ELSEVIER

European Journal of Pharmaceutics and Biopharmaceutics 44 (1997) 273–282

European
Journal of
Pharmaceutics and
Biopharmaceutics

Paper

Indices of tableting performance and application of percolation theory to powder compaction

C. Imbert, P. Tchoreloff, B. Leclerc, G. Couarraze *

Laboratoire de Physique Pharmaceutique, URA CNRS 1218, Université Paris XI, Châtenay-Malabry, France

Received 2 October 1996; accepted 17 April 1997

Abstract

The mechanical properties, tensile strength and identation hardness of compacts of different excipients with brittle or plastic characteristics are discussed, using two approaches on powder compaction. The first one, Leuenberger's exponential model extended later by percolation theory, is used to determine the compactibility, the compressibility and the characteristic relative density (ρ_r^*) of the compacts. Characteristic relative density ρ_r^* is the point when the first stable pharmaceutical compact is obtained. The second approach characterises the compact properties by using dimensionless indices, Hiestand's indices, which give insight about relative tableting performance of materials. This study showed that the two approaches are complementary. In fact, when the relative density of excipients with plastic behaviour is increased, the bonding index increases. This evolution may be interpreted by the percolation theory for the region of dense compacts by the assumption of a difference in the percolation thresholds ρ_P^* and ρ_σ^* obserbed from indentation hardness and tensile strength measurements respectively. The appearance of these transitions by 'out-of-die' measurements of the compaction properties of the studied excipients is similar to that observed earlier by the application of percolation theory to 'in process' compaction measurements. © 1997 Elsevier Science B.V.

Keywords: Powder compaction; Percolation threshold; Brittle and plastic behaviour; Tensile strength; Indentation hardness; Bonding index; Brittle fracture index

---

1. Introduction

Powder compaction complexity is linked to a great number of parameters which affect this process. Some of these parameters play a role in the compressive stress transmission through the powder bed, for example: stress intensity, speed and application time of the stress, die dimensions, and the mechanical properties of the powder. These, and other parameters, also influence the mechanical properties of the compacts obtained: size distribution, shape, crystalline state, interfacial properties, and the viscoelastic properties of powders.

Despite numerous studies which have been published about compaction of powders in different scientific fields such as metallurgy, ceramics and pharmaceutical technology [1–4], the development of a unified theory which makes it possible to predict the quality of pharmaceutical compacts based on knowledge of the particulate constituents and the general 'in process' conditions, is still a scientific and industrial challenge.

However, the compaction of pharmaceutical powders involves different mechanisms which occur in stages. It has been established that the sequence of events is highly dependent on the nature of the material considered, especially in terms of brittleness or ductility [3–6].

---

* Corresponding author. Laboratoire de Physique Pharmaceutique, URA CNRS 1218, Tour B, 1 étage, Université Paris XI, Faculté de Pharmacie, 5 rue J.B. Clément, 92296 Châtenay-Malabry Cedex, France. Tel.: +33 1 46835616; fax: +33 1 46835312; e-mail: couarraz.@phypha.u-psud.fr

PII S0939-6411(97)00134-3

Heckel treatment of compaction data [7,8] considers the compaction process to be analogous to a first order chemical reaction, the pores acting as a reactant. The Heckel equation in its final form is:

$$\ln \frac{1}{1-\rho_r} = k\sigma_c + A \tag{1}$$

where σ_c is the applied mean pressure, ρ_r is the mean relative density and A, k are two constants. k is classically related by its reciprocal value ($1/k = P_y$) to the mean yield pressure or plastic yield pressure of the material [9]. Then, a low value of P_y is characteristic of a ductile material which is deformed plastically during compression whereas high P_y values are obtained with brittle materials. Depending on the measurement of the compact relative density (in die and during compression or out-of-die after elastic recovery), the P_y values may fluctuate widely [10]. Moreover, the experimental conditions may also greatly influence P_y values (e.g. use of lubricants, compression speed) [11,12].

Hiestand also proposed a theory that describes the processes involved in tablet bonding by applying a theory of adhesion to the interpretation of the strength of compacts [3]. In this approach, the number of active contacts is a function of the solid fraction. However, the mechanism which acts at the interparticle contacts also may change with solid fraction. Specifically, some materials compacted at low compression forces may undergo isthmus formation during decompression (ductile mechanism) and then change (ductile to brittle transition) to the brittle mechanism (during decompression) at high compression forces. Indeed, it is useful to quantify the forces that come into play, to understand their origin and to describe properties in fundamental terms.

However, reducing the values of the tensile strength, shear strength, elastic modulus or hardness of compacts to a dimensionless form provides more insight and enables comparisons to be made of the properties of different materials. In this sense, Hiestand has defined three dimensionless parameters that characterise the relative tableting performance of materials. These parameters are based on dynamic indentation hardness (P) and tensile strength (σ_T) measurements [13].

The first parameter is the strain index (SI) obtained from the dynamic indentation hardness experiments. It may be interpreted as indicating the relative strain during the elastic recovery that follows plastic deformation or as the relative strain energy that could develop at a 'crack' during elastic recovery after plastic deformation has occurred:

$$\mathrm{SI} = \frac{P}{E'} \tag{2}$$

where E' is the reduced elastic modulus ($E/1 - \nu^2$ where ν is the Poisson's ratio).

The second parameter is the bonding index (BI):

$$\mathrm{BI} = \frac{\sigma_T}{P} \tag{3}$$

As it compares indentation hardness to tensile strength, BI is thought to indicate the relative survival, during decompression, of the areas of true contact that were established at maximum compression. The maximum ratio for σ_T/P should occur when the particles yield plastically at areas of true contact, during decompression. Then, the bonding forces at the particle–particle interfaces must be strong enough to induce plastic deformation (isthmus formation) instead of giving rise to the peeling apart of the interface. In the latter case, BI will have a low value. It is important to note that the maximum value of BI in Hiestand's works is 0.04 [14]. However, this value is based on experimental results, i.e. only valid for the test systems described in these studies.

In the case of determination of the P value by the quasi static indentation method, a 'best case' bonding index ($\mathrm{BI_b}$) was defined, which is greater than the 'worst case' bonding index ($\mathrm{BI_w}$), determined under Hiestand's conditions [15].

The last parameter is the brittle fracture index (BFI), obtained by comparing the tensile strength of tablets with (σ_{Th}) and without a hole (σ_T) in their centre:

$$\mathrm{BFI} = \frac{1}{2}\left[\frac{\sigma_T}{\sigma_{Th}} - 1\right] \tag{4}$$

The hole in the tablets corresponds to the insertion of a 'programmed' crack into the material. Under the conditions of the strength test, elasticity theory predicts that the stress concentration factor should be about 3 for a hole in an isotropic homogeneous solid. For most real compacts, with materials which are not completely brittle, the experimental stress concentration at failure is well below 3. Although the BFI parameter variations are in the range [0, 1], empirically, it has been observed that fracture problems are always severe when $\mathrm{BFI} \geq 0.8$ (brittle mechanism) and become negligible if BFI tends towards very low value (< 0.2).

Hiestand has pointed out that these indices are useful formulation guidelines, but, however, a single index number alone is insufficient for an understanding of tableting performance [15].

Leuenberger has developed another approach to powder compaction [16]. The compactibility is evaluated on the basis of mechanical properties of tablets compressed at different pressure levels, i.e. tablets of a wide range of porosity. Two mechanical tests, the indentation hardness (P) (Brinell hardness) and the tensile strength (σ_T) are performed.

The following equations give satisfactory results:

$$P = P_m(1 - e^{(-\gamma_p \sigma_c \rho_r)}) \tag{5}$$

Table 1
Characteristics of the powder systems

Substance	Powder true density ρ_v (g/cm)	Mean particle size (μm)	Percent Mg stearate[a] (w/w)	Mixtures calculated true density ρ_t (g/cm)
Lactose	1.525	134	1	1.518
Microcrystalline cellulose	1.530	50	1	1.522
Dicalcium phosphate	2.359	180	1.5	2.315
PVP	1.174	90	2	1.171

[a] $\rho_v = 1.048$ g/cm.

$$\sigma_T = \sigma_{Tm}(1 - e^{(-\gamma_\sigma \sigma_c \rho_r)}) \qquad (6)$$

P_m and σ_{Tm} are the maximum deformation hardness and tensile strength, respectively, when $\sigma_c \rightarrow \infty$ (i.e. $\rho_r \rightarrow 1$). γ_p and γ_s are the compression susceptibilities, related to compressibility. P_m and σ_{Tm} are considered to describe the compactibility of a powder bed.

These equations can be combined to obtain the bonding index, and a comparison with the Hiestand data has already been published [17]. In a recent review Doelker has reported extensive data with the extrapolated bonding index for various excipients [18].

Subsequently, Leuenberger et al. [6] have applied the percolation theory to the formation of a tablet compression–compaction process. In a process where a percolation mechanism occurs for a threshold value p_c of a variable p, some properties (X) of the system follow a power law such as:

$$X = S(p - p_c)^q \qquad (7)$$

where S is the scaling factor and q the critical exponent.

In the case of the indentation hardness (P) and tensile strength (σ_T), Leuenberger has shown that the exponent q is equal to unity, and corresponds to a percolation in a Bethe lattice. Two critical relative densities, a bond percolation threshold ρ_0 (value close to the relative tap density, corresponding to transition powder bed → loose compact) and a site percolation threshold ρ_r^* (corresponding to the transition loose compact → dense compact) can be determined. The corresponding equations for dense compacts are:

$$P = \frac{P_{max}}{1 - \rho_r^*}(\rho_r - \rho_r^*) \qquad (8)$$

$$\sigma_T = \frac{\sigma_{Tmax}}{1 - \rho_r^*}(\rho_r - \rho_r^*) \qquad (9)$$

The linear portion of the experimental Heckel plot at intermediate and higher pressures corresponds to the formation of dense compacts. Thus, the subsequent intercept corresponds to ρ_r^* which can be defined as the relative density at which the first stable compact, is obtained by the creation of a bonds network between the particles. This percolation threshold must be determined experimentally from both the Heckel plot and the deformation hardness or tensile strength versus relative density plots [6]. It was pointed out by Leuenberger that because of the complex phenomena that are involved in the formation of a tablet, no sharp percolation thresholds could be expected [6].

In this work, mechanical properties of compacts formed at intermediate and higher pressures (linear part of the Heckel plot) were investigated in the light of both theories. On one hand, Leuenberger's models applied to the formation of tablets were considered. On the other hand, we developed a methodology to determine Hiestand's indices BI and BFI.

A comparison of the results obtained by the two different approaches makes it possible to have a better understanding of the stages of events which occur during the compaction of granular materials.

2. Material and methods

2.1. Materials

- α-monohydrous lactose (lactose EFK®, Rhône Poulenc, GW 920414) and dicalcium phosphate dihydrate (Di-Tab®, Rhône Poulenc, 10700) were chosen as brittle substances;
- microcrystalline cellulose (Avicel PH-101®, FMC, 6044) and polyvinyl pyrrolidonne (PVP) (Kollidon 35–50®, BASF, 93068) which are both highly ductile and viscoelastic materials were also investigated because of their typical contrasting mechanical properties in the field of pharmaceutical materials.

Some characteristics of these substances are summarised in Table 1. Magnesium stearate was used as an internal lubricant.

2.2. Powder compaction

Prior to the experiment, the powders were stored 24 h in an environment with a relative humidity of 40%. Then, the powders were deagglomerated by sieving and mixed with magnesium stearate in a Turbula mixer (Type T2C, Willy A Bachofen, Basel, Switzerland) in two steps. All the magnesium stearate was mixed with one third of the powder for 1 min, and then the remainder was added and mixed for 2 min. The proportions of lubricant used are shown in Table 1.

The true densities (ρ_v) of the pure substances were determined with a helium gas pycnometer (Model 1330, Micromeritics, Norcross). The true densities of the mixtures with lubricant (ρ_t) were evaluated by using the equation:

$$\frac{100}{\rho_t}=\frac{x_1}{\rho_{v1}}+\frac{x_2}{\rho_{v2}} \tag{10}$$

where x_i and ρ_{vi} are respectively the percentage and the true density of each component. The calculated ρ_t of powder systems are compiled in Table 1.

Powders were then compressed on an instrumented Frogerais OA eccentric press at a frequency of 30 compacts/min. The punch diameter was 11.28 mm. The die depth was maintained constant (tablet weight from 0.350 g for the PVP to 0.930 g for dicalcium phosphate). Powders were compressed under various measured compressional stresses (6–10 series of 40 compacts) to cover a wide range of relative densities (intermediate and high pressure). After ejection and tablet elastic recovery (24 h) the thickness of the compacts was determined. The compact weight was also measured and the density calculated.

2.3. Tensile strength tests

The compacts were stored for 2 days (relative humidity 40%) before the test of diametral compression. The tests were performed at a constant speed of 0.1 mm/s with the TA-XT2 testing instrument (Rheo, Champlan, France) allowing the recording of both force and displacement. The tensile strength at failure was normalised to take into account the thickness differences of the compacts between materials when a theoretical zero porosity (i.e. $\rho_r \rightarrow 1$) was considered.

$$\sigma_T=\sigma_{T\exp}\frac{h_{\exp}}{h_0} \tag{11}$$

where $\sigma_{T\exp}$ is the experimental value calculated using the Fell and Newton equation [19]. $h_{\exp}$ is the thickness of the compact and h_0 is the theoretical thickness of the same compact when $\rho_r \rightarrow 1$.

2.4. Indentation hardness measurements

A stainless steel sphere ($D = 2.381$ mm) was pushed into the compact surface at a constant speed of 0.1 mm/s (TA-XT2) up to a testing load of $F = 10$ N. This load was then kept constant for 120 s. The indentation diameter (d) was measured with an optical microscope (HM-LUX, Weitzlar, Germany) equipped with a graduated ocular and under grazing light incidence. From the indentation diameter (d) and the applied load (F), the indentation hardness (Brinell hardness), (P) is calculated for each material by the following equation [4]:

$$P=\frac{2F}{\pi D(D-\sqrt{D^2-d^2})} \tag{12}$$

All the measurements were performed five times, and the mean P values were calculated.

2.5. Brittle fracture index (BFI) determination

Holes with diameters of 0.3 and 0.6 mm were bored through the compacts with a cocentred drill under very low rotational speed. The tensile strength tests on the drilled compacts were then performed under the same conditions as mentioned above.

Compactibility parameters P_m and σ_{Tm} from Leuenberger's exponential model were calculated by a non-linear regression analysis (Mac Curve Fit v. 1.2.) of the Eq. (5) and Eq. (6). The plastic yield pressures P_y (reciprocal of the Heckel slope in the linear region), the mean critical relative densities ρ_r^* (Eqs. (1), (8) and (9)) and the corresponding standard errors have been determined by a linear regression analysis.

3. Results

3.1. Heckel plot

The Heckel plots are presented in Fig. 1. Only the intermediate pressure region was considered (linear region of the Heckel plot). The correlation coefficient values of the evaluation according to the Heckel equation are compiled in Table 2. The calculated values of both the mean yield stress P_y and percolation thresholds are presented in Table 2. The critical density values (ρ_H^*) were calculated on the basis of the y-axis intercept of the linear section of the Heckel plot as suggested by Leuenberger [6] (linear regression).

The calculated P_y values of microcrystalline cellulose and PVP are lower than those of lactose and dicalcium phosphate, in good accordance with the ductile character of the first two and the brittle behaviour of the others.

It should be pointed out that the yield stress calculated values are slightly higher than those described in the literature, especially for microcrystalline cellulose ($P_y = 50$ MPa Ref. [20]). Such a difference may be explained by the out-of-die method [21]. In fact, experiments with the same batch of pure Avicel, external lubrication and in die measurements gave a P_y value of 49 MPa.

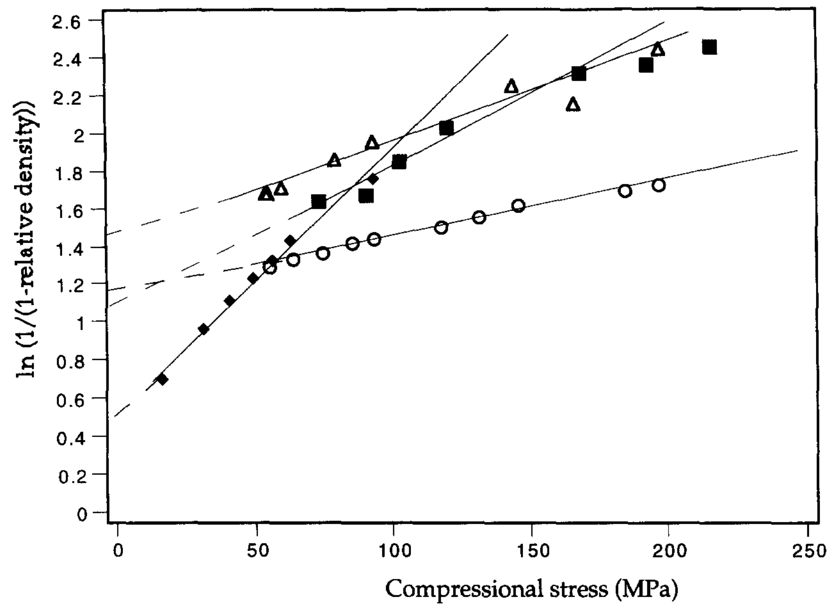

Fig. 1. Heckel plot used to determine the percolation threshold (ρ^*_H) and yield pressure (P_y) for the region of dense compacts. Key: (△) lactose; (◆) microcrystalline cellulose; (○) dicalcium phosphate; (■) polyvinyl pyrrolidonne.

3.2. Indentation hardness and tensile strength

The two models which describe the evolution of mechanical properties with regard to the relative density changes were also applied, according to Eqs. (5) and (8) for indentation hardness and Eqs. (6) and (9) for tensile strength. The graphs obtained are presented in Fig. 2a, b, according to the exponential model and the 'percolation' model respectively for the indentation hardness and Fig. 3a, b for the tensile strength. The calculated values of P_m, σ_{Tm}, and P_{max}, σ_{Tmax}, corresponding to the maximum deformation hardness and tensile strength of the substances when $\rho_r \to 1$ are compiled in Table 3a, b.

The comparison of the results and estimated standard deviations values indicates that the percolation model offers more reliable estimates of P and σ_T extrapolated values than does the exponential model. On the other hand, the correlation coefficients of the evaluation according to the percolation model are lower than those according to the exponential model. This is due to the fact that the linear model is not as flexible as the exponential one. The latter can lead, despite good r^2 values, to unreasonable values with very large standard errors [22]. Moreover, the lack of experimental data at high pressures (> 200 MPa), corresponding to the expected plateau region of the exponential model, is a heavy handicap in the pertinent use of this approach.

The extrapolated values P_m, P_{max} and σ_{Tm}, σ_{Tmax} are in good accordance for microcrystalline cellulose and PVP, but very distinct for the two brittle materials. The same kind of results were already shown by Leuenberger et al. [6,22].

The percolation thresholds were also determined from the indentation hardness P versus relative density and from the tensile strength versus relative density plots, according to Eq. (8) and Eq. (9), respectively. The critical densities obtained in these ways are denoted respectively ρ^*_P and ρ^*_s and their values are shown in Table 3b.

A comparison between the calculated critical densities ρ^*_H (Table 2) and ρ^*_P, ρ^*_s (Table 3b) makes it possible to distinguish the two, ductile and brittle, classes of behaviour. In the case of lactose and dicalcium phosphate, ρ^*_H, ρ^*_P and ρ^*_s values are very close one to the other. It is clearly not the same for microcrystalline cellulose and PVP for which ρ^*_H and ρ^*_P are very similar, but ~ 0.1 units lower than ρ^*_s.

It should be noted that other authors have obtained similar results but did not discuss them [6,22]. Consequently, this will be extensively discussed later.

Table 2
Experimental values[a] for yield strength (P_y) and relative density corresponding to site percolation threshold (ρ^*_H) according to the Heckel plot

Substance	P_y (MPa)	ρ^*_H	r^2
Lactose	196 ± 18	0.760 ± 0.013	0.952
Microcrystalline cellulose	73 ± 3	0.409 ± 0.022	0.961
Dicalcium phosphate	329 ± 12	0.681 ± 0.004	0.955
PVP	127 ± 12	0.640 ± 0.031	0.987

[a] Values are expressed as mean ± standard error of the mean.

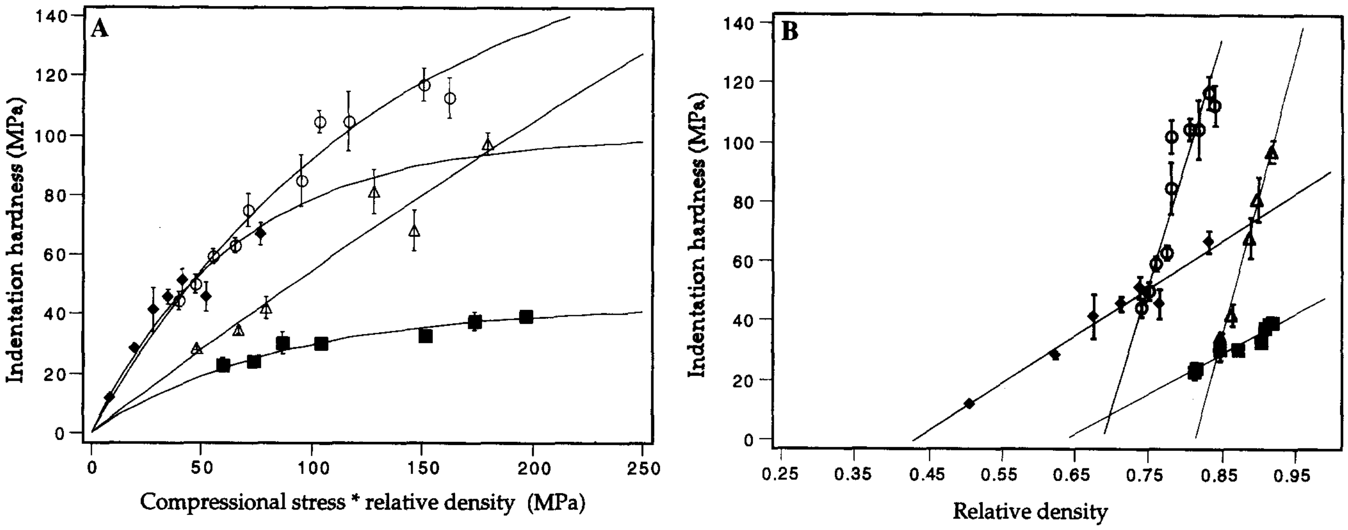

Fig. 2. Plot of indentation hardness as a function of the product of compression stress and relative density according to Eq. (5) (a), and as a function of the relative density according to percolation theory for the region of dense compacts according to Eq. (8) (b). Key: (△) lactose; (◆) microcrystalline cellulose; (○) dicalcium phosphate; (■) polyvinyl pyrrolidonne.

3.3. Brittle fracture index (BFI) and bonding index (BI)

The results obtained in terms of BFI and BI indices for compacts of relative densities between 0.85 and 0.90 (according to Hiestand's conditions) are summarised in Table 4.

BFI: The calculated BFI values are low, < 0.2 in all cases. Nevertheless, here again the two classes of materials are clearly discriminated: the calculated BFI for the two brittle substances are in the range of 0.1–0.2, while for the ductile substances they are in the range of 0.01–0.1.

Moreover, for the brittle substances, the brittle fracture indices are very similar when the measurements of the tensile strength were performed on 0.3 or 0.6 mm drilled compacts. On the other hand, BFI seems to be more sensitive to the hole diameter for the ductile materials, i.e. BFI tends to decrease when the hole diameter is increased.

We have retained the results obtained with the 0.6 mm hole diameter to stay in the same hole ratio: diameter/compact diameter, as the one used by Roberts and Rowe in their studies [23]. These authors actually considered that such experimental conditions made it possible to compare the results with Hiestand's results whereas Hiestand worked on square compacts. In fact, under a compression speed of 200 mm/s and for a solid fraction of 0.7, they determined a BFI value of 0.08 for microcrystalline cellulose, close to those presented in Table 4. Amidon [24] obtained, under Hiestand's experimental conditions, a value of BFI = 0.07 for microcrystalline cellulose with a relative density of 0.7.

Different works have also considered the influence of internal lubrication on the BFI index. Hiestand [14] noted an important decrease of BFI when NaCl is mixed with 1% of magnesium stearate. Williams [25] also considered that the lubricant contributes to a decrease in the stress concentration. This effect was suggested to affect brittle materials as well as ductile materials.

BI: The calculated bonding indices were obtained in this work from deformation hardness measured under quasi-static conditions (load application time of 120 s) (Table 4 for $0.85 < \rho_r < 0.90$). In these conditions, the calculated BI values are more related to the 'best case bonding index' (BI_b) than to the 'worst case' as defined by Hiestand. The BI values for lactose and dicalcium phosphate are low which may be associated with a poor capacity of the survival of areas, during decompression, of true contacts established at maximum compression stress. The higher BI values for microcrystalline cellulose and PVP lead to the opposite conclusion. One can note the intermediate behaviour of PVP.

It should be noted, especially for PVP (2% of magnesium stearate), that the presence of a lubricant was shown to diminish the BI values [14,25]. In the presence of increased levels of magnesium stearate, compacts seem to be unable to maintain, during decompression, the integrity of the extensive areas that were established under maximum compressive stress [25]. Similarly, the calculated BI_b for microcrystalline cellulose is lower than the values reported in the literature [24] ($BI_{b\text{microcrystalline cellulose}} = 0.12$ for $\rho_r = 0.7$). The presence of a different percentage of lubricant makes it difficult to compare the lactose and dicalcium phosphate. Nevertheless, it seems that dicalcium phosphate, in the presence of 1.5% lubricant offers a better potential for the survival of areas during decompression, than lactose with 1% of lubricant.

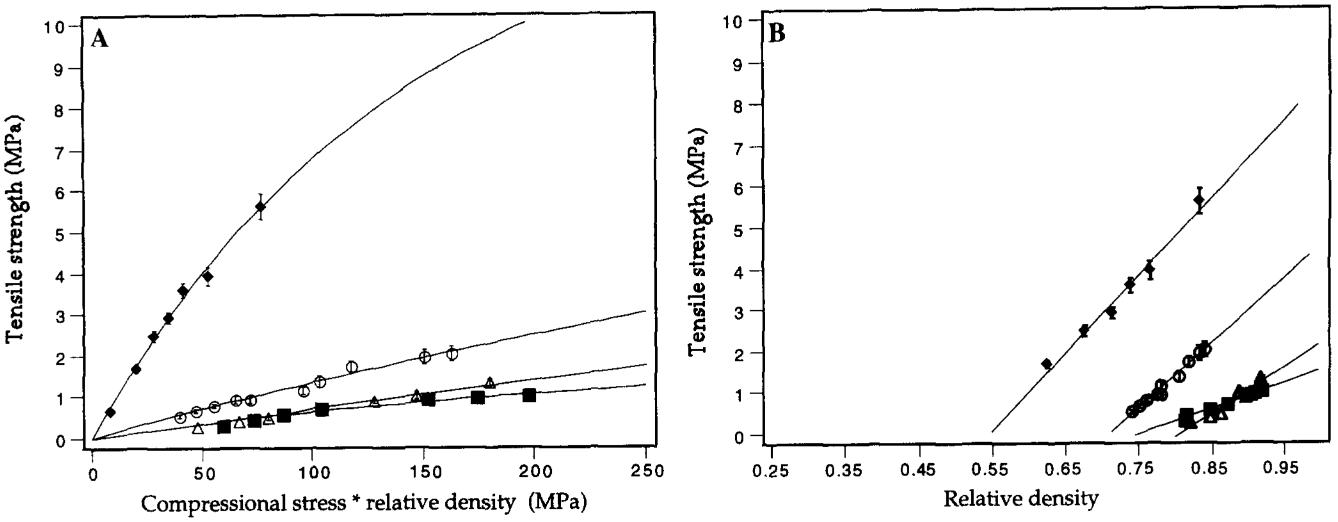

Fig. 3. Plot of tensile strength as a function of the product of compression stress and relative density according to Eq. (6) (a), and as a function of relative density according to percolation theory for the region of dense compacts according to Eq. (9) (b). Key: (☆) lactose; (◆) microcrystalline cellulose; (○) dicalcium phosphate; (■) polyvinyl pyrrolidonne.

The changes of BI values were also analysed with regard to the relative density. The plots are presented in Fig. 4. One can note an undoubted and significant increase of BI when ρ_r increases in the case of the ductile materials, microcrystalline cellulose and PVP. Such a change in BI_w values was already reported in the case of microcrystalline cellulose in a 0.4–0.9 ρ_r interval, even with 5% magnesium stearate [25].

On the other hand, for lactose and dicalcium phosphate, it could be considered that in the $0.5 < \rho_r < 0.95$ interval, no change in BI values appears (no significant differences between BI values at median and high pressures). An identical behaviour was also pointed out for a brittle material, sulfathiazole [25] (no change in BI values in the 0.6–0.9 ρ_r interval, even for high percentage of lubricants).

4. Discussion

The mechanical properties of some compacted pharmaceutical materials were considered in the light of two principal approaches. The first one describes the mechanical properties of the compacts (principally in terms of tensile strength and deformation hardness) in regard to the applied compression stress or the relative density evolution. The second one characterises the compact properties through dimensionless indices able to give insight into relative tableting performance of materials.

Whatever the method used, the expected different behaviour of the materials studied were confirmed. The chosen brittle materials, lactose and dicalcium phosphate, are characterised by high values of yield stress (P_y), extrapolated deformation hardness (P_m, P_{max}), and brittle fracture index, and by low values of bonding index with regard to microcrystalline cellulose and PVP, the two ductile materials.

The internal introduction of a lubricant did not change the expected brittle or ductile comportment of the materials studied, but did affect just the absolute values of the calculated parameters.

The mechanical properties of each of the studied substances, may be summarised briefly: In the case of microcrystalline cellulose, the low value of P_y combined with both the lowest BFI and the highest BI values show indisputably its ductile properties. The particles of microcrystalline cellulose yield plastically at areas of true contact during decompresion, and the interparticle bonding forces are strong enough to induce isthmus formation. This also results in high value of the calculated tensile strength σ_{Tmax}.

Lactose and dicalcium phosphate may be considered together despite the differences in their P_y values. Dicalcium phosphate is a more brittle substance than is lactose, as confirmed by the BFI values. On the other hand, dicalcium phosphate seems to be able to better preserve the contact areas formed at maximum compression, during decompression. Its BI is quite close to, but significantly higher than that of lactose and clearly its calculated σ_{Tmax} is twice that for lactose. Such differences may be of great relevance, in terms of capping and fracture of the compacts during decompression [15].

PVP reveals an unexpected behaviour which is most probably related to the higher percentage of lubricant required for tabletting (sticking material). Its P_y, of about 130 MPa, is intermediate but higher than expected for a highly ductile material. The low BFI value is more related to its ductility. On the other hand, the

Table 3
Experimental values[a] of indentation hardness and tensile strength when $\rho \rightarrow 1$

(a) Exponential model

Substance	Eq. (5)			Eq. (6)		
	P_m (MPa)	γ_P ($\times 10^2$ MPa^{-1})	r^2	σ_T (MPa)	γ_s ($\times 10^2$ MPa^{-1})	r^2
Lactose	631 ± 1000	0.089 ± 0.14	0.959	71.8 ± 909	0.0096 ± 0.17	0.979
Microcrystalline cellulose	108 ± 19	1.4 ± 0.2	0.983	13.3 ± 2.8	0.7 ± 0.2	0.993
Dicalcium phosphate	196 ± 63	0.65 ± 2.0	0.907	9.57 ± 300	0.015 ± 0.1	0.981
PVP	34 ± 1	1.32 ± 0.6	0.945	2 ± 0.6	0.37 ± 0.16	0.959

(b) Percolation model

Substance	Eq. (8)			Eq. (9)		
	P_{max} (MPa)	ρ^*_P	r^2	σ_{Tmax} (MPa)	ρ^*_σ	r^2
Lactose	174 ± 6.6	0.807 ± 0.02	0.980	2.4 ± 0.3	0.817 ± 0.01	0.912
Microcrystalline cellulose	94 ± 2.5	0.433 ± 0.03	0.992	7.8 ± 0.3	0.518 ± 0.01	0.991
Dicalcium phosphate	268 ± 3.1	0.672 ± 0.013	0.900	4.3 ± 0.4	0.689 ± 0.013	0.851
PVP	50 ± 2.5	0.639 ± 0.03	0.922	1.45 ± 0.04	0.733 ± 0.01	0.983

[a] Values are expressed as mean ± standard error of the mean.

(a) According to Eqs. (5) and (6) (P_m and σ_{Tm}); (b) according to Eqs. (8) and (9) (P_{max} and σ_{Tmax}) and relative density threshold ρ^*_P, ρ^*_σ according to percolation model.

PVP's BI is quite low compared to that of microcrystalline cellulose. This fact is in good accordance with the very low value of σ_{Tmax} calculated for PVP. In our experimental conditions, PVP is unable to harden when compacted.

Other more general points must be discussed from this work. A comparison between the compression parameters such as P_m, σ_{Tm}, γ_P and γ_s and the Hiestand's bonding index was already performed by Jetzer et al. [17]. These authors pointed out that the BI index is dependent on the compression parameters, and by considering the Eqs. (3), (5) and (6) the following equation may be written:

$$\mathrm{BI} = \frac{\sigma_{Tm}(1 - e^{(-\gamma_\sigma \sigma_c \rho_r)})}{P_m(1 - e^{(-\gamma_P \sigma_c \rho_r)})} \tag{13}$$

Then, BI is constant ($\mathrm{BI} = \sigma_{Tm}/P_m$) only if $\gamma_P = \gamma_s$. Thus, the exponential model is likely to take into account the variation of BI values when the relative density is increased. Unfortunately, the calculated parameters from this model were shown to be highly dispersed (unreasonable estimated standard deviations).

Conversely, the percolation model was shown to offer more reliable estimates of P and σ_T extrapolated values ($\rho_r \rightarrow 1$). Then, if one considers Hiestand's BI index with regard to the percolation model, in the intermediate and higher pressure regions, the following equations could be written, according to Leuenberger's work [6,22].

$$\mathrm{BI} = \frac{\sigma_T}{P} = \frac{\dfrac{\sigma_{Tmax}}{1 - \rho^*}(\rho_r - \rho^*)}{\dfrac{P_{max}}{1 - \rho^*}(\rho_r - \rho^*)} = \frac{\sigma_{Tmax}}{P_{max}} = \text{constant} \tag{15}$$

This equality is verified in the case of the two brittle materials. Alernatively, if microcrystalline cellulose and PVP are considered, the BI index increases as the relative density increases (Fig. 4). In fact, in this approach Leuenberger considered that the two mechanical properties (tensile strength and deformation hardness) give insight into the same percolation threshold ρ^*.

But, it had already been observed that in the case of microcrystalline cellulose and PVP, ρ^*_σ calculated values were higher (in a range of 0.1 unit) than ρ^*_P values (see Table 3b, and also the Leuenberger results in Ref. [22] for example). Such a difference should be attributed, first and foremost, to the tensile strength determination methodology. Classically, the measurement is considered as valid if the compacts break in such a manner that tensile stress is the major stress, and the specimen fails along the loaded diameter. Compacts of predominantly plastic and viscoelastic materials usually exhibit non-ideal fracture patterns, which provide an approximate value of tensile strength, limiting the range of comparison of the test. Conversely, an increase in the BI values was already pointed out in the case of microcrystalline cellulose as a consequence of a relative density increase, even by performing the experiments under Hiestand's stipulated conditions and without any internal lubrication as well as in the presence of increasing quantities of lubricant [25].

Therefore, it seems reasonable to consider as significant the differences between the critical densities calculated from tensile strength or indentation hardness measurements through the corresponding percolation equations.

Table 4
Brittle fracture index (BFI) and bonding index (BI) calculated values

Substance	BFI[a] hole diameter 0.3 mm	BFI[a] hole diameter 0.6 mm	BI[a]
Lactose	0.14 ± 0.01	0.15 ± 0.01	1.2 ± 0.1
Microcrystalline cellulose	0.064 ± 0.01	0.049 ± 0.01	7.5 ± 0.4
Dicalcium phosphate	0.16 ± 0.03[b]	0.17 ± 0.03[b]	1.6 ± 0.1[b]
PVP	0.069 ± 0.01	0.048 ± 0.01	2.7 ± 0.3

[a] Solid fraction between 0.85 and 0.90.

[b] Solid fraction for dicalcium phosphate compacts 0.80–0.85.

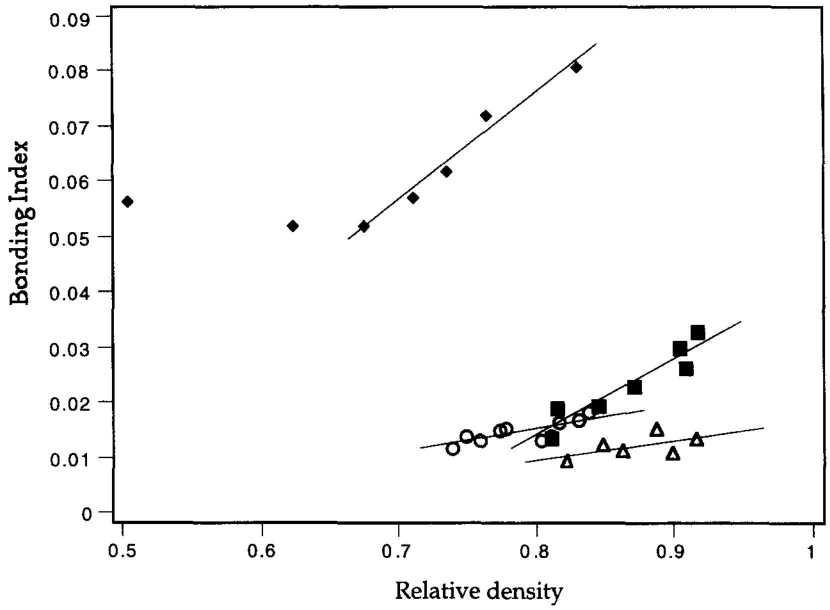

Fig. 4. Bonding index of compacts as a function of relative density. Key: (☆) lactose; (◆) microcrystalline cellulose; (○) dicalcium phosphate; (■) polyvinyl pyrrolidonne.

Two different percolation thresholds should then be defined, each of them being related to their own mechanical properties. The deformation hardness measurements are directly linked with the plastic deformation properties of the substances. In fact, the calculated ρ_P^* are very close to the ρ_H^* calculated from the linear part of the Heckel graph which is also a reflection of material's ductility. The tensile strength measurements are more related to the bonding of particles that are part of the infinite cluster formed at the percolation threshold and which represents the 'backbone' of the tablet.

To sustain the hypothesis of two separate percolation thresholds ρ_P^* and ρ_σ^*, the results obtained must be compared to those published by Holman in his in die compaction analysis [26]. Holman identified in the intermediate pressure region a bond percolation threshold and a rigidity threshold. The rigidity threshold was defined at the point where the flexible incipient percolating cluster of the particles becomes rigid. The two-stage behaviour was only exhibited by soft materials. It is of great interest to notice that in the case of microcrystalline cellulose, the bond percolation threshold was estimated in the $0.386 < \rho^* < 0.425$ interval and the rigidity threshold in the 0.532 to 0.604 relative density interval. These data are in good accordance with the ρ_P^* and ρ_σ^* values shown in Table 3b. If one takes into account the differences in methodology (particularly the 'out of die' measurements as opposed to Holman's 'in die' measurements). In the same way, Radebaugh et al. [27] have reported deviations in the relationship between the viscoelasticity and relative density of microcrystalline cellulose compacts at solid fractions levels which are very close to Holman's percolation threshold values and the values reported in this work for ρ_P^* and ρ_σ^*. Such a consistency between these results is very interesting in view of the fact that the conditions under which the tablets were made and the properties measured were different.

On the contrary, Sinko et al. [28] have identified in their work only one percolation threshold in the region powder–rigid compact for hydroxy-propyl cellulose.

This could probably be explained by the fact that the mechanical properties were performed only by indentation hardness experiments.

5. Conclusion

We have pointed out in this work the complementarity between the two approaches: the percolation theory and the dimensionless indices approach developed by Hiestand.

The bonding index behaviour, when the compact relative density is increased, exhibits an evolution which was not foreseen by the Leuenberger percolation theory. The latter is completed by a percolation threshold (ρ_σ^*) which was not initially expected.

This work illustrates the necessity to obtain the mechanical responses of compacts by different means of measurement (tensile strength masurements, indentation hardness measurements...).

References

[1] H.F. Fichmeister, E. Arzt, Densification of powders by particle deformation, Powder Metall. 26 (1983) 81–88.

[2] D. Bortzmeyer, Modelling ceramic powder compaction, Powder Technol. 70 (1992) 131–139.

[3] E.N. Hiestand, Tablet bond. I. A theoretical model, Int. J. Pharm. 67 (1991) 217–229.

[4] H. Leuenberger, B.D. Rohera, Fundamentals of powder compression. I. The compactibility and compressibility of pharmaceutical powders, Pharm. Res. 3 (1986) 12–22.

[5] W.C. Duncan-Hewitt, Uniaxial compaction modelled using the properties of single crystals, Drug. Dev. Ind. Pharm. 19 (1993) 2197–2240.

[6] H. Leuenberger, L. Ruth, Formation of a tablet: A site and bond percolation phenomenon, J. Pharm. Sci. 81 (1992) 976–982.

[7] R.W. Heckel, Density–pressure relationships in powder compaction, Trans. Metall. Soc. AIME 221 (1961) 671–675.

[8] R.W. Heckel, An analysis of powder compaction phenomena, Trans. Metall. Soc. AIME 221 (1961) 1001–1008.

[9] J.A. Hersey, J.E. Rees, The effect of particle size on the consolidation of powders during compaction. in: J.M. Groves, J.L. Sargent (Eds.), Particle Size Analysis, Soc. Anal. Chem., London, 1970, pp. 1–8.

[10] P. Paronen, in: M.H. Rubinstein (Ed.), Pharmaceutical technology: Tabletting Technology, vol. 1, Ellis Horwood, Chichester, 1987 139-144.

[11] G. Ragnarsson, J. Sjogren, The influence of die-wall friction on tablet porosity–compaction load relationship, Acta Pharm. Suec. 21 (1984) 141–144.

[12] R.J. Roberts, R.C. Rowe, The effect of the relationship between punch velocity and particle size on the compaction behaviour of materials with varying deformation mechanisms, J. Pharm. Pharmacol. 38 (1986) 567–571.

[13] E. Hiestand, D.P. Smith, Indices of tabletting performance, Powder Technol. 38 (1984) 145–159.

[14] E.N. Hiestand, D.P. Smith, Three indices for characterising the tabletting performance of materials, Adv. Ceram. 9 (1984) 47–57.

[15] E.N. Hiestand, The basis for practical applications of the tabletting indices, Pharm. Technol. 9 (1989) 54–66.

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

[17] W.E. Jetzer, W.B. Johnson, E.N. Hiestand, Comparison of two different experimental procedures for determining compaction parameters, Int. J. Pharm. 26 (1985) 329–337.

[18] E. Doelker, Assessment of powder compaction. in: D. Chulia, M. Deleuil, Y. Pourcelot (Eds.), Powder Technology and Pharmaceutical Processes, Elsevier, Amsterdam, 1994, pp. 403–471.

[19] J.T. Fell, J.M. Newton, Determination of tablet strength by the diametral compression test, J. Pharm. Sci. 59 (1970) 688–691.

[20] P. Humbert-Droz, D. Mordier, E. Doelker, Méthode rapide de détermination du comportement à la compression pour des études de préformulation, Pharm. Acta Helv. 57 (1982) 136–143.

[21] J.M. Geoffroy, J.T. Carstensen, Effects of measurement methods on the properties of materials, Powder Technol. 68 (1991) 91–96.

[22] R. Leu, H. Leuenberger, The application of percolation theory to the compaction of pharmaceutical powders, Int. J. Pharm. 90 (1992) 213–219.

[23] R. Roberts, R. Rowe, Brittle fracture propensity measurements on tablet-sized cylindrical compacts, J. Pharm. Pharmacol. 38 (1986) 526–528.

[24] G.E. Amidon, M.E. Houghton, The effect of moisture on the mechanical and powder flow properties of microcrystalline cellulose, Pharm. Res. 12 (1995) 923–929.

[25] R.O. Willams III, J.W. McGinity, Compaction properties of microcrystalline cellulose and sodium sulfathiazole in combination with talc or magnesium stearate, J. Pharm. Sci. 78 (1989) 1025–1034.

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

[27] G.W. Radebaugh, S. Babu, J.N. Bondi, Characterisation of the viscoelastic properties of compacted pharmaceutical powders by a novel nondestructive technique, Int. J. Pharm. 57 (1989) 95–105.

[28] C.M. Sinko, G.T. Carlson, D.S. Gierer, The identification of percolation and mechanical threesolds during the compaction of hydroxypropyl methylcellulose: comparaison to threesolds determined from out-of-die indentation experiments, Int. J. Pharm. 114 (1995) 85–93.