International Journal of Pharmaceutics 151 (1997) 27–34

international journal of pharmaceutics

Stress relaxation of compacts produced from viscoelastic materials

K. Van der Voort Maarschalk [a,*], K. Zuurman [a], H. Vromans [b], G.K. Bolhuis [a], C.F. Lerk [a]

[a] *Department of Pharmaceutical Technology and Biopharmacy, University of Groningen, Antonius Deusinglaan 1, 9713 AV Groningen, Netherlands*
[b] *N.V. Organon, Oss, Netherlands*

Received 5 December 1996; accepted 13 January 1997

Abstract

Stress relaxation of tablets is a phenomenon that is known to be related to elastic deformation of particles. Expressions of stress relaxation are tablet expansion and capping. It has been shown that there is a direct relation between the changes in volume of the tablet and the amount of stored energy, calculated from the elastic modulus and the yield strength of the material. The relations are, however, different for the different materials. On the basis of the assumption that the increase in tablet volume is an expression of stress relaxation and stored energy is the driving force for it, there should be a counteracting force that prevents a compact from expansion. This paper shows that the counteracting force is determined by particle bonding, quantified by the Ryshkewitch–Duckworth relation and friction of the tablet with the die wall, quantified by the ejection pressure. The data presented here suggest that the final tablet porosity is unequivocally determined by stored energy, particle attraction and friction of the tablet with the die wall. All tablets that were capped showed both high stored energies and large particle bonding. From this observation it is concluded that porous and capped tablets suffer from the same problem, but the expression stress relaxation is different for the different materials. © 1997 Elsevier Science B.V.

Keywords: Tablet; Stress relaxation; Particle bonding; Die wall friction; Porosity; Capping; Stored energy

1. Introduction

Materials with predominantly viscoelastic deformation characteristics are commonly used as filler binders in tablets, produced by direct compression. Unfortunately, these materials sometimes suffer from problems related to compaction speed, manifested as weak (porous) or capped tablets (Roberts and Rowe, 1985). In fact, these phenomena are symptoms of stress relaxation.

---

[*] Corresponding author.

PII S0378-5173(97)04889-8

Common expressions of stress relaxation are changes in tablet volume after compression (Doelker, 1993). Volume changes, however, are the net effect of many factors that are of influence on stress relaxation. Other expressions of stress relaxation, such as capped or laminated tablets, are studied separately, whereas it can be assumed that all phenomena have at least partially the same origin (relief of tablet stress). For this reason, in previous work a different approach has been suggested. A method was introduced that quantifies the energy that is elastically stored during consolidation on the basis of material properties known in polymer mechanics (Van der Voort Maarschalk et al., 1996b). The amount of stored energy is regarded as the driving force for stress relaxation. Consequently, stored energy can be related to parameters that express stress relaxation such as the increase in porosity after compression. The papers published so far reported the effects of plasticity of the excipient, the role of a plasticiser and initial particle size on viscoelastic properties and the resulting compacts from some model excipients (Van der Voort Maarschalk et al., 1996b,c,d). The present paper aims to generalise the concept suggested in the previous publications to a wider range of excipients with different molecular structures. Assuming that stored energy is the universal driving force for stress relaxation, then boundary conditions determine the way tablet relaxation is expressed. This paper pays special attention to the factors that affect the expression of stress relaxation.

2. Materials and methods

The test materials were roller dried anhydrous β-lactose (Pharmatose® DCL21, DMV, Veghel, Netherlands), sodium chloride (OPG Farma, Utrecht, Netherlands), spray-dried sorbitol (Karion® Instant, Merck, Darmstadt, Germany), microcrystalline cellulose (Avicel® PH101, FMC Europe, Brussels, Belgium), and pregelatinized potato starch (Paselli® WA4, Avebe, Foxhol, Netherlands). Before use the materials were stored at a temperature of 22°C and a relative humidity of 60% for a period of at least 7 days. Magnesium stearate Ph. Eur. grade was obtained from Genfarma (Maarssen, Netherlands).

Elastic moduli were measured as a function of deformation rate with Dynamic Mechanical Analysis (DMA) on a Rheometrics Solids Analyzer (Piscataway, NJ, USA), using the dual cantilever method. Strips of the test material of a size of about 60·6·1 mm were prepared with a hand press (Paul Weber, Stuttgart, Germany) in a specially designed punch-and-die set. The maximum applied pressure varied between 15 and 370 MPa and was held constant for about 10 s. After ejection and a relaxation period of at least 16 h the size of the strips was measured with the micrometer and the strips were weighed on an analytical balance. The maximum strain in the experiments was 0.01%. The measurement started at a frequency of 0.1 rad s^{-1} and ended at a frequency of 100 rad s^{-1}. The elastic moduli at zero porosity were calculated as previously described (Van der Voort Maarschalk et al., 1996a).

Flat-faced compacts of 500 mg and a diameter of 13 mm were prepared on a high speed compaction simulator (ESH, Brierley Hill, UK) at a temperature of 22°C and a relative humidity of 60%. The maximum applied pressures varied between about 5 and 350 MPa. The upper punch displacement profiles were sine-waves with different amplitudes in order to vary the maximum compression pressures. As sinusoidal profiles were used, a complete profile involves π rad. Knowing both the compression speed (v) and the penetration depth (A_{comp}), it is possible to calculate the angular frequency of the compression (f):

$$f=\frac{\pi \cdot v}{2 \cdot A_{comp}} \tag{1}$$

which enables to correlate DMA to compaction experiments. The average compaction speeds were 3, 30 and 300 mm s^{-1}, respectively. These values are within the range of angular frequencies as applied in DMA. Before each compression the die was lubricated with magnesium stearate. The lower punch was stationary during compression. The ejection time was always 10 s and the maximum ejection force was measured. Both upper punch and lower punch displacement and force were recorded. The resolution of the analogue-to-

Table 1
Elastic modulus, yield strength and stored energy of the test materials at different speeds of compaction

Material	Compaction speed (mm s^{-1})	Elastic modulus (Pa)	Yield strength (Pa)	Stored energy (J m^{-3})
Pregelatinized potato starch	3	$4.1 \cdot 10^9$	$1.3 \cdot 10^7$	$1.9 \cdot 10^4$
	30	$4.3 \cdot 10^9$	$1.4 \cdot 10^7$	$2.4 \cdot 10^4$
	300	$4.5 \cdot 10^9$	$1.8 \cdot 10^7$	$3.5 \cdot 10^4$
Microcrystalline cellulose	3	$5.8 \cdot 10^9$	$1.7 \cdot 10^7$	$2.4 \cdot 10^4$
	30	$6.1 \cdot 10^9$	$1.9 \cdot 10^7$	$3.0 \cdot 10^4$
	300	$6.4 \cdot 10^9$	$2.4 \cdot 10^7$	$4.4 \cdot 10^4$
Sodium chloride	3	$2.0 \cdot 10^{10}$	$2.8 \cdot 10^7$	$2.0 \cdot 10^4$
	30	$2.1 \cdot 10^{10}$	$3.3 \cdot 10^7$	$2.6 \cdot 10^4$
	300	$2.1 \cdot 10^{10}$	$4.2 \cdot 10^7$	$4.3 \cdot 10^4$
Spray-dried sorbitol	3	$6.7 \cdot 10^{10}$	$2.1 \cdot 10^7$	$3.1 \cdot 10^4$
	30	$8.0 \cdot 10^{10}$	$2.5 \cdot 10^7$	$3.8 \cdot 10^4$
	300	$9.4 \cdot 10^{10}$	$3.3 \cdot 10^7$	$5.8 \cdot 10^4$
β-Lactose	3	$1.1 \cdot 10^{10}$	$6.7 \cdot 10^7$	$1.9 \cdot 10^5$
	30	$1.2 \cdot 10^{10}$	$7.1 \cdot 10^7$	$2.2 \cdot 10^5$
	300	$1.2 \cdot 10^{10}$	$6.7 \cdot 10^7$	$2.0 \cdot 10^5$

digital conversion was 0.3 μm, the total error of the measurements appeared to be better than ± 10 μm. Corrections were made for elastic punch deformation. The yield stress of the test materials was measured according to Heckel (1961a,b). Linear interpolation was performed in the porosity range between 35% and 8%. After a relaxation period of at least 16 h, tablet dimensions were measured with the micrometer and the tablets were weighed on an analytical balance. The results of measurements of elastic moduli and yield strengths are depicted in Table 1 together with the resulting values of stored elastic energy (Van der Voort Maarschalk et al., 1996c).

The crushing strength of the tablets was measured with a Schleuniger 4N strength tester (Dr. Schleuniger Productronic, Soloturn, Switzerland). Because the good bonding properties of microcrystalline cellulose, spray-dried sorbitol and pregelatinized potato starch yield tablets with crushing strengths over 300 N (Bolhuis and Chowhan, 1996; Van der Voort Maarschalk et al., 1996a), strength measurements of tablets compacted from these materials were performed with the compaction simulator. Profiles with a linear speed of 0.25 mm s^{-1} were created, and the maximum applied pressure was recorded on an XY-recorder (Kipp and Zonen, Delft, Netherlands). There appeared to be no significant effect of the method of measurement on the value of crushing strength. The tensile strength of the tablets was calculated according to Fell and Newton (1968).

The relation between tensile strength (S) and tablet porosity (ϵ) is a quantification of interparticle bonding. Mathematical fit of this relation is possible with the Ryshkewitch–Duckworth relation (Duckworth, 1953):

$$S = S_0 \cdot e^{-k \cdot \epsilon} \qquad (2)$$

with S_0 calculated tablet strength at zero tablet porosity. The constant k is a constant that quantifies the effect of a change in porosity on tablet strength; a large value of k means that tablet strength changes strongly with porosity which points to strong bonding in the tablet. For this reason, k is called 'bonding capacity' (Van der Voort Maarschalk et al., 1996b). Table 2 shows both S_0 and k of the test materials.

Table 2
Tablet strength parameters tensile strength at zero porosity (S_0) and bonding capacity (k)

Material	S_0 (MPa)	k (−)
Pregelatinized potato starch	14.9	8.0
Microcrystalline cellulose	15.1	5.7
Spray-dried sorbitol	7.0	5.4
β-Lactose	13.6	13.0
Sodium chloride	4.9	12.6

3. Results and discussion

Fig. 1 depicts the tensile strength of both pregelatinized potato starch and of sodium chloride tablets as a function of compaction pressure at three compaction speeds. The tensile strength of tablets of both materials increases with compaction pressure, but the strength of pregelatinized starch compacts reaches a maximum value, which is less pronounced for sodium chloride tablets. Besides, there is a prominent effect of compaction speed on starch compact strength. At pressures exceeding 200 MPa, the strength of these tablets depends on the compaction speed only. It is noted that sodium chloride tablets show large scatter in strength at high compaction pressures and high compaction speed, which points to capped tablets. Some sodium chloride tablets, compacted at a speed of 300 mm s^{-1}, were also visibly capped. Moreover, Fig. 1 evidently shows that tablets compressed from pregelatinized starch are stronger than sodium chloride tablets. The data in Table 2 agree with the differences in strength between tablets of the materials. As indicated by the values of S_0, non-porous compacts compressed from pregelatinized potato starch are stronger than sodium chloride compacts. Besides, the value of k of sodium chloride is larger than that of pregelatinized potato starch, which shows that the strength of sodium chloride decreases more strongly with an increase in porosity than the strength of potato starch. And, according to Eq. (2) tensile strength is completely determined by porosity. Consequently, tablet strength is a result of both the bonding parameters and tablet porosity. Tablet porosity (ϵ) is related to compact density (ρ_c) by:

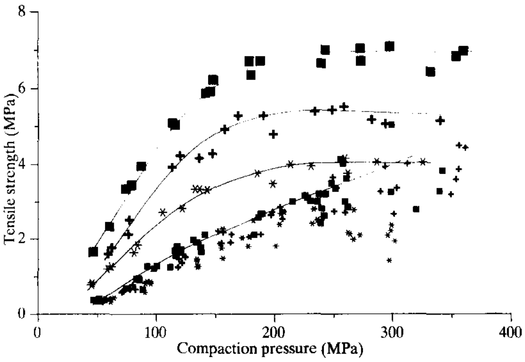

Fig. 1. Tensile strength of pregelatinized potato starch (large symbols) and sodium chloride (small symbols) compacts produced at speeds of 3 (■), 30 (+) and 300 (*) mm s^{-1}.

$$\epsilon = 1 - \frac{\rho_c}{\rho_t} \tag{3}$$

with ρ_t true density of the material. Fig. 2a and b show the compact densities (of pregelatinized potato starch and sodium chloride, respectively) after relaxation as a function of various compaction pressure of tablets compressed at different compaction speeds. In addition to this, the figure gives the true density and the compact density under pressure at a compaction speed of 3 mm s^{-1}. Tablet density of sodium chloride compacts under pressure is almost equal to the density of the tablets after 16 h relaxation (change in density 1%, Fig. 2a), while the density of pregelatinized potato starch tablets changes as much as 10–15% (Fig. 2b). This shows that the ultimate tablet porosity of sodium chloride compacts is predominantly determined by the compression stage, whereas the final porosity of potato starch is merely a result of compact relaxation phenomena. Fig. 2a shows that the density of pregelatinized starch tablets after 16 h relaxation reaches a maximum value that is independent of compaction pressure and only determined by compaction speed. This is, according to Eq. (2) and Eq. (3) in agreement with the observation that the tablet strength of starch compacts reaches a maximum value (Fig. 1). The starch compact density under pressure is larger than the true density when the pressure is larger than 147 MPa (Fig. 2a). This points to an increase in true density. Sodium

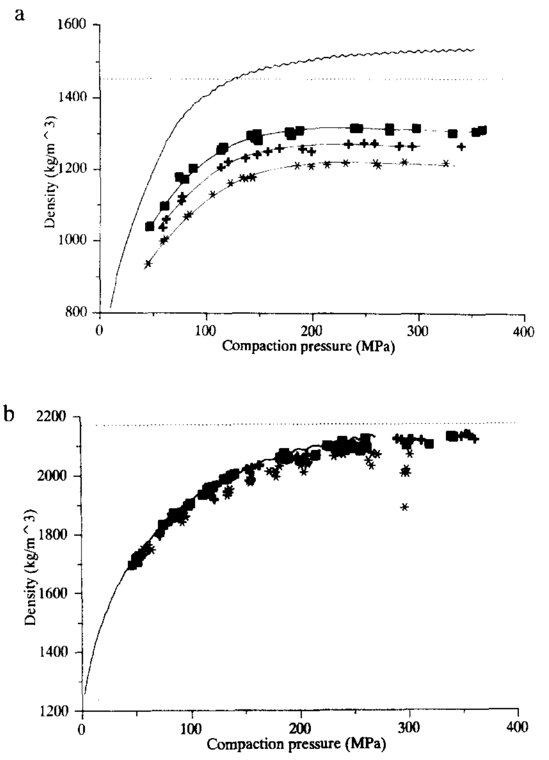

Fig. 2. Compact density of pregelatinized potato starch (2a) and sodium chloride (2b) under pressure at a compaction speed of 3 mm s^{-1}(solid line) and after compression at speeds of 3, 30 and 300 mm s^{-1} (symbols as in Fig. 1). The dotted line represents the true density of the material as measured by pycnometry.

chloride does not show increase in true density under pressure (Fig. 2b).

Table 3 shows the relative increase in true density at a pressure of 350 MPa and the volume increase upon relaxation. There are notable differences in change in volume after relaxation of the compacts. Clearly, the final compact porosity is never determined by powder densification only. Several papers suggest that change in volume is a manifestation of tablet relaxation (Doelker, 1993). However, this expansion is in fact a result of two phenomena. On the one hand, compression always leads to a certain extent of material compression, expressed as an increase in true density, which is fully reversible. On the other hand, compression leads to a build up of elastic energy ($W_{\rm rev}$, Table 1) which is responsible for the increase in porosity. Therefore, a previous paper suggested to choose porosity expansion (i.e. change in porosity, $\Delta\epsilon$) as an expression of relaxation (Van der Voort Maarschalk et al., 1996b). Evidently, porosities and hence porosity expansions over 1 are non-existent, whereas stored energy can theoretically reach any value. Consequently, the relation between porosity expansion and stored energy has an asymptote. It has been suggested to choose the increase in void fraction rather than porosity expansion ($\Delta\epsilon$) (Van der Voort Maarschalk et al., 1996d). Change in void fraction ($\Delta\Phi$) can be calculated with:

Table 3

Calculated increase in true density at a pressure of 350 MPa and increase in volume after compression

Material	Material compression at P = 350 MPa (%)	Volume change (%)
Amorphous potato starch	4.3	10–16[b]
Microcrystalline cellulose	2.4	4–6[b]
Spray-dried sorbitol	0.5	2–4[b]
β-Lactose	N[a]	3–4[b]
Sodium chloride	N[a]	1

[a] N, no measurable material compression.

[b] Depending upon compaction speed.

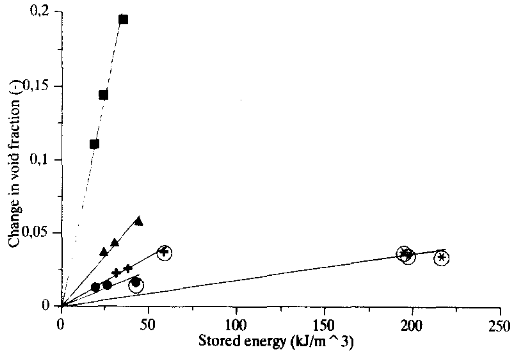

Fig. 3. Change in tablet porosity (expressed as void fraction) as a function of stored energy of pregelatinized starch (■), microcrystalline cellulose (▲), spray-dried sorbitol (+), β-lactose (*) and sodium chloride (●). The encircled symbols indicate that capped tablets were observed.

$$\Delta\Phi = \frac{\Delta\epsilon}{(1 - \Delta\epsilon)} \tag{4}$$

The relation between stored energy and change in void fraction is depicted in Fig. 3. The results indicate that there are different effects of stored energy on the changes in void fraction for the different materials.

A previous paper reported that bonding of the particles determines the relation between porosity expansion and stored energy. Weak bonds imply limited resistance against porosity expansion and consequently porous tablets. The strength of the bonds determines the (unique) relation between tensile strengths of tablets and their porosities. The proportionality constant is indicative for the strength of interparticle bonding and consequently called 'bonding capacity' (Van der Voort Maarschalk et al., 1996b). Table 2 gives the bonding capacities of the different materials. According to this table, β-lactose gives the lowest porosity expansion and spray-dried sorbitol the highest, which is evidently not the case here (Fig. 3). So this approach is too simple here.

The idea that particle bonding has a counteracting effect on increase in void fraction (or porosity expansion) is based on the assumption that increase in void fraction is the result of a driving force and a resistance to an increase in void fraction: According to a previous paper, the resistance is determined by particle bonding (bonding capacity), i.e. a consequence of interparticle attraction and the reciprocal value of the increase in void fraction

$$= \frac{1}{\text{resistance}} \cdot \text{driving force} \tag{5}$$

resistance was referred to as 'expansion capacity' (Van der Voort Maarschalk et al., 1996b). The resistance is proportionally related with the bonding capacity. However, friction forces of the tablet with the die wall may also affect the propensity of a tablet to increase its void fraction. Large frictions between the die wall and the compact may also prevent the newly formed compact from expansion. Die wall frictions were quantified by measurements of ejection forces. The ejection force was corrected for tablet size according to Hölzer and Sjögren (1977). The resulting value is by definition called 'ejection friction' (P_{ej}) here, and calculated by:

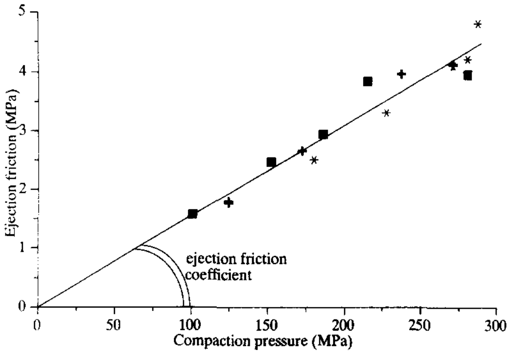

Fig. 4. Ejection friction of β-lactose as a function of compaction pressure (symbols as in Fig. 1)

$$P_{ej} = \frac{F_{ej}}{2 \cdot \pi \cdot r \cdot h} \tag{6}$$

with F_{ej} the maximum ejection force and the denominator the contact surface of the compact with the die (r is the radius and h the height of the compact). Fig. 4 gives an example of a material with large ejection friction (β-lactose). The figure shows a linear relation between ejection friction and no clear effect of compaction speed. Besides, extrapolation to zero compaction pressure shows that the ejection friction is zero, which is in accordance with observations of Hölzer and Sjögren (1977). The slope of the line in Fig. 4, defined as the 'ejection friction coefficient' (f_{ej}), was calculated for all materials in this study and the values are presented in Table 4. Assuming that 'resistance' in Eq. (5) is determined by bonding capac-

Table 4
Ejection friction coefficients

Material	Ejection friction coefficient (−)
Amorphous potato starch	$1.3 \cdot 10^{-3}$
Microcrystalline cellulose	$1.6 \cdot 10^{-3}$
Spray-dried sorbitol	$1.3 \cdot 10^{-2}$
β-Lactose	$1.5 \cdot 10^{-2}$
Sodium chloride	$2.0 \cdot 10^{-2}$

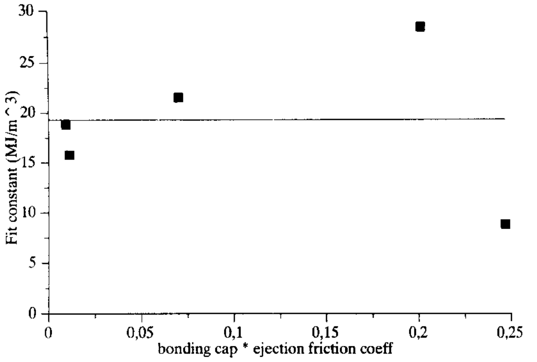

Fig. 5. The fit constant C as a function of the product of bonding capacity and ejection friction coefficient.

ity (k) and die-wall friction (f_{ej}), Eq. (5) can be rewritten as:

$$\Delta\Phi = \frac{1}{C\cdot k\cdot f_{ej}}\cdot W_{rev} \qquad (7)$$

were $\Delta\Phi$ is the increase in void fraction, W_{rev} the amount of stored energy and C is a fit constant. The constant k should be a quantification of the resistance in the tablet to pore creation (Van der Voort Maarschalk et al., 1996b) and f_{ej} should be a quantification of resistance to pore creation of the die wall-tablet interface. If the resistance to increase in void fraction is completely determined by interparticle bonding and die wall friction, the constant C will be independent on the material. According to Eq. (7) it is possible to calculate C from the slope of the line that describes the relation between stored energy and increase in void fraction and the values of bonding capacity and ejection friction coefficient. Fig. 5 gives the relation between the fit constant C and the product of the bonding capacity and the ejection friction coefficient. If C is independent of this product, the slope of te least-square fit will be zero. Fig. 5 points to values of C that are independent of the product of k and f_{ej}, suggesting that there is a relation between stored energy, bonding and friction on the one hand and creation of porosity on the other hand.

Realising again that stored energy causes stress relaxation of tablets, it is now possible to understand the varying relaxation behaviours of the different materials. The amount of stored energy of β-lactose is extremely large relative to the other materials as a result of large yield strengths (Table 1). The material has a large propensity to relieve stress. Due to high ejection friction coefficient and strong bonding, the expression of stress relief is that the tablets are capped. Sodium chloride, a material with even larger ejection friction coefficient than β-lactose, exhibits fewer capping problems because the amount of stored energy is much smaller (Table 1). At high compaction speed, and consequently large amount of stored energy, the combination of high stored energy and large ejection friction coefficient causes capping problems. The materials with small ejection friction coefficients (e.g. pregelatinized potato starch) show porous compacts because there is little resistance to increase in porosity.

On the basis of the concept described so far, it is concluded that in the consolidation stage, a compact is formed containing an amount of stress, quantified by stored energy. Stored energy will relieve and the expression of stress relaxation depends on resistance against expansion. The materials that exhibit low friction and bonding capacity (pregelatinized starch and microcrystalline cellulose) will create a porous structure. A porous compact is the result. In contrast, the materials with high resistance against increase in porosity are prevented from creation of a porous structure and the relief of stored energy will force the material to laminate or cap. It is therefore concluded that capped and porous tablets suffer from the same problem: large stored energies, but the expression of stress relief depends on the type of the material. The crystalline materials tend to suffer capping problems due to large ejection friction coefficient and bonding capacity, whereas the (partially) amorphous materials with low ejection friction coefficients show porous tablets. The frequently applied classification of materials as being either brittle or plastic is evidently not sufficient. For example, both sodium chloride and pregelatinized potato starch are classified as 'plastic' (Hardman and Lilley, 1970; Van der Voort Maarschalk et al., 1996a), but their plastic deformation characteristics are principally different, with almost incomparable relaxation properties as a result.

4. Nomenclature

A_{comp}	penetration depth
C	*constant*
f	frequency
f_{ej}	ejection friction coefficient
F_{ej}	ejection force
h	tablet height
k	bonding capacity
P_{ej}	ejection friction
r	tablet radius
$S(S_0)$	tensile strength (at zero porosity)
v	compaction speed
W_{rev}	ejection friction coefficient
$\Delta\Phi$	change in void fraction
$\epsilon(\Delta\epsilon)$	porosity (expansion)
ρ_{c}	compact density
ρ_{t}	true density

References

Bolhuis, G.K. and Chowhan, Z.T., Materials for direct compression. In: Alderborn, G. and Nyström, C., (eds.), *Pharmaceutical Powder Compaction Technology*. Marcel Dekker, New York, 1996, pp. 419–500.

Doelker, E., Comparative compaction properties of various microcrystalline cellulose types and generic products. *Drug Dev. Ind. Pharm.*, 19 (1993) 2399–2471.

Duckworth, W., Discussion of Ryshkewitch paper by Winston Duckworth. *J. Am. Ceram. Soc.*, 36 (1953) 68.

Fell, J.T. and Newton, J.M., The tensile strength of lactose tablets. *J. Pharm. Pharmacol.*, 20 (1968) 657–658.

Hardman, J.S. and Lilley, B.A., Deformation of particles during briquetting. *Nature*, 228 (1970) 353–355.

Heckel, R.W., An analysis of powder compaction phenomena. *Trans. Met. Soc. AIME.*, 221(1961a) 1001–1008.

Heckel, R.W., Density-pressure relationships in powder compaction. *Trans. Met. Soc. AIME.*, 221 (1961b) 671–675.

Hölzer, A.W. and Sjögren, J., Comparison of methods for evaluation of friction during tableting. *Drug Dev. Ind. Pharm.*, 3 (1977) 23–37.

Roberts, R.J. and Rowe R.C., The effect of punch velocity on the compaction of a variety of materials. *J. Pharm. Pharmacol.*, 37 (1985) 377–384.

Van der Voort Maarschalk, K., Vromans, H., Bolhuis, G.K. and Lerk, C.F., The effect of viscoelasticity and tabletting speed on consolidation and relaxation of a viscoelastic material. *Eur. J. Pharm. Biopharm.*, 42 (1996a) 49–55.

Van der Voort Maarschalk, K., Zuurman, K., Vromans, H., Bolhuis, G.K. and Lerk, C.F., Porosity expansion of tablets as a result of bonding and deformation of particulate solids. *Int. J. Pharm.*, 140 (1996b) 185–193.

Van der Voort Maarschalk, K., Vromans, H., Groenendijk, W., Bolhuis, G.K. and Lerk, C.F., Effect of water on deformation and bonding of pregelatinized starch compacts. *Eur. J. Pharm. Biopharm.*, Submitted (1996c).

Van der Voort Maarschalk, K., Zuurman, K., Van Steenbergen, M.J., Hennink, W.E., Vromans, H., Bolhuis, G.K. and Lerk, C.F., Effect of compaction temperature on consolidation of amorphous polymers with different glas transition temperatures. *Pharm. Res.*, Accepted (1996d).