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The identification of percolation and mechanical thresholds during the compaction of hydroxypropyl methylcellulose: comparison to thresholds determined from out-of-die indentation experiments ☆

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Abstract

Percolation theory was utilized in the interpretation of the dependence of indentation hardness and modulus on the solid fraction of hydroxypropyl methylcellulose compacts. Both out-of-die property measurements were obtained using a previously described indentation technique. These properties exhibited similar transition ranges: a bond percolation threshold at $P \sim 0.1$, a rigidity threshold at $P \sim 0.3$ and a brittle-ductile transition at $P \sim 0.6$–0.7 where P is the solid fraction normalized by the reference relative density or tapped relative density. Moreover, the sensitivity to normalized solid fraction was also similar above and below the rigidity threshold. The sensitivity above the brittle-ductile transition, however, was quite different and may be related to the different mechanical properties which are manifested in these measurements. The bond percolation threshold and the brittle-ductile transition were also observed during powder compaction in a rotary press. The appearance of these transitions in measurements of both vastly different time scales as well as mechanical displacement provides additional evidence supporting the application of percolation theory in mechanical property and compaction analysis.

Keywords: Compaction; Indentation hardness; Modulus; Percolation theory; Brittle-ductile transition; Mechanical characterization

1. Introduction

The importance of interparticulate bonding in the mechanical properties of a compact has been illustrated quite extensively in the pharmaceutical literature. Since development scientists must routinely compare the manufacturability of solid formulations, an appropriate reference state must be established to make the comparison meaningful. In a previous publication, the sensitivities of two mechanical properties, indentation hardness and modulus, to the relative density of hydroxypropyl methylcellulose compacts were described (Sinko et al., 1992). Since all powder compacts will have some porosity associated with them the apparent density of the compact was normalized by the true density. The sensitivities of these

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properties to relative density, ρ_r, were differentiated using a model which describes the impact of non-bonding contact points on tablet hardness (Leuenberger, 1982; Sinko et al., 1992).

Reports in the literature have suggested that relative density is a variable which represents an indirect measure of interparticulate bonding (Holman and Leuenberger, 1991). Using percolation theory, a more direct measure of three-dimensional particulate bonding has been recently demonstrated with the normalized solid fraction, $\rho_{r(norm)}$ (Holman, 1991; Holman and Leuenberger, 1991). The normalized solid fraction is obtained by normalizing the relative density with a reference density which is usually taken as the apparent density of the powder before the bonds begin to form between particles (Holman and Leuenberger, 1988). The tap density has been used in the past as the reference density (Holman and Leuenberger, 1988).

In this report the dependence of indentation hardness and modulus of hydroxypropyl methylcellulose compacts on the degree of three-dimensional bonding is further characterized. Using percolation theory, the dependence of these two properties on normalized solid fraction is explored through both the identification of percolation thresholds and the determination of the slopes between thresholds. Our study differs from previous reports that have described the application of this data analysis technique to the indentation hardness and complex Young's modulus of powder compacts; a much wider range of solid fraction is evaluated in the present study and the modulus described in this report is a shear modulus determined from the resistance of the compact to indentation by a spherical indenter. In addition, we compare the transitions identified in these property measurements to percolation transitions observed during an actual compaction event on a rotary press.

2. Materials and methods

2.1. Modulus and hardness determination

All of the studies described in this report were performed on hydroxypropyl methylcellulose, HPMC 2208 USP 4000 cps (Methocel, Dow Chemical, Midland, MI) and used as received from the supplier. The experimental techniques for both the modulus and hardness determination have been previously described (Sinko et al., 1992). The modulus is an apparent modulus based upon the resistance to the transit of the spherical indenter into the surface of the sample. The rate of indentation was held constant at 0.3 mm/s. Indentation hardness was calculated using the mean load under the indenter after 1200 s and the recovered surface area of the dent after the removal of the indenter (Sinko et al., 1992). The range of solid fractions and normalized solid fractions studied using this technique was $\rho_r = 0.43$–0.925 and $\rho_{r(norm)} = 0.07$–0.88, respectively. These were the practical limits which were experimentally obtainable.

2.2. Compaction analysis

The compaction analysis was performed on a Korsch Pharmapress PH106 (Korsch Tableting, Somerville, NJ). In order to establish a punch force-solid fraction relationship for HPMC during a tableting run, the punch force-punch displacement relationship had to be elucidated. Since the PH106 rotary press is only instrumented for upper and lower punch force measurement, the displacement had to be initially calculated using the analytical equations which rely on tablet press and punch geometry proposed by Rippie and Danielson (1981). Moreover, recognizing the fact that a tablet press will deflect under loads typically experienced during compression (5–50 kN), an estimate of this deflection had to be incorporated into the theoretical displacement in order to obtain a more realistic punch displacement (Oates and Mitchell, 1989).

The deflection of the press was estimated using the published values for work of compaction by Oates and Mitchell (1989) as a reference. Compression studies were performed using dicalcium phosphate dihydrate (Emcompress®, Edward Mendell Co, Carmel, NY) with the same size tooling at the identical fill weights and maximum upper punch pressures as reported by Oates and Mitchell (1989). The values of work of compaction using the analytical displacement curves, denoted as 'uncorrected work' in Table 1, are substantially higher than the reported values. The reason is that the theoretical punch displacement used in the calculation of work is greater than the actual punch displacement because the press reacts to the applied load in the opposite direction of the punch's movement, i.e., the press retracts slightly, resulting in a reduced path of movement.

In order to correct for this deflection a linear, elastic relationship between punch force and deflection was assumed (Oates and Mitchell, 1989; Dwivedi et al., 1991; Altaf et al., 1992). The deflection of the press was assumed to be the product of the punch force and a machine constant. Using the published values of work as the reference values of work, the machine constant for the PH106 press was determined to be 5.95×10^{-6} cm N^{-1} (Oates and Mitchell, 1989). This machine constant provided values of work which were very close to the literature values, denoted as shown in Table 1 (Oates and Mitchell, 1989). As a check on whether this correction could be applied to other materials, Avicel® PH102 (FMC Corp., Philadelphia, PA) and spray-dried lactose (Foremost Whey Products, Baraboo, WI) were compressed under the same conditions as reported by Oates and Mitchell (1989). Again, the uncorrected values of work result in substantially higher values, yet when the machine constant is applied to correct the punch displacement, the corrected values are reasonably close to the reported values (see Table 1). It should also be noted that the magnitude of the estimated machine constant for the Korsch Press is of the same order as the constant measured by Dwivedi et al. (1991) for their 16 station Manesty Press (2.3×10^{-6} cm N^{-1}).

2.3. Mechanical transition analysis of HPMC

The compression event for HPMC was measured on the PH106 rotary press using flat-faced, $\frac{1}{2}$ inch IPT tooling in one station while the other five were blocked off. The press speed was set to 25 rpm, which corresponds to a compression time of 232 ms and the fill weight was kept constant at 465 ± 6 mg. Punch force-time profiles were obtained using the press instrumentation and stored on a personal computer. The time points were converted to punch displacement points using the deflection-modified theoretical equation and the previously described machine constant (Rippie and Danielson, 1981). The force-displacement profiles were read into a Lotus 1-2-3 for Windows (Release 1, Lotus Development Corp., Cambridge, MA) work sheet for further analysis. The tapped density (2000 taps) was determined using a Vanderkamp Tap Density Tester (VanKel Inc., Edison, NJ) and the true density was deter-

Table 1
Work of compaction corrected for machine deflection

Material	Maximum upper punch force (kN)	Tablet weight (mg)	Uncorrected work ($N m g^{-1}$)	Displacement corrected work ($N m g^{-1}$)	Reported work [a] ($N m g^{-1}$)
Emcompress®	8.9	752	9.8	6.2	6.1
	17.7	862	20.4	9.6	9.6
	26.6	944	35.7	13.6	13.1
Avicel® PH102	8.9	542	32.6	20.0	22.7
	17.7	539	64.8	32.4	33.2
	26.6	535	281.3	41.8	39.0
Spray-dried lactose	8.9	523	13.6	9.0	8.7
	17.7	583	33.4	14.5	15.7
	26.6	674	55.4	21.4	22.0

[a] From Oates and Mitchell (1989).

mined using helium pycnometry (Quantasorb, Quantachrome Corp., Syosset, NY). The tapped density was determined to be 0.51 g/cm^3 and the true density to be 1.38 g/cm^3.

3. Results and discussion

3.1. Site-bond percolation

In a previous publication, an attempt to differentiate the dependence of indentation hardness and modulus on solid fraction was made (Sinko et al., 1992). A parameter from a relationship which characterized the impact of non-bonding contact points on tablet hardness was used as the primary variable for differentiation (Leuenberger, 1982). Since then, new material property-porosity relationships based on percolation theory have been established (Holman and Leuenberger, 1988). Holman and Leuenberger (1988) have characterized the mechanical property-porosity relationship as a site-bond percolation problem. The two components, HPMC and pores, can be distinguished as independent structures. These structures exist as either finite or infinite clusters. If the structure percolates through the entire system it is termed an infinite cluster, otherwise it is called a finite cluster. At first, no particle-particle bonds are assumed to exist in a loose powder systems. The pore structure percolates through the entire bed and is viewed as an infinite cluster. The percolation probability, P, defined as the fraction of bonds which have been formed, is zero at this point. As the system is compacted, the particles will rearrange to a critical point, called the bond percolation threshold, P_{Cs}, where the compact is considered to be first formed. At $P = P_{Cs}$ the compact is believed to contain a continuous network of particles which can resist the applied displacement, a resistance which is recorded as pressure. It is at this transition that the particle network is assumed to have converted from a finite cluster to an infinite cluster.

As the pressure increases, another threshold, P_{Ca}, the site percolation threshold, is observed. At this threshold the pore network becomes disconnected and the pore cluster is considered to convert from an infinite cluster to a finite cluster. In the above description of percolation theory, the percolation probability, P, is equated to the normalized relative density:

$$P \approx \rho_{r(norm)} = \frac{\rho_{r(com)} - \rho_{r(tap)}}{1 - \rho_{r(tap)}} \tag{1}$$

where $\rho_{r(norm)}$ is the normalized relative density, $\rho_{r(tap)}$ denotes the tapped relative density (reference relative density) and $\rho_{r(com)}$ is the relative density of compact.

3.2. Application of site-bond percolation analysis to the porosity dependence of mechanical properties

Holman and Leuenberger (1988, 1990, 1991) have applied this theory to a number of experimental observations such as the dependence of reduced modulus and indentation hardness on the solid fraction of a compact, the dependence of percolation thresholds on binary composition, the significance of the relationship between normalized solid fraction and indentation hardness between percolation thresholds and both the identification of thresholds and the delineation of the normalized solid fraction-compression stress relationship between thresholds during a compaction event (Holman, 1991). In these studies, the authors call the percolation thresholds 'effective percolation thresholds' because percolation theory should only be applied to infinitely large systems, a description which is not applicable to tablet compacts. In addition to the identification of percolation transitions, mechanical transitions, such as the so-called brittle-ductile transition and rigidity threshold, have also been observed (Holman and Leuenberger, 1988; Holman, 1991).

A plot of both indentation hardness and modulus obtained from indentation experiments vs normalized solid fraction, P, for HPMC is shown in Fig. 1. Both properties are displayed in a semilogarithmic fashion. The lines drawn through the data represent the best fit of the line to the data. The criterion for the best fit was based on the correlation coefficient, r^2. The transitions in the data were identified at the intersection for both lines. The slope and transition estimates are reported in Table 2A and B. Both the indentation hardness and modulus data exhibit two transitions, one at $P \sim 0.3$ and the second at $P \sim 0.6$–0.7. The first transition at $P \sim 0.3$ is higher than the bond percolation threshold, which for a three-dimensional compaction description can range from 0.119 for a face-centered cubic structure to 0.249 for a simple cubic structure (Leuenberger and Leu, 1992). There is, however, a slight overlap of the lower 95% confidence interval for the indentation hardness data and the bond percolation threshold for a simple cubic structure. This is due to the lower statistical power of the regression. Interestingly, the transition range at $P \sim 0.3$ is lower than the first transition range reported for both indentation hardness and reduced modulus (Holman and Leuenberger, 1988).

Table 2
(A) Percolation thresholds[a] and (B) slopes[b] from Fig. 1

(A) Property	Rigidity threshold	Brittle-ductile transition
Modulus	0.32 (0.28–0.49)	0.63 (0.61–0.67)
Indentation hardness	0.30 (0.24–0.51)	0.57 (0.55–0.63)

(B) Property	Slope		
	$P < P_R$	$P_R < P < P_T$	$P > P_T$
Modulus	9.11 (8.54–9.68)	4.82 (4.72–4.92)	1.95 (1.88–2.02)
Indentation hardness	11.49 (10.21–12.77)	5.20 (5.03–5.37)	3.62 (3.59–3.65)

[a] Ranges in parentheses represent intersection of upper and lower 95% confidence intervals.

[b] The first slope is calculated at $P < P_R$, the second slope at $P_R < P < P_T$ and the third slope at $P > P_T$. The numbers in parentheses represent the upper and lower 95% confidence intervals.

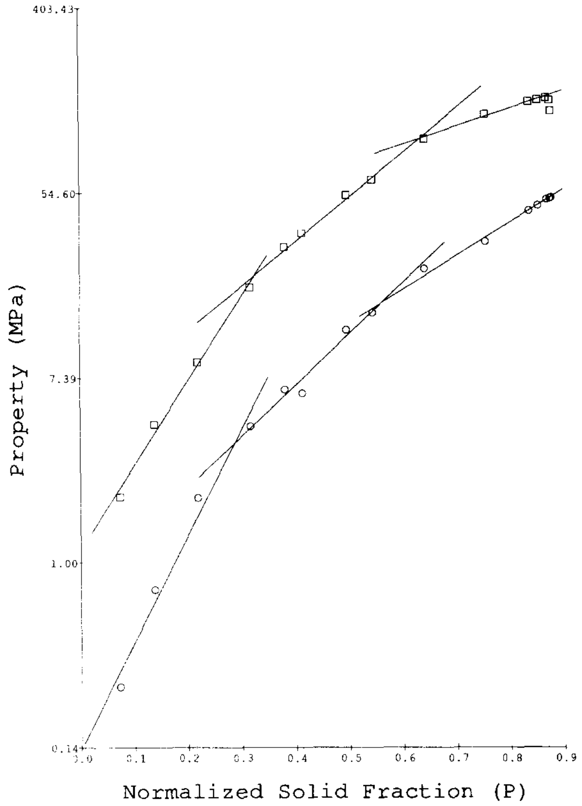

Fig. 1. Semilogarithmic representation of modulus and hardness of hydroxypropyl methylcellulose vs normalized solid fraction. Intersection of lines represent approximate regions for the rigidity threshold and the brittle-ductile transition. (□) Modulus; (○) hardness.

The most likely reason for the appearance of a transition in this range of normalized solid fraction is the presence of a 'rigidity threshold', P_R, a mechanical percolation threshold first described by Holman (1991) for compaction data. The rigidity threshold is a transition which is associated with the conversion of a compact from a flexible to a rigid state. Below P_R the compact is considered to be an infinite cluster which resists deformation through singly connected bonds. Once the compact is above P_R the system, still an infinite cluster, crosses over to a rigid body, where bonds are multiply connected (Holman, 1991). This is not a percolation threshold since the system is an infinite cluster throughout the transition. Both properties measured for HPMC appear to exhibit this transition. Although these properties represent mechanically different qualities, their dependence on the rigidity threshold is similar. One way of confirming this is to measure the properties independently using different methods. However, there is evidence which suggests that the modulus determined during the indentation experiment is not a true shear modulus but rather a post-yield modulus and that an experiment which measures this quantity will need to incorporate the yield phenomenon (Sinko et al., 1992). This would complicate the subsequent interpretation of that data since yielding itself, estimated by indentation hardness, appears to be influenced by the rigidity threshold.

The second transition corresponds to the range which has been previously associated with the brittle-ductile transition, P_T (Holman and Leuenberger, 1988; Holman, 1991). Mechanical response below P_T is associated with particle fragmentation while response above this threshold is associated with plastic deformation (Holman, 1991). This threshold has been observed for both indentation hardness and reduced elastic modulus in moderately and highly brittle materials (Holman and Leuenberger, 1988). One manifestation of ductile response is that at high solid fractions, the modulus actually drops (at $P > 0.87$). This softening phenomenon could be similar to the post-yield strain softening phenomenon observed with many polymer systems. Finally, the site percolation threshold, P_{Ca}, does not appear in either property although our data at and above the expected threshold range for three-dimensional structures ($P = 0.698$–0.802) are somewhat limited (Leuenberger and Leu, 1992).

Both properties' dependencies on normalized solid fraction are similar above and below the rigidity threshold but different above the brittle-ductile transition (denoted as 'slope' in Table 2B). The difference is not surprising considering that, in the calculation for indentation hardness, a recovered dent depth and a relaxed force (after 1200 s relaxation) are used to calculate this quantity. Consequently, both viscoelastic relaxation and an elastic recovery component factor into this parameter, whereas the force-time profiles during indentation are only used in the calculation of modulus (Sinko et al., 1992). The absence of a rigidity threshold in previously published indentation data is most likely due to the range of normalized solid fraction, generally no lower than $P = 0.45$, in which indentation hardness and reduced modulus were studied (Holman and Leuenberger, 1988). In our experiments, we were able to obtain compacts at normalized solid fractions as low as $P = 0.07$.

Although the bond percolation threshold, P_{Cs}, cannot be identified from Fig. 1, an estimate of this threshold can be obtained by invoking the fundamental equation of percolation theory (Leuenberger and Leu, 1992):

$$X = S\,|\,p - p_c\,|^q \tag{2}$$

where X is the property, S denotes the scaling factor and q is the critical exponent. The equation is only valid in the vicinity of a percolation transition but has been applied to mechanical property data from tablet compacts over a wider range of relative density because the percolation transitions in these systems are not sharp. Assuming the critical exponent, q, is equal to unity (the Bethe lattice approximation), the bond percolation threshold can be determined from the following equations (Leuenberger and Leu, 1992):

$$P = S(\rho_r - \rho_o) \tag{3}$$

and

$$S = \frac{P_{\max}}{(1 - \rho_o)} \tag{4}$$

where ρ_o is the bond percolation threshold and P represents the indentation hardness obtained at a known solid fraction, ρ_r.

The hardness and modulus data for HPMC are plotted vs solid fraction in Fig. 2. The intercept on the abscissa is the estimate of the bond percolation threshold in units of relative density. The lines drawn represent the results of a linear regression which provided the best r^2 using a minimum of four data points. For the hardness data, $\rho_o = 0.439 \pm 0.022$ and for the modulus data, $\rho_o = 0.435 \pm 0.036$. This corresponds, in units of normalized solid fraction, to $P = 0.109$ and $P = 0.103$, for hardness and modulus, respectively. These values are close to the bond percolation threshold for a face centered cubic structure (Leuenberger and Leu, 1992). The similarity of the transition ranges for both properties is a result of the fact that both properties are obtained from indentation measurements.

3.3. Percolation transitions during compaction

A semilogarithmic plot of compression stress vs normalized solid fraction, an 'in-die' estimate, is shown in Fig. 3. The solid fraction was normalized with the reference solid fraction at which the punch force began to increase substantially above the noise level of the transducers. Holman (1993) has shown that this reference density is a better estimate for the relative density at which interparticulate bond formation begins. Interestingly, this value, $\rho_{ri} = 0.366$, was very close to the experimentally determined normalized relative tapped density, 0.37. Two transitions are evident from this compression profile. The first occurs at $P \sim 0.1$–0.2 and, from the range associated with percolation transitions for three-dimensional structures, appears to be the bond percolation transition, P_{Cs}. This range is in agreement with the bond percolation thresholds calculated from the hardness and modulus data in Fig. 2. The second transition is observed at $P \sim 0.6$–0.7, similar to the range identified as the brittle-ductile transition (see Table 3A and B). As was the case with the out-of-die measurements, no site percolation threshold is visible from this data.

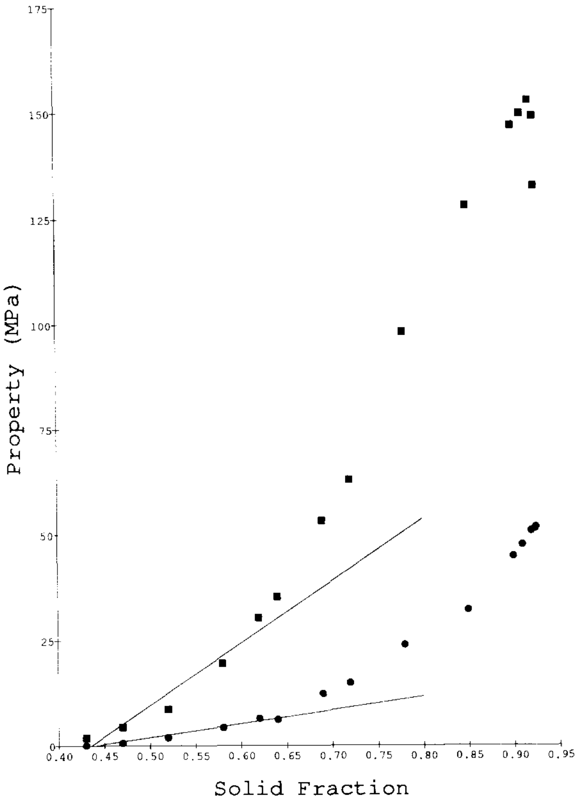

Fig. 2. Dependence of modulus and hardness on solid fraction. Intercept of lines extrapolated to the abscissa represent the bond percolation threshold. (■) Modulus; (●) hardness.

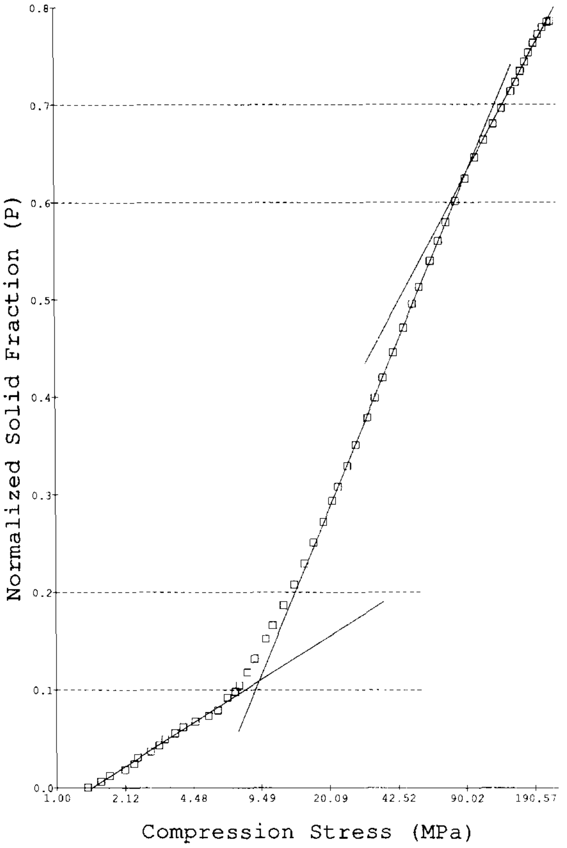

Fig. 3. Semilogarithmic representation of normalized solid fraction vs compression stress during the compaction of hydroxypropyl methylcellulose on a Korsch PH106 rotary press. The intersection of the lines represents the bond percolation threshold at $P \sim 0.1$–0.2 and the brittle-ductile transition at $P \sim 0.6$–0.7.

The absence of a rigidity threshold in this dynamic data is most likely due to the combination of mechanical events which occur during compaction: elastic, viscoelastic, plastic and fracture response. Powder systems which exhibited brittle-ductile transitions during compaction did not have rigidity thresholds and as such were viewed as being rigid above the bond percolation threshold (Holman, 1991). The powder systems with both bond percolation thresholds and brit-

Table 3
(A) Percolation thresholds[a] and (B) slopes[b] from Fig. 3

(A) Property	Bond percolation threshold	Brittle-ductile transition
Compression stress	0.108 (0.103–0.111)	0.625 (0.620–0.627)

(B) Property	Slope		
	$P < P_{Cs}$	$P_{Cs} < P < P_T$	$P > P_T$
Compression stress	0.057 (0.55–0.60)	0.228 (0.227–0.229)	0.177 (0.176–0.179)

[a] Ranges in parentheses represent intersection of upper and lower 95% confidence intervals.

[b] The first slope is calculated at $P < P_{Cs}$, the second slope at $P_{Cs} < P < P_T$ and the third slope at $P > P_T$. The numbers in parentheses represent the upper and lower 95% confidence intervals.

tle-ductile transitions were described as 'hard and moderately brittle' materials which are rigid above P_{Ca}. The lack of the appearance of a rigidity threshold in the compaction data could also be attributed to the differences in the time scale of observation. In the case of the compaction data shown in Fig. 3, the time frame corresponds to 100 ms, while the data shown in Fig. 1 are obtained in a 2.33 s time frame (Sinko et al., 1992). Moreover, materials which have been characterized as brittle do not exhibit site percolation thresholds (Holman, 1991). This may explain the absence of the site percolation threshold from the curves presented in Fig. 1 and 3. The similarity in the range of the bond percolation threshold and the brittle-ductile transition between the two experimental observations is encouraging and supports Holman's (1991) assertion that mechanical properties of a compact are dependent on the 'percolation state' and the degree of bonding, a quantity reflected through the normalized solid fraction, and not on compression stress.

It is evident that from both the compaction and out-of-die property measurements, HPMC has some brittle characteristics. The similarity in the appearance of the brittle-ductile transition for both measurements point to the dependence of this transition on the resistance of HPMC to deformation. All three material properties evaluated in this report (hardness, modulus and response to upper punch compression stress) are manifestations of mechanical resistance due to displacement, whether by a steel sphere or a flat faced punch.

In this paper we have applied some of the basic concepts of percolation theory in the interpretation of independently measured out-of-die mechanical property data for hydroxypropyl methylcellulose. This analysis was also applied to dynamic compaction data obtained on a Korsch PH106 rotary press. In accordance with percolation theory, the degree of particle bonding in a powder compact is described in terms of the normalized solid fraction. Two characteristic transitions in the modulus and the indentation hardness normalized solid fraction data have been correlated to two transitions which were observed in dynamic in-die compaction data obtained from an instrumented rotary tablet press. These transitions have been identified as the bond percolation threshold and the brittle-ductile transition. The correspondence in transitions between the out-of-die and in-die measurements provide additional evidence supporting the use of percolation theory in the interpretation of the effect the degree of bonding has on the mechanical response of a powder compact.

This work illustrates the importance of understanding the bonding state when mechanically characterizing a powder system. Since different materials require different levels of compression pressure in order to obtain the same solid fraction, the mechanical characterization of the material should be made with respect to the 'percolation state' or degree of bonding. This will provide the scientist greater power to interpret dynamic compaction events from a tablet press with data obtained from stand-alone out-of-die measurements such as indentation testing.

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References

Altaf, S.A., Xu, P. and Hoag, S.W., Linear elastic analysis of tablet machine deformation. *Pharm. Res.*, 9 (1992) S117.

Dwivedi, S.K., Oates, R.J. and Mitchell, A.G., Peak offset times as an indication of stress relaxation during tableting on a rotary tablet press. *J. Pharm. Pharmacol.*, 43 (1991) 673–678.

Holman, L.E., The compaction behavior of particulate materials. An elucidation based on percolation theory. *Powder Technol.*, 66 (1991) 265–280.

Holman, L.E., The normalization of the solid fraction of particulate compacts. *Int. J. Pharm.*, 89 (1993) R17–R21.

Holman, L.E. and Leuenberger, H., The effect of varying the composition of binary powder mixtures and compacts on their properties: A percolation phenomenon. *Powder Technol.*, 60 (1990) 249–258.

Holman, L.E. and Leuenberger, H., The relationship between solid fraction and mechanical properties of compacts – the percolation theory model approach. *Int. J. Pharm.*, 46 (1988) 35–44.

Holman, L.E. and Leuenberger, H., The significance of slopes of the semilogarithmic relationship between hardness and solid fraction of porous compacts. *Powder Technol.*, 64 (1991) 233–247.

Leuenberger, H., The compressibility and compactability of powder systems. *Int. J. Pharm.*, 12 (1982) 41–55.

Leuenberger, H. and Leu, R., Formation of a tablet: A site and bond percolation problem. *J. Pharm. Sci.*, 81 (1992) 976–982.

Oates, R.J. and Mitchell, A.G., Calculation of punch displacement and work of powder compaction on a rotary tablet press. *J. Pharm. Pharmacol.*, 41 (1989) 517–523.

Rippie, E.G. and Danielson, D.W., Viscoelastic stress/strain behavior of pharmaceutical tablets: analysis during unloading and postcompression periods. *J. Pharm. Sci.*, 70 (1981) 476–482.

Sinko, C.M., Smith, D.P. and Nixon, P.R., Mechanical characterization of hydroxypropyl methylcellulose: modulus determination from indentation loading profiles. *Int. J. Pharm.*, 81 (1992) 243–252.