proposed by York and Pilpel (57).

The Type 1 plots are exhibited by different particle size fractions of a given material which consolidates by plastic flow. Variations in initial powder bed density results in different final bed densities under any particular applied pressure.

In the Type 2 plots exhibited by the materials that consolidate by particle fragmentation, a single relationship occurs above a certain pressure irrespective of the initial bed density. This feature is also independent of particle size and is thought to be due to the progressive destruction of the particles by fragmentation and their subsequent compaction by plastic deformation.

The Type 3 plots are attributed to the absence of a particle rearrangement stage coupled with plastic deformation and the possible melting of asperities.

Using the Heckel plots, Fell and Newton (58) pointed out that density measurements made under load include an elastic component which will increase the value of $\ln[1/(1-\rho_r)]$ for a given compaction force and therefore, will result in a false (low) yield pressure value which is inversely related to the ability of a material to deform plastically under pressure.

Roberts and Rowe (59) investigated the effect of punch velocity on the compaction behaviour of a number of pharmaceutical materials by determining the change in their yield pressures. They observed that plastically deforming materials exhibited an increase in the yield pressure with increasing punch velocity. This was attributed to either a change from ductile to brittle behaviour or a reduction in the amount of plastic deformation due to time dependent nature of plastic flow. They also calculated the Percentage Strain Rate Sensitivities (SRS%) from the yield pressures determined at low and high punch velocities. The SRS%

values of the plastically deforming materials were higher than those of the brittle ones whose yield pressure values did not exhibit any significant change with increasing punch velocities.

Çelik and Marshall (13), who developed Heckel plots for a number of excipients, observed nonlinearity in many of these profiles that were obtained under dynamic conditions. They suggested that compaction data collected under static conditions, where porosity values are calculated from "out of die" measurements on tablets, would be expected to produce different results as compared with data obtained under dynamic conditions, where porosity values are determined from "in die" measurements, since presumably the elastic recovery of tablet contributes to its porosity. It must be kept in mind that, the fidelity of "in die" measurements would depend on whether the compaction data are accurately corrected for deformation of the punches and other associated machine components. The number of data points used to obtain a Heckel profile is another important factor that affects the accuracy of this method.

Rue and Rees (60) suggested that the Heckel equation should be used with caution since the Heckel profiles obtained for a given material would vary depending on the experimental conditions. Therefore, they proposed the use of area under the Heckel plots obtained at varying contact times as a quantitative method to compare the degree of plastic deformation of a range of materials.

Düberg and Nystrom (61) applied the Heckel equation to both compression and decompression phases in an attempt to distinguish plastic and elastic deformation characteristics of the materials.

In a recent work, Carstensen and others (62) proposed a modified form of Heckel equation as follows:

$$\ln \{[1/(1-\epsilon)] - V_t \rho_t \} = - AP_a + \ln (V_a \rho_t) \qquad (9)$$

where ϵ is equal to the porosity of the compact at pressure P_a , V_t is the specific solid volume, ρ_t is the true density of the material, and V_a is the apparent specific void volume.

The major difference between the original Heckel equation and its modified version is that the former equation assumes that the porosity decreases exponentially with applied pressure, whereas the latter equation assumes that the volume of air in the powder bed/compact is the quantity which will decrease exponentially with increasing pressure. Hence, the modified equation allows the linearization of plots over the entire compaction range, contrary to the traditional Heckel plots which exhibit linearity only at high pressure ranges. It was noted that the Heckel equation only applies to pressures so high that they actually are not in the range of pressures applied to pharmaceutical tablets.

Several workers (48,54,55,63) treated their compaction data using both Kawakita and Heckel equations in order to compare the applicability of these methods. Some of them (54,55) suggested that the Kawakita equation does not yield as much information as the simpler Heckel equation. Others (48,63) proposed the use of both methods together, in order to describe the mechanisms of compaction more accurately, since the linearity is observed at low pressures with the Kawakita equation and at high pressures with the Heckel equation.

Cooper and Eaton Equation:

Cooper and Eaton (64) developed an equation relating the fractional consolidation, defined as the decrease in voidage as a proportion of the original voidage, with pressure for the compaction of certain powders:

$$\frac{(V_i - V_p)}{(V_i - V_t)} = C_3 \exp(-K_3 / P_a) + C_4 \exp(-K_4 / P_a) \qquad (10)$$

where C_3 , C_4 , K_3 and K_4 are constants.

The two terms on the right hand side of the equation are related to the slippage of particles at early stages of the compaction and to the subsequent elastic deformation, respectively. Their findings supported the view that the yield strength of metal powder compacts are related to the linear portion of the Heckel plots. However, the difficulty, in practical use of the above equation, is the assignment of some physical significance to the constant parameters of this equation. Another drawback of this method is that this equation applies only to a single-component system (62).

Van der Zwan and Siskens (47), using the experimental points of the high pressure range only, proposed the simplification of the Cooper and Eaton equation to a single-term relation as:

$$\frac{(V_i - V_p)}{(V_i - V_t)} = C_5 \exp(-K_5 / P_a) \qquad (11)$$

where C_5 is equal to the sum of the constants C_3 and C_4, and K_5 is a new constant. It was, then, reported by these workers that Kawakita's constant b approximately equals to the reciprocal of the constant K_5 of the simplified Cooper and Eaton equation, although the mathematical expressions of the two methods are very different.

Leuenberger Equation:

A relatively new method used in the field of powder compaction was proposed by Leuenberger (65) who related the two important indices of powder compression; compactability (the ability of a material to yield a compact with adequate strength) and compressibility (ability of the material to undergo volume reduction under pressure). This relationship can be expressed as:

$$P_{dh} = P_{max} [1 - \exp(-\Upsilon P_a \rho_r)] \qquad (12)$$

where P_{dh} is the deformation (Brinell) hardness, P_{max} denotes the theoretical maximum deformation hardness that would be attained as P_a approaches infinity and relative density approaches 1, and Υ is the compression susceptibility.

Leuenberger and others (66-68) observed a good correlation when they applied the above equation and its modified versions to the single component powders and their binary mixtures. It was noted by these workers that a low P_{max} value shows a relatively poor compactability and this limiting value can not be exceeded, even at very high compaction pressures. A high value of Υ indicates that the theoretical limit of hardness and a sharp decrease in compact porosity may be attained with relatively low compaction pressures.

F-D Curves, Energy and Power Involved in Compaction:

A common method for assessment of the compaction behaviour of materials is the use of compression force vs punch displacement profiles (F-D curves) from which the work involved during tablet compaction can be calculated (Figure 2-a). Krycer and others (17) suggested that, since powders with different packing characteristics and different elastic/plastic deformation properties will absorb varying amounts of energy, it might be more useful to measure the 'work of compaction' rather than other characteristics. Fell and Newton (69) formed the opinion that the work done on compaction of a powder mass is utilized both for volume reduction and particle bonding, but only the latter contributes to the strength of the tablet. The total work done on compaction is, therefore, not necessarily a criterion of tablet strength. However, this conclusion was not supported by the work of Celik and Marshall (13) who observed that the rank order of total energy involved during compaction of the powders and tensile strength of their compacts were similar.

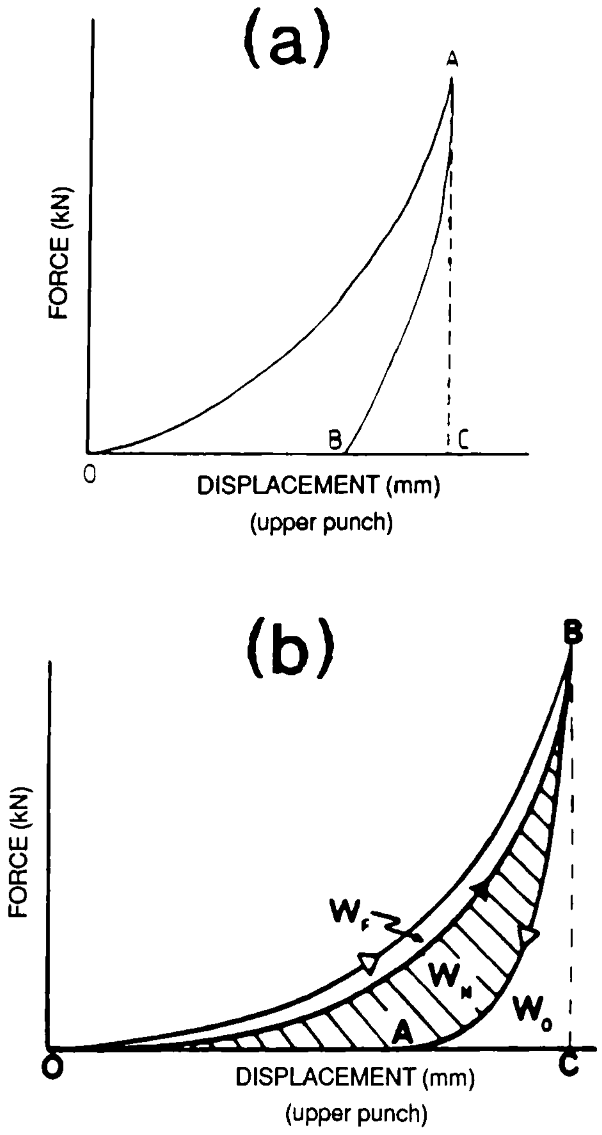


Figure 2

Force vs Displacement Profiles (F-D Curves)

(a) A diagrammatic representation

(b) W_f : Work done in overcoming friction

W_e : elastic deformation energy

W_n : net mechanical energy

(After Reference 69)

In the literature, the method of obtaining F-D curves, and the definition and utilization of work phenomenon varied considerably. In Figure 2-a, the area OAB represents the work exerted by the top punch on the material compressed. As the compact expands during decompression, some of this work will be transferred back to the upper punch. This work of expansion during decompression is represented by the area ABC. Hence, the area OAC may be considered to correspond to the total work involved in compaction. However, as Jones (16) pointed out, compact expansion due to elastic recovery may continue after the top punch has lost contact with the compact and thus, the measured work of compaction may not truly represent the complete work of compaction. In addition, the work required to overcome friction at the die wall can be calculated from the difference between the area under the curves obtained for the upper and lower punches (Figure 2-b). If this work is also deducted from the total work then the overall net work of compaction can be calculated (70). Lammens and others (71) suggested that, although the force exerted by the upper punch is usually used for obtaining F-D curves, measurement of the force transmitted to the lower punch may be of more value.

Çelik and Marshall (13) obtained F-D curves (for both single and double-ended compaction studies) by plotting the arithmetic mean of the upper and lower punch forces vs changes in the height of the powder bed during compaction. They observed hysteresis in such curves when the F-D curves were obtained by plotting the upper punch force vs its displacement. They, then calculated the total work of compaction by considering the contributions of the upper and lower punches to the total work, separately.

Assuming that the tablet has completed its plastic deformation and fully recovered elastically prior to a second compression (recompression), de Blaey and his co-workers (5,72-73) reported that the work done on the lower punch during recompression phase can be used as a measure of the elastic energy recovered on removal of the upper punch in the first compaction. However, Krycer and others (17) suggested that the above assumptions may not be strictly applicable in practice.

An alternative way of presenting work of compaction data is the use of power profiles (i.e. energy per unit time) on which very little information exists in the literature (13,74-76).

Çelik and Marshall (13) employed two different methods to analyze their power data. The first technique involved the calculation of instant power by analyzing the force and displacement data of the total tabletting cycle in small fractions. It was observed that the peak of the instant power vs pressure plots corresponded to the point of inflexion on the force vs time profiles. The second technique was termed as the average power consumption which was calculated by dividing the cumulative total work of compaction by the corresponding contact time. In their work, the slopes of the average power consumption vs pressure plots could be clearly divided into two groups, those where strong or weak tablets were produced.

The method used to determine the time interval variable and to present the power data can change both the magnitude and rank order of power consumption, significantly. Applying three different power equations to the same data, Armstrong and Palfrey (75) obtained different total power expenditures. Therefore, power data must be used with caution if power consumption is to be correlated with the compaction characteristics of a powder.

B. Utilization of Transmitted Pressure Data

Upper to Lower punch stress transmission:

During a single ended compaction of a powder mass, a rather complicated force transmission pattern, with major components of, F_a , the axial force causing compression of the powder and F_r, the radial force exerted upon the die wall, occurs (77), as shown in Figure 3. The force sensed by the lower punch, F_b, is less than F_a because of the existence of a frictional force, F_d, between the die wall and the solid being compacted.

If μ is the coefficient of friction between the particulate solid and the die wall, then:

$$F_d = \mu F_r \tag{13}$$

Shaxby and Evans (78) found a logarithmic relationship between applied pressure, P_a, and transmitted pressure to the lower punch, P_b , as:

$$P_a = P_b \exp(4H_c K_6 / D) \tag{14}$$

where H_c is the thickness of the compact; D is the diameter and K_6 is a material constant.

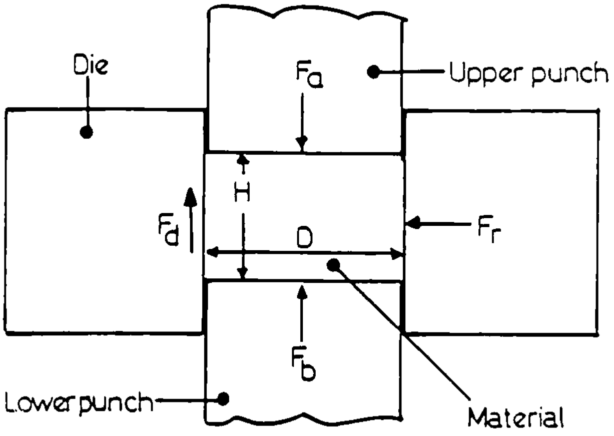


Figure 3

A diagrammatic representation of the forces operating in a die (After Reference 77)

Unckel (79), and Toor and Eagleton (80) modified this equation to include the ratio of radial to axial stress, Ω, (which is equal to the Poisson ratio, ν) and the coefficient of friction, μ, as:

$$P_a = P_b \exp(4\mu\Omega H_c/D) \qquad (15)$$

This equation can also be expressed as:

$$\ln(P_a/P_b) = 4\mu\Omega H_c/D \qquad (16)$$

In practical terms, the above equations are useful to show the importance of a low H_c/D ratio for the tablet being compacted and the influence of the coefficient of friction between the powder and the die wall. When the H_c/D ratio is high, there will be a considerable decay of the applied pressure down the compact length resulting in a poorly compacted region adjacent to the stationary punch. In the case of a rotary machine, the effect is reduced by employing two moving punches to apply pressure to the compact.

Since Nelson and others (81) elucidated the potential usefulness of the following ratio:

$$R = F_b \; / \; F_a \tag{17}$$

where R, which is termed as R value, is the coefficient of lubricant efficiency, a number of authors (82-83) used this ratio to study the efficiency of lubricants in tablet formulations. However, studies of de Blaey and Polderman (5) indicated that since force transmission is not constant during the complete compaction cycle, a large variation occurs in the amount of work required to overcome the friction with the die wall, especially during the initial phase of compaction. Consequently, it was concluded that R values measured at the end of the cycle may not truly represent the values prevailing during compaction.

Guyot and others (84) have suggested that the work input calculated from the area under the curves of the upper punch displacement and the mean value of upper and lower punch forces can be used instead of the R value as a lubrication index.

Axial to Radial Stress Transmission (Compression Cycles):

Examination of the axial to radial stresses during a complete compression cycle (i.e., application, relaxation and dissipation phases of the applied pressure) can yield data to obtain quantitative values for a number of compaction properties of the powders.

Using load cells and strain gauges, Nelson (29) studied the transmission of forces to the die wall during the application of axial pressure. However, this work was not extended to cover the relaxation and dissipation stages of the applied pressure.

Long (30) employed a split die to measure the radial pressure over a complete compression cycle. Assuming that the die was perfectly rigid, and there was no die wall friction, he described two possible compression profiles for ideal isotropic systems:

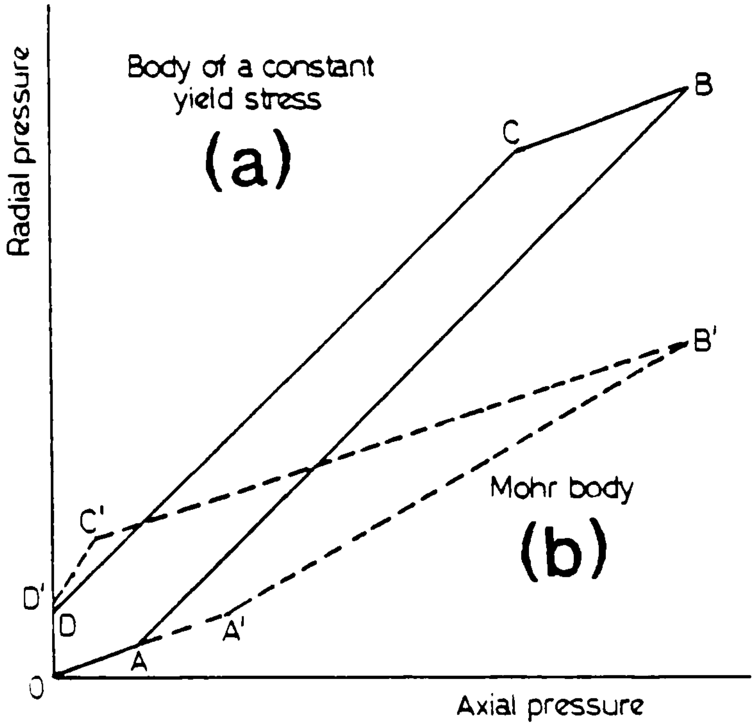
a- A body with a constant yield stress in shear (Figure 4-a).
b- A Mohr's body (Figure 4-b).

Initially, as the upper punch descends into a filled die, the powder particles are rearranged to form a closer packing and then, begin to undergo elastic deformation. During this phase, the axial pressure (P_a) transmitted through the powder mass generates a radial pressure (P_r) which can be determined from the following equation:

$$P_r = \nu P_r \qquad (18)$$

where ν is termed as the Poisson ratio.

With further increase in P_a, the elastic limit (i.e., the yield point which is denoted by A and A' in Figure 4-a and b, respectively) of the material



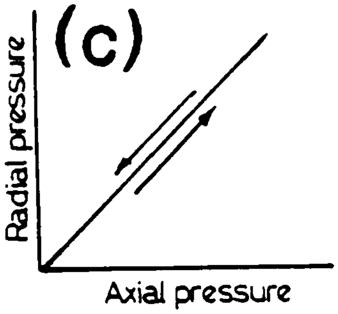


Figure 4

Diagrammatic representation of radial vs axial pressure cycles

(a) A body with a constant yield stress in shear (After Reference 30)

(b) Mohr body (After Reference 30)

(c) An ideal elastic body (After Reference 31) is exceeded, beyond which either brittle fracture or plastic deformation takes place and bonds form between the particles. At this stage, the radial force is no longer determined by Poisson's ratio but either:

i) exhibits constant yield in stress where the relationship between P_a and P_r is unity (AB).

ii) behaves as a Mohr's body in which the yield stress is a function of the normal stress across the shear plane and the slope of A'B' may vary in magnitude.

In the first case, after the maximum force has been applied (B and B' in Figure 4-a and b, respectively), the change in P_r is once again the Poisson's ratio times the rate of change of P_a. Therefore, the slope BC is equal to the slope of OA. In the second case (Mohr's body), on release of P_a, the radial pressure diminishes following the line B'C' and its slope is equal to slope of the initial curve OA'. Then, the yield takes place (C and C' in Figure 4-a and b, respectively) and it continues until P_a has returned to zero. At this point (D and D' in Figure 4-a and b, respectively), there is a residual radial stress still exerted on the compact and in the case of a Mohr's body, this residual die wall stress is somewhat larger.

Leigh and others (31) suggested a third possible compression profile presenting the behaviour of a perfectly elastic body or a body compressed below its elastic limit (Figure 4-c). On unloading, the radial force returns to zero. There will be no residual radial force exerted on the die wall and the body will be free to move out from the die. These authors also suggested that the above concepts, developed for solid isotropic bodies, can be explained in particulate systems in terms of the following stages of compact deformation.

OA (or OA') = Elastic deformation
AB (or A'B') = Plastic flow/crushing

It was reported by Leigh and others (31) that the analysis of the compression cycles of materials may indicate the formation of satisfactory or unsatisfactory compressed tablets. These workers observed that acetaminophen granulations behaving as a Mohr's body tended to cap and laminate and found that the change from a compact which readily caps and laminates to an intact one was associated with the transformation from a Mohr's body type compression cycle to one with a constant yield stress in shear.

Contrary to these findings, Shotton and Obiorah (85), observed no tendency to cap or laminate although their materials behaved like a Mohr's body, as well. Instead, they suggested that materials possessing low residual die wall pressure would yield weak tablets which might cap on ejection.

C. Miscellaneous Techniques

Measurements of Elastic Expansion of the Compacts:

It has been pointed out that (86-88) on release of compression force, the compact can expand within the die and may continue to do so after ejection. This expansion may generate stresses that are the main cause of some tabletting problems, such as capping and lamination. Employing the acoustic emission technique, Rue and others (88) observed that both capping and lamination occurred completely within the die during decompression and not during ejection.

Numerous techniques have been employed to determine the magnitude and the disruptive effects of the elastic recovery of formed compacts. Some of these were evaluated by Krycer and others (89).

Several workers (89-91) used the percentage recovery (E) defined as:

$$E = 100 * (H_e - Hc)/Hc \tag{19}$$

where H_c and H_e are the heights of the compacts under pressure and after ejection, respectively. However, the expansion of compacts has been measured at varying times following their ejection by different authors (89,92-93) and, therefore, the values may include the slower viscoelastic recovery as well as the rapid elastic expansion.

Another technique of studying elastic expansion is the use of the work done on the lower punch in a second compaction (73,94). As cited earlier, this method assumes that the tablet fully recovers elastically prior to recompression and only elastic deformation occurs on the recompression stage. However, it is questionable whether the above assumptions apply in practice.

Summers and others (94) employed an elastic modulus (EM) defined as:

$$EM = P_a H_c \;/\; \Delta H_c \tag{20}$$

where ΔH_c is the decrease in the height H_c .

An alternative technique to measure the disruptive effects of elastic expansion was suggested by Çelik (34), and Çelik and Travers (8) who proposed the Elastic Recovery Index (ERI) defined as:

$$ERI = ER \;/\; SM \tag{21}$$

where ER is the magnitude of elastic recovery undergone by the compact during decompression (corrected for punch deformation) and SM is the strain movement (i.e., the magnitude of further plastic and viscoelastic deformation under a constant stress). It was suggested that if a material has a high ERI value, it forms weak, possibly capped and/or laminated tablets. Using a similar ratio, ER/PC, where PC is the plastic compression determined under constant strain conditions) some others workers (95-96) observed high ratio values for the compacts of materials with capping tendencies.

Percolation Theory and Fractal Geometry:

A recent development in the field of pharmaceutical compaction is the application of percolation theory and fractal geometry by Leuenberger and his co-workers (97-99).

Percolation theory deals with the number and properties of clusters of randomly occupied sites in a geometric lattice (100). It describes a phenomena whereby a property of a system as a function of a continuously varying parameter which diverges, vanishes or just begins to be manifested at one sharply defined point. This point, referred as the 'percolation threshold', is where a component of the system just begins to percolate or to form continuous structure throughout the length, width, and height of the system (101).

Three types of percolation have been described (101):

a- site percolation where a cluster is a group of neighboring occupied sites

b- bond percolation where all sites are occupied and the cluster is a group of neighbors connected by bonds

c- site-bond percolation which is a combination of the above two.

Depending on dosage form design, important changes in mechanical and biopharmaceutical properties of the tablet occur at percolation threshold. The percolation threshold of a powder system vary with the material characteristics of different substances depending on the geometric arrangement of the particles. Therefore, the particle size, size distribution and shape may also influence the value of percolation threshold (102).

It has been suggested that the data obtained from the compaction of binary powder systems can be satisfactorily explained with the help of the percolation theory (102). However, more work is needed to verify the applicability of this theory to the pharmaceutical compaction.

Measurements of Tablet Strength:

The need to quantify the strength of tablets has long been recognized both in compaction research and in industrial practice as a quality control parameter. The mechanical strength of the tablets has been described by several means including the crushing strength (103-104), the axial (105-107) or radial tensile strength (108-110), hardness (111-114), and the work required to cause tablet failure (115).

A common method of assessing the strength of tablets involves the measurement of the force required to break a tablet in a diametral compression test. Using a load transducer in place of a tablet, Brook and Marshall (103) compared several crushing strength testers and observed variations in crushing strength values due, partially, to inaccuracies in the instrument scale values and varying methods of applying load.

The Radial Tensile strength (T_s) of tablets can be calculated from the following equation:

$$T_s = 2F_c / \pi D H_e \tag{22}$$

where F_c is the force needed to break the tablet, D and H_e are the diameter and the thickness of the ejected tablet, respectively. Several precautions must be taken when using this equation. Various factors (e.g., test conditions, deformation properties of the material, adhesion conditions between the compact and its support, tablet shape) may influence the measurements of the tensile strength (105,109). A modified form of the above equation can be used for the measurement of tensile strength of convex-faced tablets (110).

Some authors (105-107) suggested the determination of axial tensile strength because of the sensitivity of radial tensile strength measurements to crack propagation variations. The axial tensile strength (T_{sx}) can be calculated from the following relationship:

$$T_{sx} = 4F_c / \pi D^2 \tag{23}$$

The measurements of tablet strength in axial direction were found to be valuable for the assessment of capping and/or lamination tendencies of the materials (116).

Crushing strength is often imprecisely termed as hardness which is, in fact, a surface property measured by the resistance of a solid to local permanent deformation. Hardness can be determined by either the static methods (e.g., the Brinell, Vickers, and Rockwell hardness tests) or the dynamic methods (67). The static indentation methods involve the formation of a permanent indentation on the surface of the material tested and the hardness is determined by means of the load applied and size of the indentation formed (34,111,113). In the dynamic indentation tests, either a pendulum is allowed to strike from a known distance or an indenter is allowed to fall under gravity onto the surface of the test material. The hardness is then determined from the rebound height of the pendulum or the volume of the resulting indentation. Using an apparatus consisting of a steel sphere pendulum acting as an indenter, Hiestand and others (112) estimated the hardness (i.e,, the mean deformation pressure) of compacted materials by dividing the energy consumed during impact by the volume of the indentation.

Hiestand and Smith (117) used the indentation hardness and the tensile strength measurements to formulate the following three dimensionless indices to characterize the relative tabletability of single components and mixtures:

- Bonding Index (BI) is defined as the ratio of the tensile strength to the dynamic indentation hardness, and is claimed to be the indicator of the survival success of areas of contact.

- Brittle Fracture Index (BFI) is a measure of brittleness which is the principal cause of capping and lamination.

- Strain Index (SI) is obtained during the determination of dynamic indentation hardness and is indirectly related to the proximity of the surfaces that remain in contact after decompression.

CONCLUSIONS

A number of compaction data evaluation techniques that are used to assess the deformation characteristics of pharmaceutical powders have

Table 2

Recommended Methods to Study the Important Compaction Parameters

	Information required	Preferred Method
1.	stages of compaction	- Heckel Equation - Kawakita Equation
2.	compressibility	- Leuenberger Equation - Kawakita Equation (at low pressures) - Heckel Equation (at high pressures)
3.	consolidation	- Heckel Equation - Leuenberger Equation - BI, Bonding Index
4.	elastic deformation/ elastic expansion	- E, Percentage Elastic Recovery - Work done on the lower punch in a second compression
5.	plastic deformation/ brittle fracture	- Heckel Equation - Compression Cycles
6.	yield strength/ yield pressure	- Heckel Equation - Compression Cycles
7.	work of - elastic deformation - die wall friction net work of compaction	- F-D curves
5.	lubricity	- R value - Compression Cycles - Unckel/Shaxby-Evans Equations
7.	capping tendency/ lamination tendency	- ERI, Elastic Recovery Index - PC/ER, Plasto-elasticity Index - BFI, Brittle Fracture Index

been reviewed. None of them was found to be fully satisfactory for the comprehensive analysis of the compaction mechanisms.

It was observed that the most commonly used compaction equations were based on the relationship between the applied pressure and volume reduction of a material being compacted. These equations were found to yield useful information on determining the stages of compaction and predominant mechanisms taking place. In many cases, especially before the introduction of instrumented machines, this relationship was often examined by determining the volume of compacts from the out of die measurements which may give different results than in die measurements. It is, therefore, critically important that the validated data monitoring and analysis methods be applied consistently to all materials under investigation in order to minimize the occurrence of conflicting findings over the compaction behaviour of the same material or in order to compare the data obtained for various materials, properly. It must be kept in mind that the above suggestion is valid for all compaction data analysis techniques used.

In conclusion, more than one data evaluation technique may have to be applied in order to increase the validity of the conclusions drawn from the results of a compaction study. Such methods can be selected from Table 2 that summarizes the recommendations of this review article which focuses on the methods involved during compaction.

LIST OF SYMBOLS

a	constant in Equations 3 and 4

A	constant in Equation 5
b	constant in Equations 3 and 4 (coeff. of compression)
B	constant in Equation 8
BFI	brittle fracture index
BI	bonding index
C	degree of volume reduction
C_1	constant in Equation 1
C_2	constant in Equation 2 (coeff. deformability)
C_3	constant in Equation 10
C_4	constant in Equation 10
C_5	constant in Equation 11
D	compact diameter
E	percentage elastic recovery
EM	elastic modules
ER	elastic recovery during decompression
ERI	elastic recovery index
ER	strain movements under constant stress
F_a	axial force exerted by the upper punch
F_b	axial force exerted upon the lower punch
F_c	crushing force
F_d	friction force
F_r	radial force exerted upon the die wall
H_c	compact thickness under pressure
H_e	compact thickness after ejection
K	constant in equation 5
K_1	constant in Equation 1
K_2	constant in Equation 2 (pressing modulus)

K_3	constant in Equation 10
K_4	constant in Equation 10
K_5	constant in Equation 11
K_6	constant in Equation 14
N	number of tapping
P_a	applied pressure
P_b	transmitted pressure to the lower punch
PC	plastic compression
P_{dh}	deformation (Brinell) hardness
P_{max}	theoretical maximum deformation hardness
P_r	transmitted pressure to the die wall
P_y	yield pressure
R	coefficient of lubricant efficiency
SI	strain index
SRS	strain rate sensitivity
T_s	radial tensile strength
T_{sx}	axial tensile strength
V_a	the apparent specific void volume
V_i	initial apparent volume
V_p	powder volume under pressure P_a
V_r	relative volume
V_t	the specific solid volume
Y	yield strength
ρ_a	apparent density
ρ_r	relative density
ρ_t	the true density

ϵ	porosity
μ	coeff. of friction
Ω	the ratio of radial to axial stress
ν	Poisson's ratio
Υ	compression susceptibility

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