RESEARCH PAPER

Use of Tablet Tensile Strength Adjusted for Surface Area and Mean Interparticulate Distance to Evaluate Dominating Bonding Mechanisms

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ABSTRACT

In this study, tablet tensile strength has been adjusted for tablet surface area and the average distance between particles in compacts of different materials. The aim of the study was to evaluate the feasibility of using this concept to assess the dominating interparticulate bonding mechanisms. Adjustment of the tensile strength for both tablet surface area and mean pore radius gave similar bonding strength values for materials bonding mainly by weak distance forces (crystalline lactose, sucrose, and microcrystalline cellulose) almost independently of compaction pressure. However, particle size and other factors may still affect the compensated strength values. The bond strength was much higher and more varied for materials bonding also with solid bridges (potassium chloride, sodium chloride, and possibly also sodium bicarbonate and amorphous lactose). For these materials, particle size and compaction pressure had a substantial effect on the bond strength. It is probably the formation of continuous bridges between adjacent particles that is important in these materials rather than the surface properties and the average distance between particles positioned at some distance from each other. Hence, adjusting the tensile strength of compacts does not necessarily reflect all the dominating factors responsible for interparticulate bonding. Nonetheless, adjustment for tablet surface area and mean pore radius allowed discrimination between different dominating interparticulate bonding mechanisms in these compacted materials.

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INTRODUCTION

Although the component and processing variables affecting tablet strength have been studied extensively over the years, interparticulate bonding mechanisms in compacts have not yet been characterized in a simple and comprehensive manner. Several workers have suggested parameters thought to be important for determining tablet strength (1-6). Nyström (7) stated that the parameters primarily responsible for compact strength are the dominating bonding mechanism and the surface area over which interparticulate bonds are active. These parameters are in turn affected by several secondary factors, such as particle size, particle shape, and volume reduction behavior of the material. Since it is difficult to measure the primary parameters directly, more indirect methods have been used to describe the mechanical strength and bonding surface area of a compact (8). However, it has not yet been possible to obtain a good estimation of the effective bonding surface area (i.e., the actual surface area participating in bonding). Nonetheless, some studies (9–11) have concluded that the bonding surface area must be very small compared to the total surface area of the tablet.

It is necessary to consider the dominating bonding mechanism when determining the effects of surface area on the compact strength. The interparticulate bonds may be solid bridges, weak distance forces (intermolecular attraction forces), or mechanical interlocking (12). Several studies investigating different qualities and particle size fractions of crystalline lactose (3,13–15) and starch (16) found a linear relationship between the surface area of the tablets and their strength when crushed. It was suggested that the tablet surface area was a function of the powder surface area and the pressure applied to the tablet. The linearity of the relationship was believed to indicate that the particles within the compacts were held together by the same type of interparticulate bonds irrespective of compaction pressure and particle size. In contrast, this unique relationship between tablet strength and tablet surface area was not reported by Eriksson and Alderborn (17) or Juppo (18). However, the results may be difficult to compare due to differences in experimental procedures.

Nyström et al. (11) investigated the surface-specific tablet strength by adjusting the value for the strength of the tablet according to the compact surface area. If the surface-specific strength of a tablet was high, it was inferred that solid bridges contributed significantly to the bonding mechanism. Similarly, a low value would indicate that weak distance forces were the primary bonding mechanism. It should thus be possible to distinguish be-

tween the different types of bonds. Bonding by mechanical interlocking of rough or needle-shaped particles may also contribute to the strength of some compacts.

However, it is not sufficient to compensate only for the surface area of the particles in the compact. The strengths of a powder and a tablet made of the same powder, although having the same surface area, will obviously differ considerably. The distance between the particles will thus also influence the mechanical strength of a powder bed. In this study, the tensile strength of tablets made of different materials has been adjusted with regard to both the tablet surface area and the average distance between the particles in the compacts.

The surface area and interparticulate distances of compacted powders can be estimated using different techniques, such as gas adsorption, mercury porosimetry, and air permeametry. The aim, however, is to estimate the relationship between the total particulate surface area and that fraction of the surface area that is actually participating in bonding. Each of the different techniques is associated with drawbacks. For example, the material might change/collapse during mercury intrusion under high pressures. The surface area calculated from mercury porosimetry and gas adsorption data might include the area of cracks and pores inside the particles (i.e., surfaces not taking part in interparticular attraction). Consequently, air permeametry (which measures only the external surfaces) may be preferable. However, the air flowing through the tablet during permeametry measurements may not be able to permeate the tiny distances between particles that contribute to interparticulate bonding. Nonetheless, it is also unlikely that all these surfaces are accounted for in gas adsorption or mercury porosimetry measurements. Therefore, it is believed that the surface area values obtained using permeametric techniques may be as accurate a reflection of the surface area taking part in interparticulate bonding as is currently available. The risk of overestimating the tablet surface area in dense compacts was pointed out by Alderborn, Duberg, and Nyström (19) and should also be borne in mind. Only a proportional relationship between the measured surface area and the bonding surface area should be expected. The advantages and disadvantages of the different techniques have been discussed in more detail elsewhere (19,20).

The mean interparticulate distance can be calculated from slip-flow corrected permeametric surface area determinations (21). Although it is not plausible that the air flowing through the tablet will reach all the areas where bonding actually takes place, it is considered likely that the mean pore radius is proportionally related to the num-

ber of surfaces at these small interparticulate distances. Generally, van der Waals forces are believed to act up to a distance of 100–1000 Å, while solid bridges operate at much smaller distances, approaching atomic separation (22). As discussed above, it is difficult to distinguish between inter- and intraparticulate areas within the compacts. Therefore, to reduce the effects of pores and cracks within the particles, air permeametry was chosen to reflect the bonding surface area.

The aim of this study was to evaluate the feasibility of using the tensile strength of a tablet, compensated for tablet surface area and mean interparticulate distance, to assess the dominating interparticulate bonding mechanisms in the compact.

MATERIALS

Seven different materials were studied (Table 1). Potassium chloride (crystalline, puriss, Kebo-lab, Sweden), sodium chloride (crystalline, puriss, Kebo-lab, Sweden), sodium bicarbonate (crystalline, puriss, Kebo-lab, Sweden), spray-dried amorphous lactose, and Avicel PH101 (FMC) were chosen to represent materials consolidating

mainly by plastic deformation. Lactose (crystalline, α -monohydrate, Pharmatose, The Netherlands) and sucrose (crystalline, Svenskt socker AB, Sweden) represented materials possessing an intermediate or high degree of fragmentation.

The amorphous lactose was prepared by spray-drying a lactose solution made of crystalline α -monohydrate lactose (Pharmatose) and water in a ratio of 1:6 in a Niro Automizer (Germany). The pressure was 4.5 kg/cm², the inlet temperature was 175°C–185°C, and the outlet temperature was 70°C–80°C.

The amorphous lactose obtained from the Automizer was further dried in an oven. The solid-state characteristics of the dry amorphous material were evaluated using differential scanning calorimetry (DSC) (Mettler, TC10A/TC15, Switzerland) by measuring the mean glass transition temperature $T_{\rm g}$ from three repeated measurements (109°C; standard deviation 3°C).

Two particle size fractions were prepared for the microcrystalline cellulose and the crystalline lactose (10–20 μm and 40–60 μm), and three were prepared for the other materials (10–20 μm , 40–60 μm , and 90–150 μm). The amorphous lactose was not fractionated. Sodium bicarbonate, sodium chloride, and sucrose were milled in

Table 1
Primary Characteristics of the Test Materials

Material	Sieve Size Fraction (μm)	Density ^a (g/cm ³)	Volume-Specific Surface Area (cm ² /cm ³)
Potassium chloride	10-20	1.973 (0.000)	3200 (40) ^b
	40-60		1410 (30) ^b
	90-150		290 (0)°
Sodium chloride	10-20	2.152 (0.000)	6070 (270) ^b
	40-60		2510 (20) ^b
	90-150		790 (10)°
Sodium bicarbonate	10-20	2.215 (0.001)	4990 (420) ^b
	40-60		2470 (120) ^b
	90-150		$680 (0)^{c}$
Amorphous lactose	_	1.531 (0.000)	4860 (140) ^b
Avicel PH 101	10-20	1.569 (0.003)	10290 (80) ^b
	40-60		4800 (20) ^b
Lactose	10-20	1.534 (0.000)	3630 (210) ^b
	40-60		1920 (90) ^b
Sucrose	10-20	1.588 (0.001)	7350 (10) ^b
	40-60		2360 (30) ^b
	90-150		1900 (20)°

^a Measured using a helium pycnometer (Accu Pyc. 1330, Micromeretics). Mean value of three determinations; standard deviation in parentheses.

^b Measured using Blaine permeametry (19). Mean value of three samples; standard deviation in parentheses.

^c Measured using Friedrish permeametry (23). Mean value of three samples; standard deviation in parentheses.

a pin disk mill (Alpine 63C, Alpine AG, Germany) to reduce the particle size. Manual dry sieving was used to obtain the particle size fraction of $90-150~\mu m$. The particle size fractions of $10-20~\mu m$ and $40-60~\mu m$ were obtained by elutriation (Alpine 100~MZR, Alpine AG). The apparent particle densities (B.S. 2955, 1958) of all the materials were determined by helium pycnometry (Accu Pyc 1330, Micromeretics) (Table 1). The volume-specific surface areas of the test materials were measured using air permeametry (Table 1). The powders were stored at constant relative humidity (40%) and room temperature (22°C \pm 2°C) for at least 48 hr before compaction, except for the amorphous lactose, which was stored at 0% relative humidity to prevent crystallization.

METHODS

Compaction of Powders

The powders were compacted in an instrumented single-punch press (Korsch EK 0, Germany) using flatfaced punches with a diameter of 1.13 cm. Before each compaction, the die and punch faces were lubricated with magnesium stearate powder. The material was weighed on an analytical balance and manually poured into the die. The maximum upper punch pressure during compression was recorded for each tablet, and 20 tablets were prepared for each load. A deviation from the desired compaction load not exceeding 3% was acceptable. The applied compaction pressures were 25, 50, 75, and 100 MPa for potassium chloride, sodium chloride, microcrystalline cellulose, sucrose, and lactose. Because of difficulties in obtaining compacts strong enough to handle, the applied loads for sodium bicarbonate were 50, 75, 100, and 125 MPa, and those for amorphous lactose were 75 and 100 MPa. The distance between the punch faces at the lowest position of the upper punch in all cases was 3 mm at zero pressure. The different loads were obtained by varying the amount of material in the die.

After compaction, the tablets were stored at 40% relative humidity (except for the amorphous lactose compacts, which were stored at 0% relative humidity) and room temperature for at least 48 hr before their weight, thickness, diameter, and strength were evaluated.

Specific Surface Area Measurements of the Tablets and Determination of Pore Radius

The volume-specific surface area of two tablets from each compaction load and size fraction was measured using a Blaine permeameter (19), and the mean value was calculated. The mean pore radius was also calculated from these measurements (21).

Determination of Tensile Strength

The radial tensile strength was calculated using the diametral compression test (24). The tests were carried out on eight tablets from each compaction load and size fraction at a speed of 4 mm/min (Holland, C50, Great Britain).

Adjustment for Surface Area and Pore Radius

The adjusted radial tensile strength of the compact was obtained by dividing the mean measured radial tensile strength by the mean volume-specific surface area of the tablets as obtained by permeametry. The distance between the particles in the compact was accounted for by multiplying the strength by the mean pore radius obtained by permeametry.

$$\partial_A = \frac{\partial_R}{S_V} * r \tag{1}$$

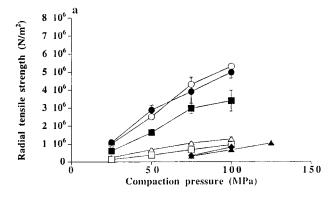
where ∂_A = adjusted radial tensile strength (N); ∂_R = radial tensile strength (N/m²); S_V = volume-specific surface area (m²/m³); r = pore radius (m).

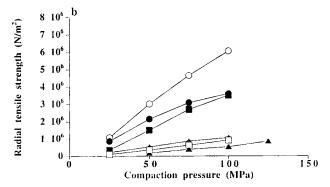
RESULTS AND DISCUSSION

Tensile Strength of Tablets

The tensile strength of the compacts was almost linearly proportional to the applied pressure (Figs. 1a–1c). Microcrystalline cellulose, potassium chloride, and sodium chloride formed the strongest compacts. Sucrose and lactose (crystalline and amorphous) gave compacts of intermediate strength compared to the other materials. Generally, sodium bicarbonate produced tablets of the lowest strength.

There was a tendency for a decrease in particle size to produce an increase in tensile strength, although the effect of particle size on tablet strength seemed to be the opposite for microcrystalline cellulose (Figs. 1a and 1b). It is possible that, although there were fewer bonds between the coarser particles of microcrystalline cellulose, these bonds were stronger, or that the increase in surface area obtained by reducing the particle size for this material was not effectively utilized for the development of bonds.





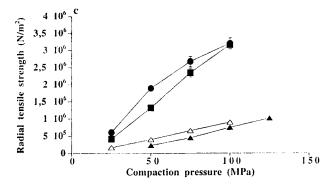


Figure 1. Radial tensile strength as a function of compaction pressure for \blacksquare , potassium chloride; \blacksquare , sodium chloride; \blacktriangle , sodium bicarbonate; \spadesuit , amorphous lactose; \bigcirc , microcrystalline cellulose; \square , crystalline lactose; and \triangle , sucrose. Confidence intervals for p=.05 are given: (a) particle size fraction 10-20 μ m (except for amorphous lactose, for which the raw material was used); (b) particle size fraction 40-60 μ m; (c) particle size fraction 90-150 μ m.

In this study, amorphous lactose produced compacts of lower tensile strength than crystalline lactose (Fig. 1a). It has been suggested by Sebhatu, Ahlneck, and Alderborn (25) that moisture may act as a plasticizer within the compacts, thus inducing an increase in particle deformability, and that this could facilitate the development of bonds over large surfaces. The absence of moisture during storage of the amorphous lactose powder and amorphous lactose compacts (0% relative humidity) and the rather low compaction pressures used with this material probably accounted for the low strength of the amorphous lactose tablets.

Surface Area of Tablets

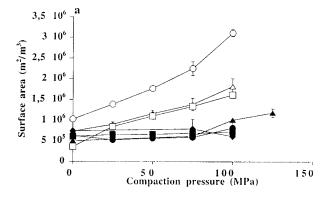
Almost linear relationships between compaction pressure and the permeametric tablet surface area were obtained for all materials and particle sizes (Figs. 2a–2c). The effect of compaction pressure on the tablet surface area was most pronounced for tablets of materials known to undergo volume reduction mainly by fragmentation (i.e., lactose and sucrose), but was also pronounced for microcrystalline cellulose. Although the compression of microcrystalline cellulose is usually considered mainly to involve plastic deformation, the agglomerate structure of the material may have contributed to the relatively large effect of compaction pressure on the tablet surface area in this case (26).

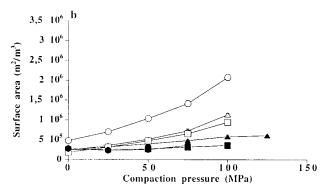
Compaction pressure appeared to have very little effect on the surface area of tablets made from sodium chloride, sodium bicarbonate, potassium chloride, and amorphous lactose. This is in agreement with earlier studies, which reported that compacts of these materials undergo volume reduction mainly by plastic deformation (25,27,28).

Relationship Between Tablet Strength and Tablet Surface Area

The effect of tablet surface area on radial tensile strength was most pronounced for the fragmenting materials, that is, the new surfaces exposed by fragmentation were used for creation of interparticulate bonds (Figs. 3a–3c). Tablet surface area seemed to be of less importance for the radial tensile strength of compacts made from more plastic materials. Microcrystalline cellulose (Figs. 3a and 3b) and sodium bicarbonate (Fig. 3c) gave intermediate relationships compared to the other materials.

These results indicate that the radial tensile strength is not related directly to the tablet surface area, as reported by Vromans et al. (13), for instance. Thus, param-





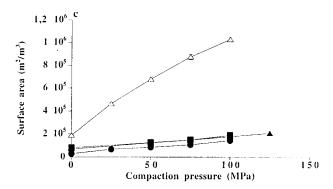
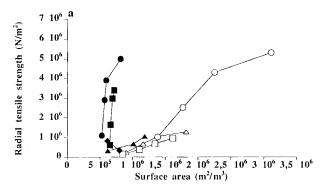


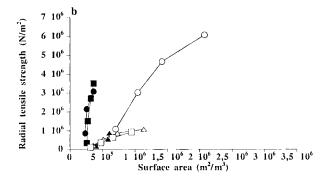
Figure 2. Tablet surface area as a function of compaction pressure. Symbols as in Fig. 1. Standard deviations for n=2 are given: (a) particle size fraction $10-20 \mu m$ (except for amorphous lactose, for which the raw material was used); (b) particle size fraction $40-60 \mu m$; (c) particle size fraction $90-150 \mu m$.

eters other than surface area will affect the strength of tablets made from this range of materials.

Interparticulate Distance Within Tablets

The relationship between the pore radius and the compaction pressure was nonlinear (Figs. 4a–4c). This rela-





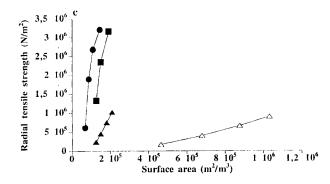
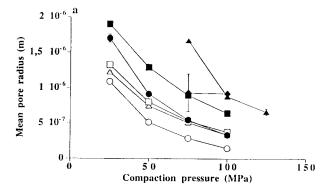
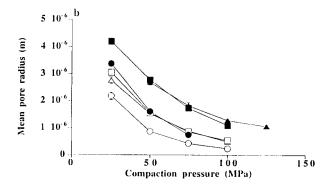


Figure 3. Radial tensile strength as a function of tablet surface area. Symbols as in Fig. 1: (a) particle size fraction $10-20 \mu m$ (except for amorphous lactose, for which the raw material was used); (b) particle size fraction $40-60 \mu m$; (c) particle size fraction $90-150 \mu m$.

tionship is supported by theoretical equations that describe the relationship between interparticulate distance and bond strength (29). A relationship between tablet porosity and pore radius might be expected, especially when the compact consists of monodispersed particles. However, it is doubtful whether the amount of air in the compact (expressed as tablet porosity) will provide any information about the distribution of that air within the





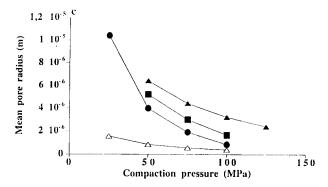


Figure 4. Mean pore radius calculated from the permeametric tablet surface area data as a function of compaction pressure. Symbols as in Fig. 1. Standard deviations for n=2 are given: (a) particle size fraction $10-20~\mu m$ (except for amorphous lactose, for which the raw material was used); (b) particle size fraction $40-60~\mu m$; (c) particle size fraction $90-150~\mu m$.

compact or the influence of the pores on tensile strength since particles within real compacts are of varying size. Therefore, it is suggested that the pore radius is more directly related than the porosity to the strength of a compact. This was also concluded by Juppo (18).

Effect of Tablet Surface Area on the Interparticulate Bond Strength

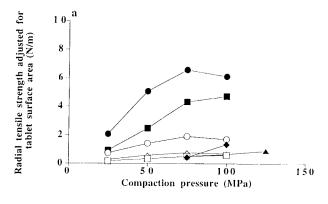
The surface area over which bonds may act is a determining factor for the strength of a tablet. When the tensile strength was divided by the corresponding tablet surface area, the relationship between surface area and strength was obvious. Potassium chloride and sodium chloride formed compacts of higher compensated tensile strength than the other materials (Figs. 5a–5c). High surface-specific tensile strength values for compacted sodium chloride were also reported by Nyström et al. (11), who suggested that these high values corresponded to strong interparticulate bonds.

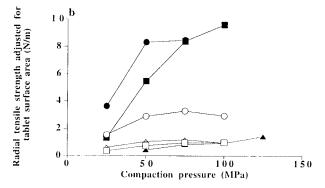
The development of solid bridges during compaction requires certain prerequisites; for instance, the material should have a simple structure and a certain level of plasticity. A high concentration of stress at contact points between particles is also thought to be important. These prerequisites are probably fulfilled by both sodium chloride and potassium chloride. The importance of solid bridges in determining the strength of tablets is believed to increase with an increase in compaction load and particle size (30).

Generally, the surface-specific tensile strength of lactose (crystalline), sucrose, and sodium bicarbonate compacts was lower than that of the other compacts (Figs. 5a–5c), indicating that the particles within the tablets are held together by weaker bonds.

Intermediate values were obtained for microcrystal-line cellulose (Figs. 5a and 5b) and also for amorphous lactose, especially at a compaction pressure of 100 MPa. It is likely that the high compactibility of microcrystalline cellulose is due to the increase in surface area during compaction, as reported earlier (9). However, mechanical interlocking may also have contributed to the tablet strength. Amorphous lactose (Fig. 5a) compacted at 100 MPa appeared to develop somewhat stronger bonds than bicarbonate, sucrose, and crystalline lactose. The capacity for amorphous lactose to develop relatively strong interparticulate bonds when compacted has been reported earlier (25), although it was suggested by these workers that the presence of water may have played a significant role in the bond formation process.

The effect of particle size on the surface-specific tensile strength was most pronounced for sodium chloride and potassium chloride; in these compacts, the strength increased with an increase in particle size. Particle size, however, had a moderate influence on the strength of compacts from all materials (Figs. 5a–5c). It has been suggested that increasing particle size will facilitate de-





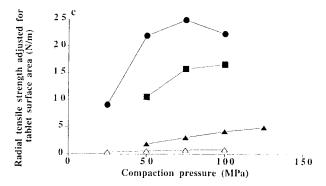


Figure 5. Radial tensile strength adjusted for tablet surface area as a function of compaction pressure. Symbols as in Fig. 1: (a) particle size fraction $10-20~\mu m$ (except for amorphous lactose, for which the raw material was used); (b) particle size fraction $40-60~\mu m$; (c) particle size fraction $90-150~\mu m$.

velopment of solid bridges. When the particle size is increased, there will be a corresponding reduction in the number of interparticulate contact points; consequently, the stress at each contact point will increase (30,31). Increasing the concentration of compaction stress on the particles may even reduce the melting point of the

material and further facilitate development of solid bridges (32).

For materials that are believed to develop solid bridges during compaction, the relationship between the total surface area of the tablet and the bonding surface area is less clear since a decrease in tensile strength has been associated with a decrease in particle size for sodium chloride (31). This effect was not, however, seen in this study (Figs. 1a–1c), probably because of the rather limited range of particle sizes studied. In addition, the effect of particle size on tensile strength is often more pronounced when higher compaction loads are applied.

When the compaction pressure was increased, the surface-specific tensile strength reached a plateau. This might indicate that the increased compaction pressure, rather than increasing the number of solid bridges, caused an increase in the bonding surface area over which weak distance forces are active.

Effect of Tablet Surface Area and Pore Radius on the Interparticulate Bond Strength

Generally, the distance between particles is related to the interparticulate attraction force in a nonlinear way. Equations describing the effect of interparticulate distance on the magnitude of interaction energy between atoms, ions, and molecules have been proposed for the various types of bond (29). However, in this study, the relationship between radial tensile strength and interparticulate distance was assumed for the sake of simplicity to be linear.

As discussed above, it seems reasonable to adjust the tensile strength of a compact according to both the interparticulate distance and the tablet surface area (Eq. 1) to obtain information about the nature and strength of interparticulate attraction forces in compacts made of different materials. In this study, however, the relationship between interparticulate distance and the strength of the materials appeared to be less important, except for microcrystalline cellulose. The small distances between microcrystalline cellulose particles appeared to encourage the development of bonds in this material, resulting in high compactibility.

The mean pore radius for sodium bicarbonate compacts was generally relatively large and similar to that for sodium chloride (Figs. 4a–4c). Adjusting the tensile strength of the sodium bicarbonate and sodium chloride compacts for the pore radius resulted in values close to those obtained for sucrose and lactose. However, a value

significantly higher than expected was obtained for the coarsest size fraction. This may have been the result of an increasing proportion of solid bridges as the particle size increased.

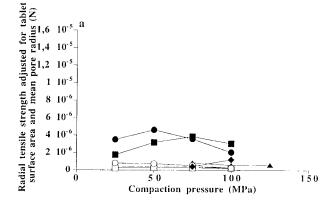
After adjustment for both interparticulate distance and surface area, the tensile strength of the rest of the materials resulted in a ranking order similar to that seen after adjustment for surface area alone (Figs. 5a–5c and 6a–6c). However, when the compaction pressure was increased, interparticulate distance appeared to have a much more profound effect on tensile strength. This effect was most pronounced for materials in which solid bridges are believed to contribute significantly to bond formation (e.g., sodium chloride and potassium chloride). For these materials, the tensile strength, after adjustment for surface area and mean pore radius, is probably not an accurate reflection of the surface area participating in interparticulate bonding.

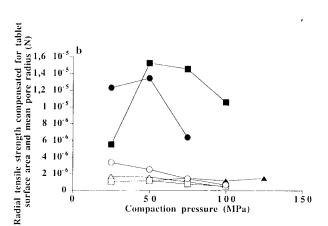
Comprehensive evaluation of the interparticulate bonding mechanisms in compacts may also require consideration of the effect of differences in surface energy among the materials since this is believed to affect the bond strength, and hence the radial tensile strength, of compacts (33). The surface energy of a material may be affected by any treatments it has undergone before use (34). However, in the present study, all size fractions of the same material were produced by the same procedure. Thus, differences in tensile strength between the particle size fractions for one material are probably not the result of differences in surface energy.

Specific Evaluation of the Effect of Particle Size and Compaction Pressure on the Radial Tensile Strength of Tablets After Adjustment for Surface Area and Mean Pore Radius

The rationale behind evaluating the effects of particle size and compaction pressure on the strength of compacts separately from the effects of surface area and interparticulate distance is that it is important to obtain a tensile strength value that reflects each distinct bonding type. Consequently, a change in both particle size and compaction pressure should not influence the adjusted strength value provided that changes in these factors do not also result in a change in bonding type.

The effect of particle size on the adjusted radial tensile strength was most pronounced for sodium chloride and potassium chloride and also for the largest particle size fraction of sodium bicarbonate (Fig. 7b).





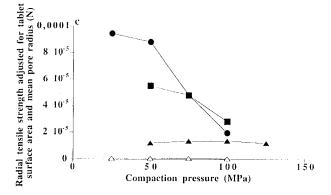


Figure 6. Radial tensile strength adjusted for tablet surface area and mean pore radius as a function of compaction pressure. Symbols as in Fig. 1: (a) particle size fraction $10-20~\mu m$ (except for amorphous lactose, for which the raw material was used); (b) particle size fraction $40-60~\mu m$; (c) particle size fraction $90-150~\mu m$.

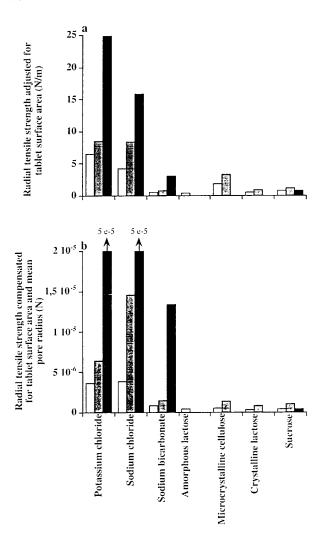


Figure 7. Effect of particle size on adjusted tensile strength of the tablets at a compaction pressure of 100 MPa, with particle size fractions \Box , $10-20~\mu m$; \blacksquare , $40-60~\mu m$; and \blacksquare , $90-150~\mu m$: (a) adjustment for tablet surface area; (b) adjustment for tablet surface area and mean pore radius.

The effect of particle size on the adjusted tensile strength of materials that are believed to bond principally by weak distance forces (crystalline lactose, sucrose, microcrystalline cellulose) appeared to be minute (Fig. 7b). Hence, particle size appears to have a greater effect on the strength of interparticulate bonds in materials with a capability to develop solid bridges during compaction. Also, the effect of compaction pressure on the adjusted strength values (Figs. 6a–6b) were more pronounced for the materials that are believed to develop solid bridges

during compaction (sodium chloride, potassium chloride, sodium bicarbonate, and amorphous lactose) than for the others.

CONCLUSIONS

The test materials in this study could be divided into two groups of opposite character regarding compaction behavior, expressed by the effects of compaction pressure on tablet strength and surface area. The first group includes sodium chloride and potassium chloride. These materials formed the strongest tablets with the least increase in surface area during compaction. This is in agreement with earlier studies (11,30) in which these materials were associated with strong bonds, such as solid bridges or ionic bonds. The second group comprised crystalline lactose and sucrose. Tablets of these materials were rather weak, but the surface area increased extensively during compaction of the powders. Consequently, these materials are believed to develop interparticulate attractions that are weak and act over greater relative distances. Some of the test materials (microcrystalline cellulose, amorphous lactose, and sodium bicarbonate) were difficult to classify. These materials may probably best be described as bonding mainly by weak attraction forces acting over relatively great distances.

Ranking of the materials according to tensile strength adjusted for specific surface area resulted in approximately the expected ranking for the type of bond, that is, lower adjusted strength values were associated with the more fragmenting materials, which bind mainly by weak attraction forces. However, this type of adjustment did not result in a single unique value for each material, independent of compaction pressure and particle size. Generally, the adjusted strength increased with compaction pressure. Thus, factors other than the surface area affect the tensile strength of compacts. The mean interparticulate distance should also be taken into account for materials bonding with weak distance forces. Adjusting the tensile strength of compacts made of these materials for interparticulate distance provided a better reflection of the dominating bond type, independent of both compaction pressure and particle size.

Conversely, adjustment of the tensile strength values for interparticulate distance and tablet surface area would not be expected to improve the description of the type of bonding for materials bonding predominantly with solid bridges. It is probably not the space between the particles that is important for these materials, but rather the actual bridges developed between the particles. In other words, the compensation for tablet surface area and mean interparticulate separation distance will probably not represent any meaningful way of expressing a value that reflects the nature of dominating bond type. Compaction pressure and particle size have a substantial effect on the adjusted tensile strength values for these materials.

Particle size also affects compacts made of sodium bicarbonate. The finer particle size fractions appeared to bind almost entirely by weak attraction forces, but bonding in the coarsest fraction seemed more to involve solid bridges.

The purpose of this study was to evaluate the dominating bonding mechanism of different materials and to estimate whether a material binds primarily with weak distance forces or by additional contribution from solid bridges. In this study, no attempts have been made to develop a complete model capable of quantifying and compensating for the behavior of different particle size fractions of the same material during compaction. A unique value of the tablet strength adjusted for surface area and mean interparticulate distance would therefore not be accomplished for each material independent of particle size. Thus, to obtain a model that also takes into account and compensates fully for the effect of different particle size fractions of the same material, the concept of adjustment for tablet surface area and mean pore radius obviously must be further refined and developed. In addition, it is important to realize that several factors other than those investigated in this study can alter tablet tensile strength and compaction behavior. The data could also be interpreted in terms of mechanical interlocking between particles. However, this mechanism does not appear to be an important factor for the results obtained. In addition, adjustment of the data to account for the surface energy of the materials may, in principle, provide a better understanding of the compaction behavior of some materials. The results in this study regarding the dominating interparticulate bonding mechanism in compacts of different materials are supported by other studies performed at our laboratory (e.g. 11, 30), but it is necessary to investigate additional materials to evaluate fully the concept of adjusting the tensile strength of tablets for specific surface area and mean interparticulate distance.

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REFERENCES

- A. McKenna and D. F. McCafferty, J. Pharm. Pharmacol., 34, 347 (1982).
- H. Vromans, A. H. de Boer, G. K. Bolhuis, C. F. Lerk, and K. D. Kussendrager, Drug Dev. Ind. Pharm., 12, 1715 (1986).
- H. Vromans, G. K. Bolhuis, C. F. Lerk, and K. D. Kussendrager, Int. J. Pharm., 39, 207 (1987).
- 4. G. Alderborn, E. Börjesson, M. Glazer, and C. Nyström, Acta Pharm. Suec., 25, 31 (1988).
- P. G. Karehill, M. Glazer, and C. Nyström, Int. J. Pharm., 64, 35 (1990).
- 6. L. W. Wong and N. Pilpel, Int. J. Pharm., 59, 145 (1990).
- 7. C. Nyström, Indian J. Pharm. Sci., 50, 15 (1988).
- 8. M. Duberg and C. Nyström, Int. J. Pharm. Technol. Prod. Mfr., 6, 17 (1985).
- C. Nyström and P. G. Karehill, Powder Technol., 47, 201 (1986).
- G. Alderborn and M. Glazer, Acta Pharm. Nord., 1, 11 (1990).
- C. Nyström, G. Alderborn, M. Duberg, and P. G. Karehill, Drug Dev. Ind. Pharm., 19, 2143 (1993).
- 12. C. Führer, Labo-Pharma Probl. Technol., 25, 759 (1977).
- H. Vromans, A. H. de Boer, G. K. Bolhuis, C. F. Lerk, K. D. Kussendrager, and H. Bosch, Pharm. Weekbl. Sci., 7, 186 (1985).
- A. H. de Boer, H. Vromans, C. F. Lerk, G. K. Bolhuis, K. D. Kussendrager, and H. Bosch, Pharm. Weekbl. Sci., 8, 145 (1986).
- H. Leuenberger, J. D. Bonny, C. F. Lerk, and H. Vromans, Int. J. Pharm., 52, 91 (1989).
- G. H. P. te Wieriket, J. Bergsma, A. W. Arends-Scholte, T. Boersma, A. C. Eissens, and C. F. Lerk, Int. J. Pharm., 134, 27 (1996).
- M. Eriksson and G. Alderborn, Pharm. Res., 12, 1031 (1995).
- 18. A. M. Juppo, Int. J. Pharm., 127, 95 (1996).
- G. Alderborn, M. Duberg, and C. Nyström, Powder Technol., 41, 49 (1985).
- 20. T. Allen, in *Particle Size Measurement*, 5th ed., Chapman and Hall, London, 1997, p. 149.
- 21. T. Allen, in *Particle Size Measurement*, 5th ed., Chapman and Hall, London, 1997. p. 1.
- C. Nyström and P. G. Karehil, in The Importance of Intermolecular Bonding Forces and the Concept of Bonding Surface Area (G. Alderborn and C. Nyström, Eds.), Pharmaceutical Powder Compaction Technology, Marcel Dekker, New York, 1996, p. 17.

- 23. M. Eriksson, C. Nyström, and G. Alderborn, Int. J. Pharm., 63, 189 (1990).
- J. T. Fell and J. M. Newton, J. Pharm. Sci., 59, 688 (1970).
- 25. T. Sebhatu, C. Ahlneck, and G. Alderborn, Int. J. Pharm., 146, 101 (1997).
- R. Ek, G. Alderborn, and C. Nyström, Int. J. Pharm., 111, 43 (1994).
- E. T. Cole, J. E. Rees, and J. A. Hersey, Pharm. Acta Helv., 50, 28 (1975).
- M. Duberg and C. Nyström, Powder Technol., 46, 67 (1986).

- 29. J. N. Israelachvili, in *Intermolecular and Surface Forces*, 2nd ed., Academic, London, 1992, p. 28.
- 30. Å. Adolfsson, H. Olsson, and C. Nyström, Eur. J. Pharm. Biopharm. 44, 243 (1997).
- 31. G. Alderborn and C. Nyström, Acta Pharm. Suec., 19, 381 (1982).
- 32. A. S. Rankell and T. Higuchi, J. Pharm. Sci., 57, 574 (1968).
- N. A. El Gindy and M. W. Samaha, Int. J. Pharm., 13, 35 (1983).
- G. Buckton, A. Choularton, A. E. Beezer, and S. M. Chatham, Int. J. Pharm., 47, 121 (1988).

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