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Effect of magnesium stearate on bonding and porosity expansion of tablets produced from materials with different consolidation properties

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Abstract

The negative effect of magnesium stearate on tablet strength is widely known. This strength reduction is always considered to be the result of reduction of interparticle bonding. It is also known that interparticle bonding affects relaxation of tablets. Relaxation increases with decreasing bonding. Microcrystalline cellulose is an example of a material with a high lubricant sensitivity, which effect is caused by its plastic deformation behavior during compression. This paper shows for microcrystalline cellulose that the porosity under pressure was equal for unlubricated tablets and for tablets containing 0.5% magnesium stearate. This points to equal densification properties. The lubricated tablets show, however, a much larger relaxation than the tablets without magnesium stearate. This difference can be ascribed to the reduction of interparticle bonding by the lubricant, because a strong interparticle bonding counteracts tablet relaxation. In contrast to microcrystalline cellulose, aggregated γ-sorbitol (Karion Instant) has a low lubricant sensitivity. Both porosity under pressure and tablet relaxation were found to be equal for lubricated and unlubricated sorbitol tablets. This phenomenon is caused by the particle structure of γ-sorbitol. During compression, a lubricant film will be destroyed by fragmentation of the sorbitol aggregates. For this reason, magnesium stearate will hardly affect the interparticle bonding between sorbitol particles and hence have only a small or no effect on tablet relaxation.

Keywords: Stored energy; Particle bonding; Relaxation; Tablet strength; Magnesium stearate; Microcrystalline cellulose; Sorbitol

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1. Introduction

Pharmaceutical tablets are normally composed of several ingredients. One of the ingredients is usually a lubricant that prevents the tablet from sticking to the die and punches and minimizes wear of them. Magnesium stearate is the most commonly used pharmaceutical lubricant. In several papers, however, it has been shown that magnesium stearate can have an adverse effect on bonding between particles (Strickland et al., 1956; Bolhuis et al., 1975; De Boer et al., 1978; Duberg and Nyström, 1982; Vromans and Lerk, 1988).

Additionally, it was recently demonstrated that interaction between particles affects the relaxation behavior of tablets (Rees and Tsardaka, 1994; Van der Voort Maarschalk et al., 1996b). Tablets produced from materials with low interparticle attraction tend to suffer from more relaxation than tablets made from materials where interparticle attractions are large. Realizing that magnesium stearate affects interparticle bonding and that the latter has an effect on tablet relaxation immediately after compression, it can be assumed that magnesium stearate is a component that alters the relaxation properties of tablets.

The present paper discusses the effect of magnesium stearate on bonding between particles in a compact and the consequenses of alterations in particle attractions on tablet relaxation.

2. Materials and methods

The materials used were magnesium stearate, (Genfarma, Maarssen, The Netherlands), microcrystalline cellulose (Pharmacel 102, DMV, Veghel, The Netherlands) with a mean particle size of 100 μm (15% was smaller than 32 μm and 96% was smaller then 200 μm, determined using an Air Jet Sieve), and spray-dried γ-sorbitol with a particle size between 106 and 212 μm. The sorbitol fraction was sieved from Karion Instant (Merck, Darmstadt, Germany) using an Air Jet Sieve (Alpine, Augsburg, Germany) equiped with USA Standard testing sieves (W.B. Tyler, Mentor, OH, USA).

The elastic modulus was measured by dynamic mechanical analysis (DMA) with a Rheometrics Solids Analyzer (Piscataway, NY, USA), at a frequency of 0.63 rad/s. The method has previously been described in more detail (Van der Voort Maarschalk et al., 1996a).

Compaction of 500 mg powder into flat-faced tablets with a diameter of 13 mm was carried out on a compaction simulator (ESH, Brierley Hill, UK). The upper punch displacement profiles were sine waves with different amplitudes in order to vary the maximum compression pressures. The average compaction rate was 3 mm/s, corresponding with the DMA frequency of 0.63 rad/s. The lower punch was stationary during compression. The ejection time was always 10 s.

For the production of tablets containing magnesium stearate ('lubricated tablets'), mixing of the filler-binder with magnesium stearate was performed with a Turbula-mixer, model 2P (W.A. Bachofen, Basle, Switzerland) at 90 rev/min for a period of 30 min. Before compression of the compacts from unlubricated matarial, the die was prelubricated with magnesium stearate.

Yield stress of the test materials was calculated from the force displacement profiles according to Heckel (1961a,b). Corrections were made for elastic punch deformation as previously described (Van der Voort Maarschalk et al., 1996b).

Tablet dimensions were measured at least 16 h after compaction with an electronic micrometer (Mitutoyo, Tokyo, Japan) and the tablets were weighed on an analytical balance.

Crushing strengths of the tablets were measured at least 16 h after compaction using the compaction simulator as previously described (Van der Voort Maarschalk et al., 1997a). Tensile strength of the tablets was calculated according to Fell and Newton (1968).

3. Results and discussion

Fig. 1 shows the relation between tensile strength and compaction pressure for tablets compressed from unlubricated microcrystalline cellulose and microcrystalline cellulose lubricated with 0.5% magnesium stearate, respectively. It can be seen that the presence of the lubricant causes a

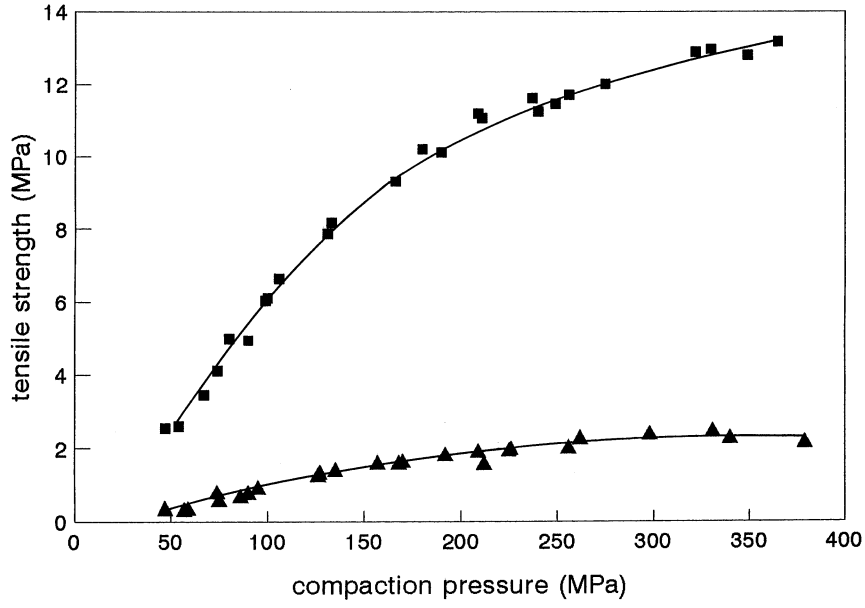

Fig. 1. Tensile strength of unlubricated (■) and lubricated (▲) microcrystalline cellulose compacts.

strong decrease in tablet tensile strength. The high lubricant sensitivity of microcrystalline cellulose and other excipients that undergo plastic deformation under compression has been explained in previous work by film formation of magnesium stearate upon the substrate particles during the mixing procedure (Bolhuis et al., 1975; De Boer et al., 1978). As shown in Fig. 2 (closed symbols) tablets containing magnesium stearate have a higher porosity than unlubricated ones that were compressed at the same compaction load. This observation suggests that either the densification (that is the porosity reduction of the microcrystalline cellulose/magnesium stearate blend under load) is more difficult, compared to the powder without magnesium stearate, or the lubricated tablets show a larger increase in volume due to a higher stress relaxation after compaction.

Powder densification can be studied by the determination of the yield strength of a material. A high yield strength is related with difficult densification, i.e. larges pressures are necessary to reach a certain porosity. Table 1 shows that the presence of 0.5% magnesium stearate results in a small decrease in yield strength of this microcrystalline cellulose mixture. This effect points to facilitating of powder densification by magnesium stearate, just as has been found previously for a number of directly compressible materials (Vromans and Lerk, 1988). The open symbols in Fig. 2 show, however, that the minimal attainable porosity under pressure is simular for unlubricated and lubricated microcrystalline cellulose powder, when pressed at a certain load. Based on this observations one would expect about the same porosities (after ejection) for unlubricated and lubricated tablets when compressed at equal loads.

However, the closed symbols in Fig. 2 show a higher porosity of lubricated tablets after relaxation. The latter must hence be caused by a higher porosity expansion after compression of the powder blend. From previous data (Van der Voort Maarschalk et al., 1998) it became clear that all pore formation was a result of phenomena occuring after decompression (i.e. after punch release). These data demonstrate that the compacts produced from a blend of microcrystalline cellulose and magnesium stearate suffer from more stress relaxation than compacts made from microcrystalline cellulose only.

A method to estimate the stress relaxation propensity is calculation of the amount of elastic

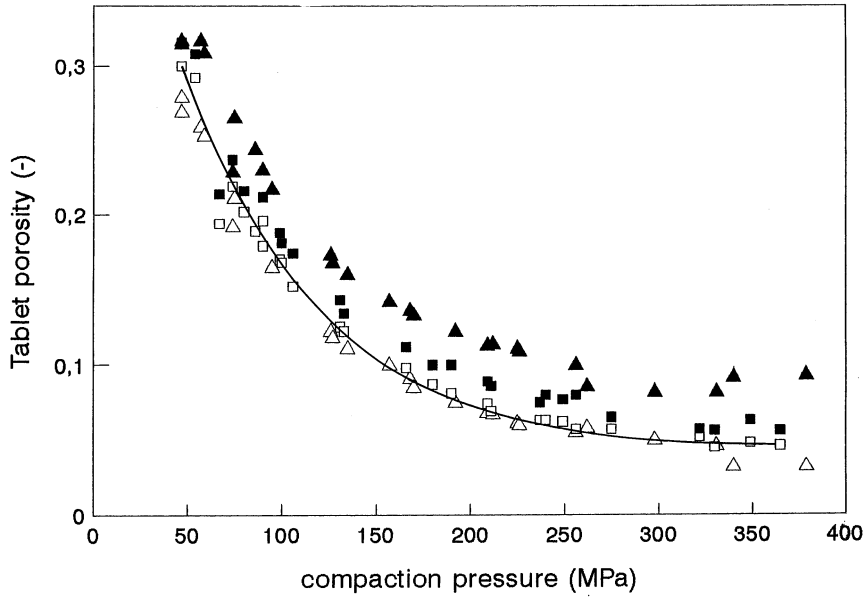

Fig. 2. Tablet porosity under pressure (open symbols) and after relaxation (closed symbols) as a function of compaction pressure. Symbols as in Fig. 1.

energy stored during compression (Van der Voort Maarschalk et al., 1996a):

$$W = \frac{1}{2} * \frac{\sigma_c^2}{E} \quad (1)$$

in which: E is the elastic modulus; and σ_c the yield strength of the material.

Table 1 lists yield strengths, elastic moduli and calculated stored elastic energy for microcrystalline cellulose, the blend of microcrystalline cellulose with 0.5% magnesium stearate and magnesium stearate. The data suggest that the amount of stored energy increases enormously upon addition of magnesium stearate. The reason for this large increase is the extremely small elastic modulus measured for the lubricated material.

The elastic modulus of the non-porous compacts is calculated by extrapolation of data obtained from compacts with different porosities to zero porosity. The validity of this approach is questionable, however. The stress relaxation expressed by stored energy is a property of the bulk of the material: it expresses the propensity of the particles to regain their original shapes. As already indicated, mixing with magnesium stearate covers the surface of microcrystalline cellulose and this phenomenon may have a large influence on the bonding of the particles in the strips used in DMA measurements. Table 1 suggests that strips without magnesium stearate are much stiffer than strips with magnesium stearate. However, there are no reasons to suppose that the rigidity of the microcrystalline cellulose particles in a strip changes upon the addition of a small amount of lubricant. For this reason, the data for the elastic modulus of strips containing magnesium stearate must be considered as an artefact: it is more a measure of the stiffness of the bonding between the particles than a measure of the stiffness of the particles themselves (Van der Voort Maarschalk et al., 1996b). Consequently, simple measurement of the elastic modulus of compacts made from binary mixtures may lead to erroneous values. Exactly the same consideration is applicable when explaining the neglectible effect of magnesium stearate addition on yield strength. The yield strength is a measure of the force necessary to deform a particle permanently. This value is clearly related with the bulk properties of the material. The small amount of magnesium

Table 1
Yield strength, elastic modulus and stored energy of microcrystalline cellulose (mcc) without and with magnesium stearate (MgSt)

PRIVATE Material	Yield strength (Mpa)	Elastic modulus (GPa)	Stored energy (kJ/m^3)
mcc (pure)	21	12	18
mcc + 0.5% MgSt	19	2	89
mcc + 1.0% MgSt	18	1	166
MgSt (pure)	6	_[a]	_[a]

[a] Not measurable.

stearate will not have a significant effect in this type of yield strength determination.

Another approach is to estimate the stored energy on the basis of the stored energy of the individual components. Assuming that the presence of a second material does not affect the viscoelastic properties of the first material in a mixture, the energy stored by deformation of the individual particles can be calculated by:

$$W_{\text{mix}} = W_{\text{cell}} * \varphi_{\text{cell}} + W_{\text{mgst}} * \varphi_{\text{mgst}} \quad (2)$$

with φ_{cell} and φ_{mgst} the volume fractions microcrystalline cellulose and magnesium stearate, respectively.

The stored energies can be calculated as described in Eq. (1) using the yield strength and elastic moduli of the individual components.

So, Eq. (2) may be written as:

$$W_{\text{mix}} = \frac{1}{2} * \frac{\sigma^2_{\text{c,cell}}}{E_{\text{cell}}} * \varphi_{\text{cell}} + \frac{1}{2} * \frac{\sigma^2_{\text{c,mgst}}}{E_{\text{mgst}}} * \varphi_{\text{mgst}} \quad (3)$$

The volume fraction of magnesium stearate is always very low relative to the fraction microcrystalline cellulose. Moreover, the yield strength of magnesium stearate is low compared to that of microcrystalline cellulose (Table 1). Unfortunately, it is impossible to determine the elastic modulus of magnesium stearate, so the relative contribution of the lubricant cannot be calculated. However, if the elastic modulus of magnesium stearate is not extremely low, its contribution to the amount of energy stored in a tablet upon compression will be neglectible. As the volume fraction of magnesium stearate in a tablet is low, it is very plausible to conclude that the amount of stored energy in a tablet with a small amount of magnesium stearate is about the same as that in a tablet without magnesium stearate.

The data discussed so far show that relaxation phenomena in terms of stored energy are equal for tablets formed within or out of the presence of magnesium stearate. The different relaxation for lubricated and unlubricated tablets in terms of volume or porosity change implies that bonding phenomena play an important role here.

The latter is important, because it counteracts tablet relaxation (Van der Voort Maarschalk et al., 1996a).

In previous work, it has been demonstrated that the interaction between particles in a tablet can be derived from the relationship between tensile strength and porosity (Van der Voort Maarschalk et al., 1996b). Fig. 3 shows profiles for both unlubricated and lubricated microcrystalline cellulose tablets and it can easily be seen that the relationship between tensile strength and porosity changes dramatically as an effect of the presence of magnesium stearate. The profiles are fitted according to the Ryshkewitch–Duckworth relation (Duckworth, 1953):

$$\ln\frac{S}{S_0} = -k \cdot \varepsilon \quad (4)$$

in which S is the tensile strength, S_0 is the tensile strength at zero porosity, ε is the porosity of the tablets, and k is a constant, in previous work referred to as 'bonding capacity' (Van der Voort Maarschalk et al., 1996b).

Table 2 lists the parameters obtained by means of Eq. (4). These calculated values indicate that the bonding capacity as quantified by k is larger in compacts containing magnesium stearate. This is in sharp contrast with any other observation. It

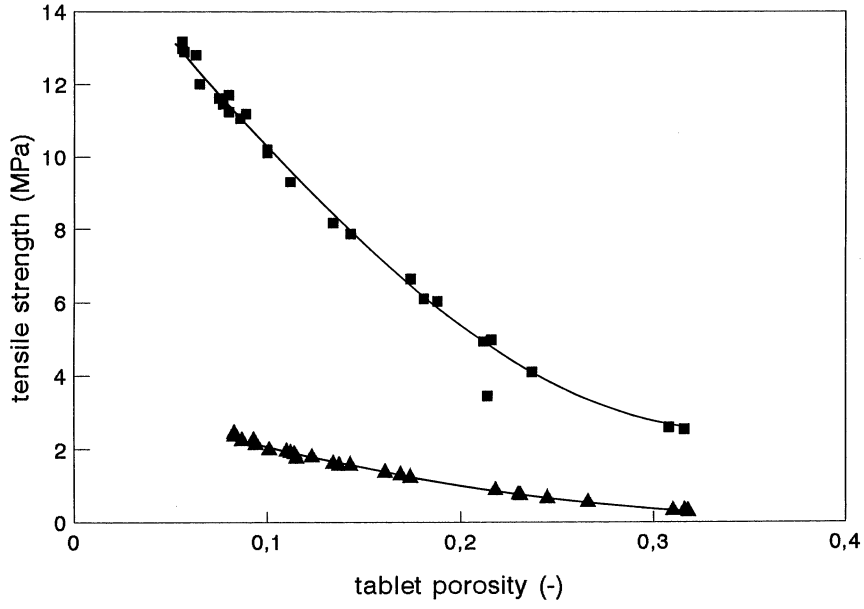

Fig. 3. Tensile strength as a function of tablet porosity. Symbols as in Fig. 1.

implies that the previous interpretation of k is not possible when dealing with a system containing more than one component. Addition of magnesium stearate to microcrystalline cellulose turns the powder into a binary system. It is noted that according to the correlation coefficients (depicted in Table 2), the Ryshkewitch–Duckworth equation fits the data acceptably.

In a binary system of components A and B, there are three types of particle interaction: a cohesive interaction A–A, a cohesive interaction B–B and an adhesive interaction A–B. For a binary system of a filler-binder (A) and a lubricant (B), the cohesive attraction A–A is strong, because otherwise the material would not be a good filler-binder for direct compaction. It is generally known that adhesive interaction A–B between a lubricant such as magnesium stearate and a filler-binder is poor (Bolhuis and Hölzer, 1996). The cohesive interaction B–B between magnesium stearate particles is also poor and has the same order of magnitude as the interaction A–B between magnesium stearate and a filler-binder (Rowe, 1988).

Table 2
Tensile strength at zero porosity and constant k calculated from the Ryshkewitch–Duckworth relation of tablets compressed from microcrystalline cellulose and sorbitol, respectively, with and without magnesium stearate

PRIVATE Material	S_0 (MPa)	k (−)	R^{2a}
mcc (pure)	19.1	6.5	0.979457
mcc + 0.5% Mgst	4.9	8.0	0.993529
Sorbitol (pure)	11.5	6.6	0.915007
Sorbitol + 0.5% Mgst	8.8	9.1	0.994256

[a] R^2 = correlation coefficient.

Which type of interparticle attraction dominates the tablet strength is determined by the type of consolidation of the main component. With the exception for filler-binders which show completely plastic deformation (e.g. starch) or completely fragmentation under load (e.g. dicalcium phosphate dihydrate), most filler-binders show various extends of fragmentation, which means that particle fracture will be a function of the pressure exerted (Van der Voort Maarschalk and Bolhuis, 1998a,b). As an effect of fragmentation, the dominating attraction type will change. During mixing with magnesium stearate, the filler-binder will be covered with the lubricant and attraction types B–B and A–B will dominate. At increasing compaction pressures, however, attraction type A–A will become more and more important as an effect

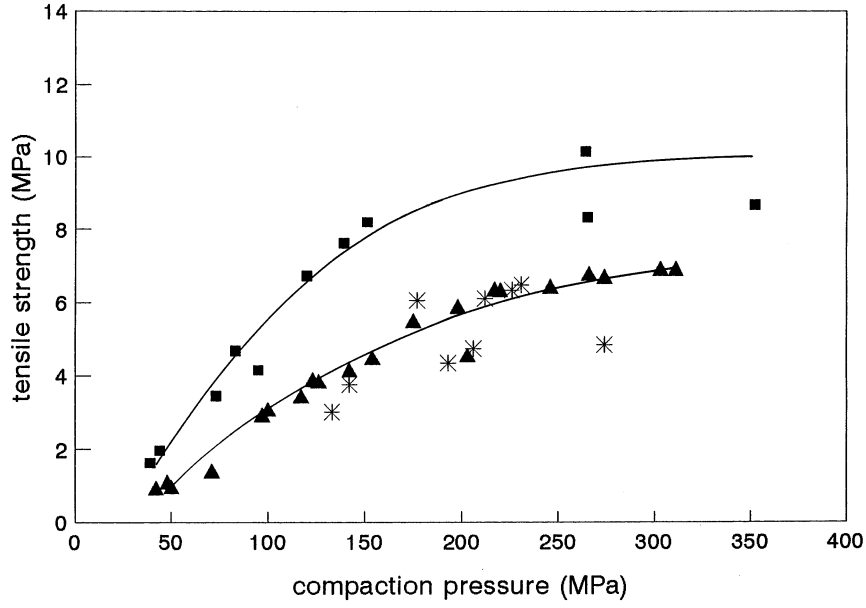

Fig. 4. Tensile strength of unlubricated (■) and lubricated (▲) sorbitol compacts. Data plotted by (*) reflect unlubricated sorbitol compacts which show beginning of capping.

of particle fragmentation, which successively replaces the continuous network of the lubricant by a network of the filler-binder. The increase of the importance of attraction type A–A and the decrease of the importance of the attraction types A–B and B–B at increasing compaction forces means that the bonding capacity k in Eq. (4) will be a function of the compaction pressure and hence of the tablet porosity. Just as could be expected, Table 2 shows a dramatic decrease in tensile strength at zero porosity for lubricated tablets. It should be realized, however, that extrapolation to zero porosity leads to unreliable results because the slope of the relation in Eq. (4) is k. Consequently, it must be concluded that the use of both k and S_0 leads to an erronous interpretation of particle bonding when the material under study is a binary system of a filler-binder and a lubricant.

Without currently being able to quantify interparticle attraction of binary systems, the data in this paper indicate that relaxation of compacted material increases when interparticle attraction is disturbed. There are no reasons to accept that the driving force for relaxation changes because it is a bulk property of the particles. Consequently the increased relaxation is purely a result of decreased interparticle bonding.

Fig. 4 depicts the relationship between tensile strength and compaction pressure of tablets produced from pure sorbitol and sorbitol lubricated with 0.5% magnesium stearate. Data plotted by an asterix reflect unlubricated sorbitol tablets which do not fit the corresponding curve. This discrepancy must be ascribed to beginning capping of the tablets, according phenomena reported by, for example Marshall et al. (1993). As compared with microcristalline cellulose (Fig. 1), the lubricant has a much smaller effect on the tensile strength. Fig. 5 shows the relationship between tablet porosity and compaction pressure for unlubricated and lubricated sorbitol tablets, respectively. Porosities below zero proves densification of the material under pressure (Van der Voort Maarschalk et al., 1997b). Just as found for microcrystalline cellulose tablets, the porosity under compression was similar for unlubricated and lubricated sorbitol tablets, which effect points to a similar amount of stored elastic energy. In contrast to microcrystalline cellulose tablets, however,

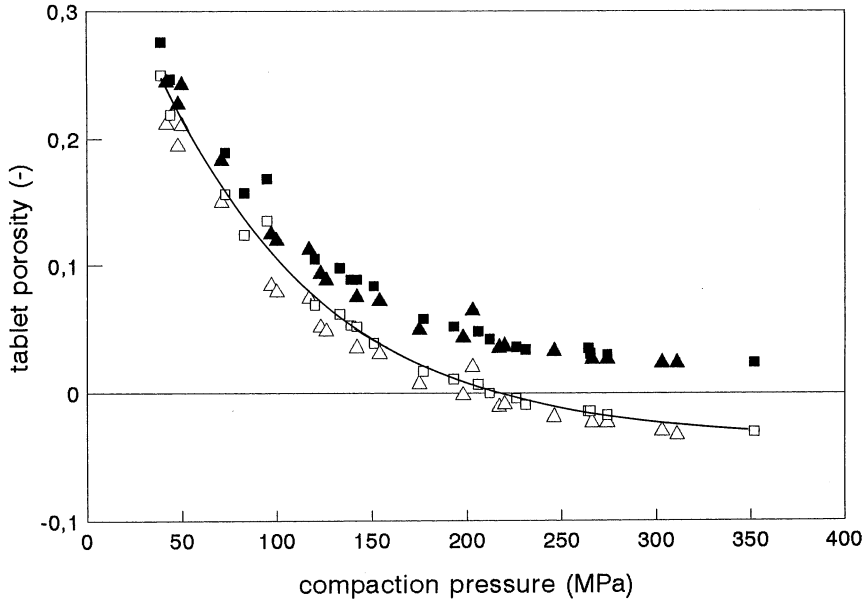

Fig. 5. Tablet porosity under pressure (open symbols) and after relaxation (closed symbols) as a function of compaction pressure. Symbols as in Fig. 4.

the relaxation of lubricated sorbitol tablets was about the same as that of unlubricated sorbitol tablets, which is in agreement to the small difference in tensile strength of lubricated and unlubricated tablets.

The relatively small effect of admixing magnesium stearate can easily be understood when the particle structure of the material is known. Spray-dried γ-sorbitol particles consist of aggregates of very small primary particles (Bolhuis and Chowhan, 1996). Mixing the powder with magnesium stearate during 30 min, the aggregates will completely be covered by the lubricant. The fact that the powder particles are aggregates implies that they have a brittle fracture behavior. During compaction a lot of fresh, new surfaces will be formed. This means that the interparticle attraction will predominantly be of type A–A. Apparently, fracture occurs already in the early stages of compression, which leads to isolated patches of magnesium stearate rather than a continuous network of it (Riepma et al., 1993).

The strong interparticle attraction between sorbitol particles which counteracts relaxation is almost similar for both lubricated and unlubricated sorbitol tablets. Consequently there is only a small effect of magnesium stearate on tablet strength.

In conclusion, this paper shows that a part of the decrease in tablet strength by mixing pharmaceutical powders such as microcrystalline cellulose with magnesium stearate is caused by a more extensive relaxation of the lubricated tablets.

As the amount of stored elastic energy was found to be simular for lubricated and unlubricated tablets, the increased relaxation of the lubricated tablets will be caused by their smaller particle attraction and the consequent reduced resistance against relaxation. The increase of tablet relaxation as an effect of mixing with magnesium stearate is smaller when using materials which fragment during the compaction process.

4. Nomenclature

k; bonding capacity
S (S_0); tensile strength (at zero porosity) (Pa)
ε; porosity

$W_{(mix)}$; calculated amount of stored energy in a mixture (J/m^3)
$W_{(cell)}$; calculated amount of stored energy in microcrystalline cellulose (J/m^3)
$W_{(mgst)}$; calculated amount of stored energy in magnesium stearate (J/m^3)
φ_{cell}; volume fraction of microcrystalline cellulose
φ_{mgst}; volume fraction of magnesium stearate
$\sigma_{c,cell}$; yield strength of microcrystalline cellulose (Pa)
$\sigma_{c,mgst}$; yield strength of magnesium stearate (Pa)
E_{cell}; elastic modulus of microcrystalline cellulose (Pa)
E_{mgst}; elastic modulus of magnesium stearate (Pa)

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