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Compaction and measurement of tablets in liquids with different dielectric constants for determination of bonding mechanisms—evaluation of the concept

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Abstract

In order to study bonding mechanisms in tablets, liquids with increasing dielectric constants have been used to filter out weak long range distance forces. The aim of this study was to further critically evaluate this concept.

Tablets of sodium chloride, sodium bicarbonate, Avicel®, Emcompress®, lactose and sucrose were compacted in media with dielectric constants from 1 to 24 and the remaining tensile strength of tablets compacted in liquid was calculated. With increasing dielectric constant a continuos decrease in tensile strength was obtained and at a dielectric constant above approximately 10–15, a plateau level was reached for all materials except for Avicel®. This level was assumed to reflect the proportion of solid bridges in the compact and the values were consistent with previous data reported from our laboratory.

The results also showed that by compacting particles suspended in a liquid a more effective reduction of long range distance forces was obtained, than if tablets were compacted in air followed by a soaking process in liquid.

Compaction in liquids may be unsuitable for some materials due to swelling or changes in volume reduction behaviour. Nevertheless, the method appears to be favourable for studying bonding mechanisms, especially for tablets with a low porosity.

Keywords: Bonding mechanism; Compaction; Dielectric constant; Liquid; Remaining tensile strength; Tablet

1. Introduction

Generally the tensile strength of a compact is considered to be primarily determined by two parameters: the type of bonding mechanism between the powder particles in the tablet and the area over which these bonding forces act (Nyström et al., 1993). Different bonding mechanisms have been described (Führer, 1977; Rumpf, 1958), but generally the bonding mechanisms in pharma-

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ceutical compacts are divided into three different types (de Boer et al., 1978; Führer, 1977): solid bridges, weak long range forces (intermolecular forces) and mechanical interlocking.

A method of distinguishing between the bonding mechanisms is necessary in order to evaluate their relative importance. In order to develop such a method, the bonding mechanisms must first be clearly defined.

1.1. Types of interparticulate bonding mechanisms

Solid bridges, or sinter bridges, are often described as areas of particle to particle contact on an atomic level and can thus be considered as a continuous phase of powder material between the particles. The molecules or ions in the solid bridge between particles are thus assumed to be arranged and bonded in the same manner as those inside each particle.

Weak long range distance forces, i.e. van der Waals forces, hydrogen bonds and electrostatic attraction forces, are likely to occur when the distance between the particles is less than approximately 100–1000 Å (Israelachvili, 1992a). Van der Waals forces occur between almost all molecules and particles. Their strength is dependent on the type of material, the distance between the molecules or particles and the medium surrounding them (Israelachvili and Tabor, 1973). They are considered to be the dominating bonding mechanism between solid surfaces when the surrounding medium is air. Hydrogen bonds occur primarily through electrostatic interaction, either intra- or intermoleculary. In order for these bonds to be established, a hydrogen atom must be in connection with an electron attracting atom in the molecule (Israelachvili, 1992b). Electrostatic forces arise during mixing and compaction due to tribo-electric charging. These forces are neutralised with time via electrostatic discharging. For compacts stored at normal relative humidities or in liquids this is likely to be a relatively fast process since the electrostatic charge is highly diffusable in the liquid or the adsorbed liquid layers (Shirvinskii et al., 1984).

The third important bonding mechanism is mechanical interlocking, which implies that particles can hook or twist together and thus contribute to the strength of the compact. This would normally occur if the particles were elongated and/or irregular (Führer, 1977).

1.2. Studies of bonding mechanisms

Different approaches have been used to distinguish between solid bridges and weak long range distance forces. These include conductance measurements in the compacts (Bhatia and Lordi, 1979) and the use of magnesium stearate as a barrier against distance forces between particles (de Boer et al., 1978; Nyström et al., 1993). The first method requires that the material has some ability to conduct an electrical current. In the second method, the added magnesium stearate may possibly affect the force distribution and thus the compaction process.

An alternative to these methods involves the use of liquids with different dielectric constants which have the ability to screen out weak long range distance forces. This approach has been used in experiments where tablet tensile strength has been measured after soaking the tablet in various liquids (Fraser, 1973; Luangtana-anan and Fell, 1987; Luangtana-anan and Fell, 1988; Luangtana-Anan and Fell, 1990) and also in disintegration studies of tablets (Luangtana-anan et al., 1992). Karehill and Nyström (1990) used a technique where the tablets were both compacted and their strength was characterised in liquid.

The concept of soaking tablets in liquids with different dielectric constants after compaction in air has advantages in that an ordinary instrumented tablet machine may be used. The actual soaking of the tablet is, however more difficult. The viscosity, surface tension and the angle of contact between the liquid and the solid material as well as the pore structure of the tablet may affect the penetration of liquid into every pore (Washburn, 1921), which is a prerequisite for reduction of the weak long range distance forces. The possible formation of dense peripheral zones in the tablet ('tablet skin'), caused by high shear forces developed during compaction (Train and Hersey, 1960), could also decrease liquid penetration. However, wetting of the powder is simplified if the powder is suspended in a liquid during compaction. This has the added advantage of avoiding pores containing air forming during compaction. The change of medium from gas to liquid may, however, affect the compacts formed, for example by altering the volume reduction behaviour, force distribution and post compaction phenomena.

The concept of using liquids with different dielectric constants as a means of reducing weak long range distance forces between surfaces may be derived from the following equations (Luangtana-Anan and Fell, 1990).

$$W = -A/12\pi d^2 \quad (1)$$

The van der Waals energy of interaction (W) between two surfaces is dependent on the Hamaker constant (A) and the distance between the two surfaces (d). The Hamaker constant is an expression of the interactive forces between the surfaces and can according to Luangtana-Anan and Fell (1990) be expressed as (Eq. (2))

$$A_{s/l} = 24\pi d^2 \gamma_{s/l} \quad (2)$$

where γ is the surface energy of the particles in the system and s/l denotes the two phases—in this case the solid particle and the medium surrounding it.

The surface energy of a particle is affected by the dielectric constant of the medium surrounding the particle (Luangtana-Anan and Fell, 1990). A high dielectric constant results in lower surface energy and thus a reduction of the strength of the van der Waals forces. As a consequence, the strength of the van der Waals forces holding the tablet particles together is proportional to the dielectric constant of the medium separating the particles from each other. A high dielectric constant results in lower surface energy and thus a reduction in the strength of the van der Waals forces in the compact.

Van der Waals forces between two surfaces may be defined as dispersion or polar forces, each of which acts independently. Consequently, the discussion above is true for materials which have a significant polar component to the surface free energy (Luangtana-Anan and Fell, 1990). All materials in this study are considered to fall into this category. An increase in the dielectric constant of the medium separating the powder particles was therefore assumed to reduce the tensile strength of the compacts in this study.

Solid bridges are unlikely to be affected by a moderate increase in dielectric constant, since they consist of a continuous phase of solid material. If the dielectric constant is increased to a greater extent, however, the subsequent increase in solubility of the material is likely to affect the bonding structure of the compact and thus limit the feasibility of the test.

According to Karehill and Nyström (1990), the tensile strength of tablets compacted in liquids decreases with increasing dielectric constant, reaching a plateau at a dielectric constant of between 10 and 20. The authors suggest that this is the point where the van der Waals forces are totally annulled by the dielectric constant. Thus, if the tablet still possesses a measurable tensile strength, this could be caused by solid bridges and/or mechanical interlocking. By using this approach, the complicated measurements of surface energies and distances between particles in the compact are avoided, but at the expense of assuming that the change of media does not affect anything except the degree of van der Waals forces.

The aim of this study was to further study and critically evaluate the concept of compaction and strength characterisation of tablets in media with different dielectric constants, in order to evaluate bonding mechanisms.

2. Materials and methods

2.1. Powders

The following materials were investigated: sodium chloride (crystalline, puriss Ph Eur., Kebo Lab., Sweden), sodium bicarbonate (crystalline, puriss Ph. Eur., Kebo Lab., Sweden), microcrystalline cellulose (Avicel® pH 101, FMC, USA),

Table 1
Primary characteristics of test materials

Material	Size fraction (μm)	Apparent particle density (g/cm^3)	Melting point (°C)	Solubility in ethanol (g/ml)[1,2]	Solubility in water (g/ml)[1]
Sodium chloride	180–355	2.152	801	0.004 (25°C)	0.36 (25°C)
Sodium bicarbonate	90–180	2.214	270 (with decomposition)	Practically insoluble	0.09
Avicel®	Used as supplied	1.571	260–270 (charring temperature)	—	Practically insoluble
Emcompress®	180–355	2.341	decomposes below 100	Practically insoluble	Practically insoluble
Lactose	180–355	1.535	201–202	Practically insoluble (25°C, 100% ethanol)	0.22 (25°C)
Sucrose	180–355	1.588	160–186 (with decomposition)	0.006	2.0

American Pharmaceutical Association, Handbook of Pharmaceutical Excipients, London 1994.
[1] At 20°C unless otherwise stated.
[2] 95% ethanol unless otherwise stated.

calcium hydrogen phosphate dihydrate (Emcompress® USP/NF, Albright and Wilson LTD, UK), lactose (α-monohydrate, Swedish Sugar Co., Sweden) and sucrose (crystalline, Swedish Sugar Co., Sweden). A size fraction of 180–355 μm was prepared for all materials, except for Avicel® which was used as supplied, and sodium bicarbonate where a size fraction of 90–180 μm was used. The size fractions were obtained by dry sieving with laboratory sieves (Retsch, Germany). All compounds were stored in a desiccator over saturated chrome trioxide in water (40% relative humidity) (Nyqvist, 1983) for at least 2 days before using. The apparent particle densities of the raw material were measured using an helium pycnometer (AccuPyc 1330, Micromeritics, USA). The results are shown in Table 1. The range of materials chosen for testing had significantly polar surface free energy and represented both plastically deforming materials and those that fragmented under pressure.

2.2. Media

The liquids used for compaction and strength measurements included n-hexane, ethyl benzoate, (1)-hexanol, (1)-butanol and ethanol. All liquids except for ethanol had a water content less than 2% and were obtained from Kebo Lab, Sweden. Ethanol (water content 5%) was obtained from Kemetyl, Sweden. Before the liquids were used they were saturated with the respective test material in order to avoid dissolution problems. The dielectric constants and other characteristics of these liquids are given in Table 2. When tablets were compacted in air the dielectric constant was approximated to unity, which is the dielectric constant of vacuum.

2.3. Compaction

All compactions were made using a hydraulic press (Apex, UK) and flat faced punches with a diameter of 1.13 cm in a specially designed apparatus described by Karehill and Nyström (1990). The punches and die were fitted into a chamber containing the medium used. The powder for each tablet was weighed on an analytical balance and the die was then filled manually. The compaction procedure was carried out as described by Karehill and Nyström (1990).

The maximum compression load (100 MPa) was within ± 3% of the mean value presented. The die was not lubricated prior to compaction, except with the Emcompress® tablets, since ejection from the die was not possible without pre-

Table 2
Liquid media used in bond testing

Medium	Dielectric constant[a]	Boiling point (C)	Thermal conductivity (W/mK)	Surface tension (dynes/cm)[c]
Air	1.0	—	0.03	—
n-hexane	1.9 (20°C)	69.0	0.14	18.4 (air)
Ethyl-benzoate	6.0 (20°C)	211-213[b]	—	35.5
(1)-hexanol	13	158	0.16	—
(1)-butanol	18	117	0.15	24.6 (air or vapour)
Ethanol	24	78.5	0.17	22.8

CRC, Handbook of Chemistry and Physics, Cleveland 1970 unless otherwise stated.
[a] At 25°C unless otherwise stated.
[b] Merck and Co. Inc. The Merck index, Rahway 1976.
[c] In contact with vapour unless otherwise stated.

compaction lubrication with 1% magnesium stearate suspended in ethanol. However, when the Emcompress® tablets were compacted in liquids, lubrication was not used so as to avoid interaction between the lubricant and the bonding forces in the compact. After compaction the tablets were stored for 48 h in the same medium that was used for compaction. The tablets compacted in air were stored at 40% relative humidity as described for the storage of the powders.

2.4. Characterisation of the tensile strength

The diametral compression test according to Fell and Newton (1970) was performed to investigate the tensile strength of the tablets. The fracture force of the tablets was measured in a steel cup containing the same medium that the tablets were compacted and stored in, using a material tester (M 30 K, Lloyd Instruments, UK).

2.5. Characterisation of powder and tablet surface area

The surface areas of sodium chloride, sodium bicarbonate, Emcompress®, lactose and sucrose powders were determined by permeametry ($n = 3$) using Friedrich equipment as described by Eriksson et al. (1990). The surface area of Avicel® powder was also determined by permeametry but by using a Blaine apparatus ($n = 3$).

The surface area of the tablets compacted in air was also investigated by permeametry using a Blaine apparatus ($n = 3$). Each tablet was fitted to the top of the apparatus using a device described by Alderborn et al. (1985a). The tablets compacted in butanol were left on a metal net for 48 h for the butanol to evaporate. They were then put in a desiccator for 48 h before the surface area was measured ($n = 6$) as for the tablets compacted in air. The surface areas were calculated using the Kozeny-Carman equation corrected for slip flow, and the porosities of the tablets were calculated from their dimensions (Alderborn et al., 1985b). The results are shown in Table 3.

2.6. Tensile strength as a function of alternating drying and wetting/soaking of compacts

Tablets compacted in butanol or air were alternately stored in butanol and in air (40% relative humidity). The tensile strength was tested before each transfer to a new storage medium. After this process tablets compacted in butanol were placed in a mercury porosimeter (AutoPore III, Micromeritics, USA) and the pressure was brought down to 20 μm Hg for approximately 3 min to ensure maximum evaporation of liquids from the tablet pore system. The tablets were then left in a desiccator for 48 h before the tensile strength was again tested.

Table 3
Primary characteristics of powders and compacts

Material	Powder Sv (cm-1)	Tablet Sv—dry compacted (cm-1)	Tablet Sv—compacted in butanol (cm-1)	Tablet porosity—dry compacted (%)	Tablet porosity—compacted in butanol (%)
Sodium chloride (180–355 μm) 100 MPa	235 (2.8)	974 (239)	870 (148)	13.76 (1.55)	14.71 (1.50)
Sodium bicarbonate (90–180 μm) 100 MPa	651 (4.2)	2088 (270)	3066 (114)	21.85 (0.98)	21.71 (0.86)
Avicel® (raw material) 100 MPa	5773 (69.1)	24 675 (2741)	14 163 (1019)	20.84 (2.02)	26.34 (0.95)
Emcompress® (180–355 μm) 100 MPa	757 (10.3)	37 469 (2004.3)	18 290 (6660)	24.46 (1.44)	33.31 (0.48)
Lactose (180–355 μm) 100 MPa	392 (6.3)	3999 (100)	11 773 (1391)	14.10 (0.75)	18.01 (3.14)
Sucrose (180–355 μm) 100 MPa	265 (0.9)	3289 (401)	18 345 (4188)	15.28 (0.78)	18.90 (3.27)

Average values of at least three measurements and the corresponding standard deviation in parentheses. Sv denotes the volume specific surface area.

3. Results and discussion

3.1. Compaction of tablets in media with different dielectric constants

3.1.1. Absolute changes in tensile strength

The tensile strength of all tablets made in this study decreased as the dielectric constant of the liquid medium used in compaction increased (Fig. 1a and 1b). For all materials except Avicel® the tensile strength decreased rapidly to reach a plateau at higher dielectric constants. The tensile strength of the Avicel® tablets continued to decrease at higher dielectric constants. For two of the materials zero strength was reached within the range of dielectric constants applied.

The bonding mechanisms in this study are assumed to be comprised predominantly of solid bridges and weak long range distance forces and the assumption was made that the plateau seen in Fig. 1a occurred because all weak long range distance forces were filtered out. Thus, the remaining tensile strength could be considered as an estimate of the strength of the solid bridges in the compact.

Relatively stable plateaus were achieved for sodium chloride, sodium bicarbonate, lactose and sucrose above a dielectric constant of approximately 10–15. The tensile strength of tablets compacted in liquids with higher dielectric constant than 24 was not investigated, but it seems likely that the remaining tensile strength would eventually decrease since the solubility of the material increases, leading to the rupture of strong bonds such as ion bonds.

Avicel® differed from the other materials in that the tensile strength continued to decrease with increasing dielectric constant without reaching a stable plateau (Fig. 1b). This may be attributed to the increased tendency for this material to swell in media with higher dielectric constants (Ek et al., 1995; Ferrari et al., 1996; Reier and Shangraw, 1966). This can also be seen in Fig. 1b where the increase in tablet height at a dielectric constant of 24 coincides with a considerable drop in tensile strength.

A tensile strength close to zero was obtained at dielectric constants above 18 for Emcompress®. The extensive fragmentation tendency and the complex crystallographic structure of this material resulted in low values of tensile strength when compaction was carried out in liquids with increasing dielectric constants.

The results of compacting sodium chloride, Avicel® and lactose in liquids with different dielectric constants were in accordance with data reported by Karehill and Nyström (1990).

3.1.2. Relative changes in tensile strength

In order to facilitate the evaluation of dominating bond type and to compare the importance of solid bridges as a bonding mechanism for different materials the percentage remaining tensile strength (RTs) was calculated according to equation 3 where $Ts_{(l)}$ and $Ts_{(a)}$ denote the tensile strength in liquid and air respectively.

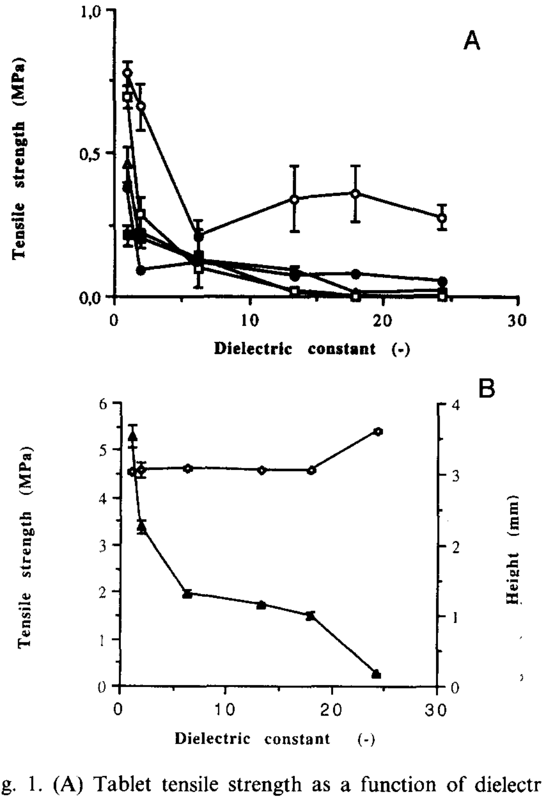

Fig. 1. (A) Tablet tensile strength as a function of dielectric constant. ○ sodium chloride; ● sodium bicarbonate; △ Emcompress®; ■ lactose; □ sucrose. (B) Tablet tensile strength (▲) and tablet height (◇) as functions of dielectric constant for Avicel®. Standard deviations shown where they exceed the dimensions of the symbol.

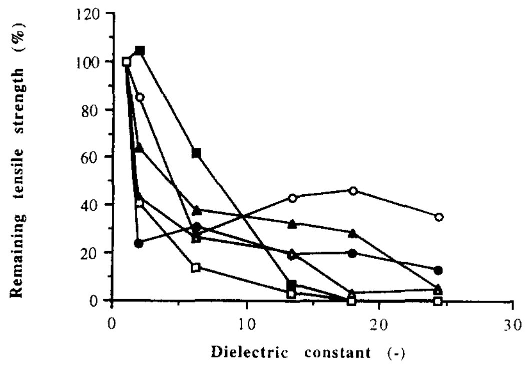

Fig. 2. Remaining tablet tensile strength as a function of dielectric constant. Legends as in Fig. 1.

$$RTs = \frac{Ts_{(l)}}{Ts_{(a)}} 100 \tag{3}$$

The percentage remaining tensile strength is shown as a function of dielectric constant in Fig. 2.

The remaining tensile strength of sodium chloride at the plateau level is significantly higher than for the other materials, which suggests a greater propensity for this material to form solid bridges. Support for the conclusion that coarse sodium chloride in particular has a greater tendency to form solid bridges than the other materials in this study can be found in the literature (de Boer et al., 1978; Führer, 1977; Karehill and Nyström, 1990; Nyström et al., 1993).

Sodium bicarbonate has been described as a material with a similar volume reduction behaviour to that of sodium chloride, but a considerably higher yield pressure (Duberg and Nyström, 1986). This and the relatively more complex crystallographic structure have been used to explain the observation that sodium bicarbonate has a lower propensity to form solid bridges than sodium chloride (Adolfsson et al., 1996). In Fig. 2 the remaining tensile strength at the plateau level is significantly lower than for sodium chloride.

According to Duberg and Nyström (1985), the fragmentation of a material increases the number of particles and thus the number of contact points between particles. This may lead to a more even force distribution throughout the compact during compression, which probably results in a lower

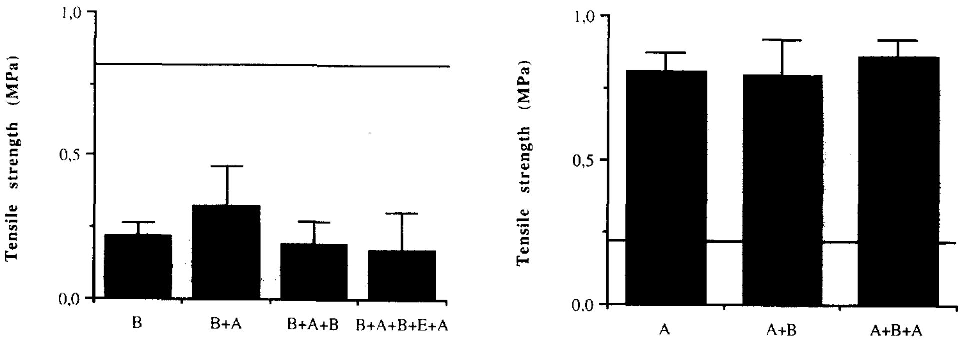

Fig. 3. (A) Alternating soaking and drying of sodium chloride tablets. Tensile strength in butanol of tablets compacted in butanol (B); tensile strength in air of tablets compacted in butanol and dried in air (B + A); tensile strength in butanol of tablets compacted in butanol, dried and soaked again in butanol (B + A + B); and tensile strength in air of tablets compacted in butanol, dried, soaked in butanol and evacuated to < 20 μm Hg (B + A + B + E + A). The line represents the tensile strength in air of the corresponding tablets compacted in air. (B) Alternating drying and soaking of sodium chloride tablets. Tensile strength in air of tablets compacted in air (A); tensile strength in butanol of tablets compacted in air then soaked in butanol (A + B); and tensile strength in air of tablets compacted in air, soaked in butanol and dried in air (A + B + A). The line represents the tensile strength in butanol of the corresponding tablets compacted in butanol.

energy at each contact point. Energy may also be consumed in the creation of new surfaces during the fragmentation. Volume reduction and consolidation by fragmentation would thus decrease the likelihood of solid bridges forming. At a dielectric constant exceeding approximately 15-20, the two fragmenting materials lactose and sucrose have almost no remaining tensile strength, which is in accordance with the hypothesis that such materials are less prone to develop solid bridges.

The remaining tensile strength of Emcompress® is more difficult to interpret since no distinct plateau was obtained. The true plateau level may occur at dielectric constants above 18. In this case the effects of solubility are not likely to affect the results since Emcompress® is virtually insoluble, even in water with a dielectric constant of 78. Alternatively, the extensive friction during ejection of these tablets may have reduced their tensile strength, resulting in a false low value of the remaining tensile strength.

The estimation of the proportions of solid bridges in these materials appears to be consistent with previous data reported from our laboratory (Nyström et al., 1993). Furthermore, a dielectric constant of 18 appeared to be appropriate for evaluation of solid bridges in a compact.

3.2. Tensile strength as a function of alternating drying and wetting/soaking of compacts: Comparison of the two methods

A prerequisite for the application of the concept of using liquid media between the tablet particles during compression, specifically to reduce the weak long range distance forces, is obviously that the presence of liquid will not affect other processes involved during compression. It is thus assumed that the creation of local friction and stress leading to high temperatures and subsequent formation of solid bridges is not hindered. Further, it is assumed that volume reduction and especially the degree of fragmentation is not affected.

Likewise, when applying the technique of soaking tablets compacted in air, it is a prerequisite that the liquid used is capable of penetrating the compact and its pore structure.

3.2.1. Tablets compacted in butanol

The tensile strength of all tablets compacted in butanol, except those made of sodium chloride (Fig. 3a), was significantly increased when the tablets were left in open air (Fig. 4a, Fig. 5a and Fig. 6a). This was probably because evaporation of butanol from the tablet allowed re-establish-

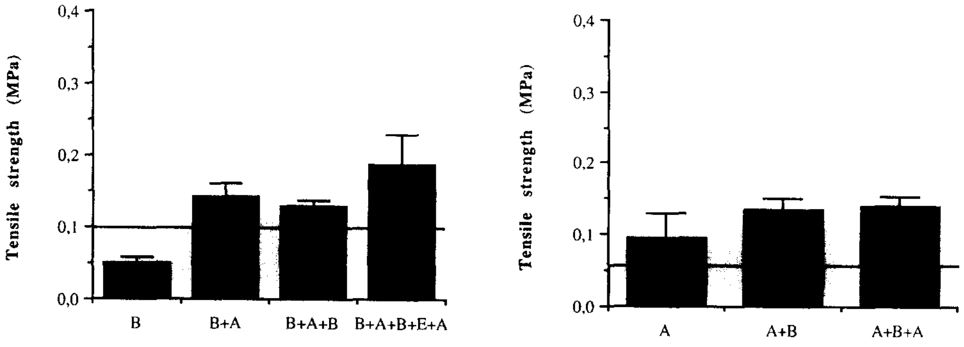

Fig. 4. (A) Alternating soaking and drying of sodium bicarbonate tablets. Legends as in Fig. 3a. (B) Alternating drying and soaking of sodium bicarbonate tablets. Legends as in Fig. 3b.

ment of the weak long range distance forces between particles in the compact, thus increasing the tensile strength.

The tensile strength of sodium bicarbonate tablets was higher for tablets compacted in butanol and thereafter evaporated (Fig. 4a), than for tablets compacted in air (Fig. 4b). A possible explanation could be that the butanol lubricated the system and reduced the creation of flaws and cracks, which resulted in a tablet of higher tensile strength.

The tensile strength of Avicel® and Emcompress® (Fig. 5a and Fig. 6a) was as expected reduced when the dried tablets were re-soaked in butanol. For sodium chloride and sodium bicarbonate a slight tendency to a reduction in tensile strength was obtained (Fig. 3a and Fig. 4a).

For sodium bicarbonate (Fig. 4a), and perhaps also for sodium chloride (Fig. 3a), butanol appears to be able to evaporate from the compact, but does not seem to be able to re-enter it.

The tensile strength of the tablets compacted in butanol and then left to dry in open air was not as high as for the tablets compacted in air. This may have been caused by some butanol remaining present in sealed pores. The problem of effectively evaporating the tablet was demonstrated with sodium bicarbonate and Emcompress® (Fig. 4a and Fig. 6a): evacuation of the tablets probably caused a substantial further increase in the tensile strength.

The tensile strength of evacuated Avicel® tablets is increased to the same level as for the Avicel® tablets dried in open air. This may possibly indicate that the presence of a liquid may have affected the compaction process so that the bond formation was changed, as described above. In this case the results may indicate that the evaporation of butanol in open air was sufficient.

The evacuation of sodium chloride tablets did not result in any significant change in tensile strength, since neither drying nor soaking of these tablets affected the tensile strength significantly. This result was expected and can probably be explained by the incapability of the liquid to penetrate the compact.

3.2.2. Tablets compacted in air

The tensile strength of tablets of all materials compacted in air except for those made of Avicel® was not significantly affected by soaking the tablets in butanol or by evaporation of the butanol (Fig. 3b, Fig. 4b, Fig. 6b, Fig. 7 and Fig. 8). This was probably because butanol does not enter the compact because of the formation of dense peripheral zones in the tablet, or the appearance of air pockets in the tablet, which makes the soaking procedure less effective. If butanol does not enter the compact, the subsequent process of drying tablets would not be expected to affect the tensile strength of the compact (Fig. 3b, Fig. 4b, Fig. 6b, Figs. 7 and 8). A slight increase in tensile strength after soaking in butanol was obtained with sodium bicarbonate. This was also seen for the corresponding tablets compacted in butanol.

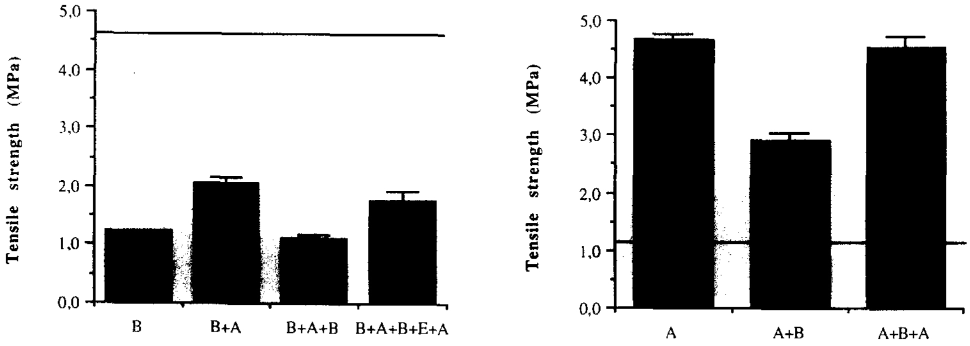

Fig. 5. (A) Alternating soaking and drying of Avicel® tablets. Legends as in Fig. 3a. (B) Alternating drying and soaking of Avicel® tablets. Legends as in Fig. 3b.

The tensile strength of Avicel® compacted in air was reduced significantly on the addition of butanol, but not to the same low level as for the corresponding tablets compacted in butanol (Fig. 5b and Fig. 5a). The reason that Avicel® compacted in air was most affected by the soaking process may be that the absorption of butanol into the tablet was facilitated by the presence of amorphous regions in this material in the same way as when water is absorbed into the amorphous structure of microcrystalline cellulose (Kahn et al., 1988). Alternatively, the high porosity of the cellulose tablets may have been implicated. The decrease in tensile strength may also have been further promoted by swelling of the tablet. Dissolution is unlikely to have been involved since the solubility of the material is low (Table 1). The tensile strength of tablets compacted in air and then soaked in butanol, however, was not as low as for the corresponding tablets compacted in butanol. This was probably because the dense structure of the outside layer of the tablets prevented the liquid from entering, as described above. When the cellulose tablets were dried again, the tensile strength was restored to the original value (Fig. 5b).

To sum up these experiments the tensile strength of sodium bicarbonate and Emcompress® tablets compacted in butanol was restored by evacuation to a value similar to that of the corresponding tablets compacted in air. For sodium bicarbonate drying in air was also sufficient to restore the tensile strength. The tensile strength of sodium bicarbonate, Emcompress®, lactose and sucrose compacted in air was not significantly affected by soaking or drying. For sodium chloride tablets compacted in butanol, as well as in air, the structure of the tablet was probably too dense in places to allow the transport of liquid (Fig. 3b and Fig. 3a). The irreversible swelling of Avicel® in butanol, which resulted in destruction of the tablet structure, implies that this was probably not a suitable choice of test material.

3.3. Comparison of surface areas of tablets compacted in butanol and under ambient conditions

The plastic nature of materials such as sodium chloride, sodium bicarbonate and Avicel® is indicated by the moderate increase in surface area when powders of these materials are compacted in air (Table 3). The corresponding compaction of Emcompress®, lactose and sucrose resulted in an extensive increase in surface area that can be explained by the fragmenting nature of these materials.

The porosity and surface area of sodium chloride compacted in butanol do not differ from the corresponding values obtained when compacting tablets in air. For sodium bicarbonate, however, the surface area of tablets compacted in butanol was somewhat higher than for the corresponding tablets compacted in air.

Avicel® and Emcompress® tablets compacted in butanol showed higher porosity but lower surface

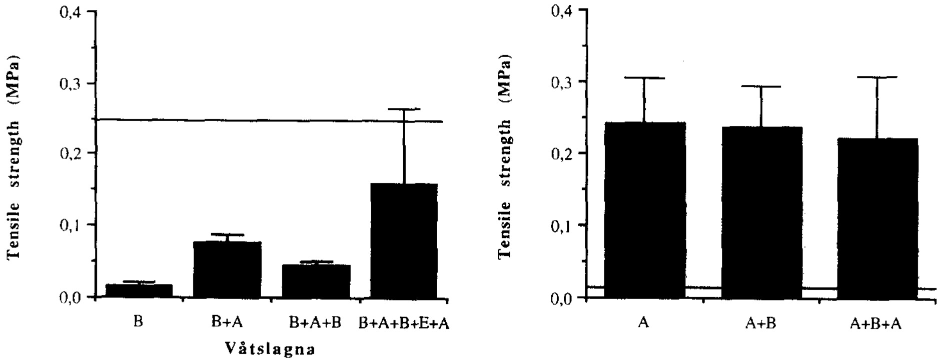

Fig. 6. (A) Alternating soaking and drying of Emcompress® tablets. Legends as in Fig. 3a. (B) Alternating drying and soaking of Emcompress® tablets. Legends as in Fig. 3b.

area than the corresponding tablets compacted in air. The possible lubricating effect of the liquid, which could result in a reduced interparticulate friction may explain the decrease in surface area obtained, but such an interaction by the liquid would then also result in a decreased porosity due to both reduced friction and attraction forces between the particles. However, an increase in porosity was obtained.

In the case of lactose and sucrose the surface area increased when compacted in butanol. This may indicate an increased fragmentation tendency in butanol, but is probably an artefact caused by the tablet still containing liquid. This type of artefact would then decrease the measured permeability of the compact and thus result in an erroneously high value of surface area.

The presence of a liquid phase surrounding the particles during compression probably affects local friction within the tablet. For some materials this will lead to a reduced fragmentation tendency as was possibly the case with Emcompress® and Avicel®. This effect is obviously also linked to reduced development of bonding surface area and bonding. It may in such cases be valuable to study a range of compaction loads corresponding to different degrees of friction and fragmentation tendency. However, the somewhat confusing and contradictory results reported here indicate that the permeametric technique may be less suitable for such an evaluation. Unfortunately gas adsorp-

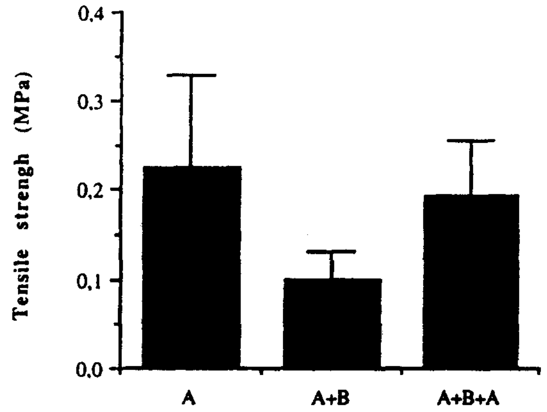

Fig. 7. Alternating drying and soaking of lactose tablets. Legends as in Fig. 3b.

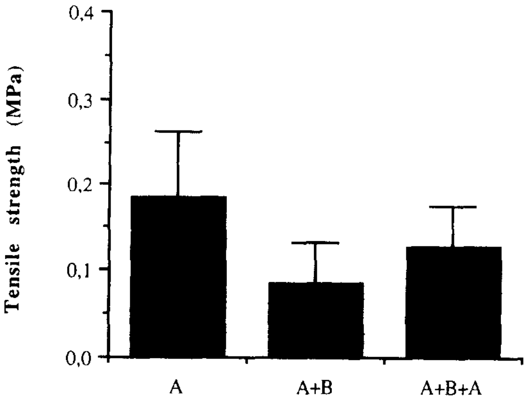

Fig. 8. Alternating drying and soaking of sucrose tablets. Legends as in Fig. 3b.

tion and mercury intrusion techniques are probably of limited use in this context.

4. Conclusions

Liquids with different dielectric constants have previously been used to evaluate bonding mechanisms in tablets. The most common and straightforward method, where tablets are compacted in air and then soaked in liquids with different dielectric constants to eliminate weak long range distance forces, offers advantages in allowing more convenient experimental methods. The main drawback of this method is that the liquid may not be able to enter the pore system completely, in order to reduce the weak long range distance forces. Results from this study have emphasised the importance of this problem.

When using the method of compacting the powder suspended in a liquid it is important to chose a liquid with an appropriate dielectric constant. The construction of a graph such as that seen in Fig. 2 is helpful in this respect. The use of several liquids representing a range of dielectric constants may also reveal potential problems such as swelling.

It is important to clarify when a liquid medium is used between powder particles in a tablet, in order to reduce weak long range distance forces, whether the change in dielectric constant is the only parameter affecting the tensile strength or whether other, unwanted changes in the system also occur. These unwanted changes may be due to innate differences in the media used, e.g. lubricating effect and thermal conductivity. The best correlation between the physicochemical properties of the liquids, evaluated in this study, and the gradual reduction in tensile strength, however, was achieved using the dielectric constant. Changes in thermal conductivity alone were not sufficient to explain the gradual decrease in tensile strength. In the cases where the surface area was changed by changing the compaction medium from air to butanol no distinct pattern of effect on fragmentation tendency was seen. Thus, compacting tablets in liquids with different dielectric constants in order to evaluate bonding mechanisms in tablets appears to produce plausible results.

It has also been shown that the compaction of tablets in different media increases the probability of satisfactory elimination of weak long range distance forces as compared to the alternative method of soaking tablets compacted in air in liquid. This results in an accurate and reliable method, which can be used for the investigation of bonding mechanisms in tablets. As a consequence, this also appears to be a favourable method for studying the effect of compaction load, especially high loads, on bonding mechanisms.

For the materials in this study a dielectric constant of approximately 18 appears to be a reasonable choice for quantification of the remaining tensile strength.

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