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Studies on direct compression of tablets

XXI. Investigation of bonding mechanisms of some directly compressed materials by strength characterization in media with different dielectric constants (relative permittivity)

P.G. Karehill and C. Nyström

Department of Pharmaceutics, Uppsala Biomedical Center, Uppsala University, Box 580, S-751 23 Uppsala (Sweden)

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Summary

Three substances with varying properties regarding compactability and volume reduction mechanisms were compressed both in air under ambient conditions and in liquids with different dielectric constants. The relative importance of bonding with intermolecular forces compared with that with solid bridges and mechanical interlocking was evaluated by comparison of the radial tensile strengths of compacts under ambient conditions vacuum, and in liquids with increasing dielectric constant. All investigated materials increased in radial tensile strength in vacuum, which corresponds to a medium with a dielectric constant of unity. The increase was greater for materials with a high surface area, indicating that the increase in strength in vacuum is primarily caused by increased surface interactions due to removal of adsorbed water vapor and surface contaminations which act as a filter, reducing bonding with intermolecular forces in the compact. An increase in the dielectric constant of the liquid generally decreased the radial tensile strength of the investigated compacts. The compact strength decreased monotonically down to a plateau value or to zero. For all materials, these minimum values were obtained at dielectric constants between 10 and 20. It is suggested that the remaining strength seen in the plateau values is predominantly due to solid bridges or interlocking mechanisms. The difference between the radial tensile strength in vacuum and these minimum strength values obtained in liquids was thus used as an indication of the amount of bonding with intermolecular forces. Bonding with intermolecular forces seems to be the dominating bonding mechanism for all the investigated materials. Bonding with solid bridges and mechanical interlocking contributes to a minor degree to the compact strength of the model substances except for the coarse fraction of sodium chloride. The results obtained support the idea that pharmaceutical compacts can generally be regarded as agglomerates of primary particles that are mainly attracted to each other by bonding with intermolecular forces.

Introduction

The process of forming a compact from a powder can be divided into several stages, i.e., rearrangement of the particles, followed by elastic deformation, plastic deformation and particle fragmentation (Duberg and Nyström, 1982). If these volume reduction mechanisms are to cause a permanent consolidation into a compact, it is required that bond formation takes place between solid surfaces in the compact.

Rumpf (1958) and Führer (1977) have pro-

Correspondence: C. Nyström, Department of Pharmaceutics, Uppsala Biomedical Center, Uppsala University, Box 580, S-751 23 Uppsala, Sweden.

posed several possible bonding mechanisms in this context. For pharmaceutical tablets, three types are normally considered: (a) solid bridges formed, e.g., by a melting process or recrystallization; (b) attractive forces active over distances, i.e., intermolecular and electrostatic forces; (c) mechanical interlocking, depending on strongly irregular shapes of the particles, i.e., hooking or twisting together of the packed material. It can generally be assumed that for a compressed powder material more than one bonding mechanism contributes to the overall effect, but only one or possibly two of these mechanisms will dominate for a specific system. Hitherto, few reports have discussed the relative importance of these mechanisms.

Several difficulties could complicate such an evaluation for typical pharmaceutical compounds. Normally, the microstructure of the compact cannot be characterized and described quantitatively. Thus, the amount of solid surface area taking part in the interparticulate attraction and the distances between such surfaces are not known. One approach to distinguishing between different bonding mechanisms could then be to change test parameters that will specifically influence only one mechanism but not the others.

In an earlier study by Karehill et al. (1989), molecular films of magnesium stearate were applied to reduce the strength of intermolecular and electrostatic forces. The results indicated that bonding with intermolecular forces was the dominating bonding mechanism for the tested plastically deformed compounds. It was not, however, possible to distinguish between bonding with solid bridges and mechanical interlocking. This is usually not a major problem, since bonding with mechanical interlocking by definition depends on the shape of the particles and can be regarded as contributing much less to the compact strength than bonding with solid bridges and intermolecular forces in regularly formed grains. However, for irregularly formed particles mechanical interlocking can be of substantial importance (Führer, 1977).

Another means could be to compress and measure compact strength firstly in normal ambient surroundings (room temperature and normal relative air humidity) and then to change the ambient surroundings by conducting the experiments in better defined media such as liquids and vacuum.

Sartor (1978) has evaluated the crushing strength of limestone compacts in vacuum. A substantial increase in crushing strength was found when the compacts were compressed and measured at low pressures. This is in good agreement with the fact that all materials in ambient air are covered with a thin film, a few molecular layers thick, of adsorbed impurities and water vapor. Friction will increase for most metal materials and graphite if the surface contamination is removed in vacuum (Bowden and Tabor, 1950). When the film is removed the materials' surface free energy will increase and hence the ability for bond formation with intermolecular forces between the surfaces will increase. In the field of tribology this technique has been used to study the adhesive component of friction.

If a surface is covered with a liquid, the liquid will act as a barrier for the adhesion forces and hence reduce the interaction between surfaces in close proximity. However, if more liquid condenses on the surface, liquid bridges may be formed between surfaces in close contact. These bridges are strong, and could thus increase the compact strength. However, it should be noted that only the interfacial forces at the liquid-gas interface contribute to the bonding force between the grains. As soon as the liquid completely envelopes the compact, all capillary bonding force vanishes (Rumpf, 1962).

Shirvinskii et al. (1984) reported that the adhesion forces for a number of different particulate materials (silicon, aluminum and calcite) adhering to surfaces of silicon, quartz, teflon and steel, decreased with increasing dielectric constant for liquid binary media or along a curve with a minimum plateau value. This plateau level in adhesion force was found in some cases for liquids with relatively high dielectric constants compared to the dielectric constant of the solid substance. This is in agreement with Lifshits theory that the most stable suspensions are those whose dispersion media have relative permittivities close to those of the particles (Shirvinskii et al., 1984; Israelachvili, 1985a). The basic idea of this theory is that the forces interacting between surfaces in close contact are considered to be due to a fluctuating electromagnetic field. Because of the quantum-mechanical fluctuations, this field is always present in the interior of a material medium, and it also extends beyond its boundaries. This theory is applicable to any material, irrespective of its molecular nature (Dzyaloshinskii et al., 1961; Israelachvili, 1985b).

From the Hamaker and Lifshits theories, some general conclusions related to the forces interacting in a medium between particles can be drawn:

(a) The London-Van der Waals forces between two particles of the same material dispersed in a fluid are always attractive, provided there is no marked orientation of the fluid molecules. If the particles are of different composition, the resultant force may be repulsive in its nature (Hamaker, 1937; Dzyaloshinskii et al., 1961).
(b) The London-Van der Waals forces between any two bodies in vacuum are always attractive (Hamaker, 1937; Dzyaloshinskii et al., 1961).
(c) A decrease in London-Van der Waals forces with an increase in the dielectric constant of the medium could be expected (Dzyaloshinskii et al., 1961; Shirvinskii et al., 1984).
(d) The solubility of a salt in different solvents will be proportional to $e^{-\text{constant}/e}$, where e is the dielectric constant of the solvent (Israelachvili, 1985c).
(e) Electrostatic forces do not contribute to the adhesion forces in organic liquids because of the high diffusibility of the electric double layer in organic media containing small amounts of electrolyte (Shirvinskii et al., 1984).

It seems, therefore, reasonable to determine the tablet strength for a number of pharmaceutical materials compressed in liquids with different dielectric constants, and to compare these strength values with those of the compact strength obtained in both ambient air and in vacuum. The importance of solid bridges or mechanical interlocking in relation to bonding with intermolecular forces could then be obtained, since these latter forces are at a minimum for liquids with dielectric constants of 10–20 (Shirvinskii et al., 1984). For higher dielectric constants, the usefulness of this technique is limited due to dissolution of easily soluble compounds.

The objective of the present study was to evaluate the relative importance of different bonding mechanisms, i.e., bonding with intermolecular forces, solid bridges and mechanical interlocking for pharmaceutical compacts characterized by mechanical strength in media with different dielectric constants.

Experimental

Materials

Powders Sodium chloride and Avicel® PH 101, two powder materials undergoing volume reduction mainly by plastic deformation, and lactose, undergoing fragmentation, were chosen as test materials.

TABLE 1

Primary characteristics of powders and compacts

Material	Density [a] ($g\ cm^{-3}$)	Surface area of powders ($cm^2\ g^{-1}$)	Surface area of compactsi	
			Air ($cm^2\ g^{-1}$)	Liquid ($cm^2\ g^{-1}$)
Avicel PH 101	1.54	3490	18542	18512
Sodium chloride 250–355 μm	2.17	100	507	358
Sodium chloride < 63 μm	2.17	925	6395	3735
Laktos 350	1.56	4964	15689	18318
Laktos 150–180 μm	1.56	576	5853	6824

[a] Measured with an Air Comparison Pycnometer Model 930 (Beckman, U.S.A.).

[b] Measured by permeametry according to Alderborn et al. (1985).

TABLE 2

Primary characteristics of test liquids, including calculated solubility values for sodium chloride

Liquid (−)	Dielectric constant (−)	Supplier (−)	Purity (%)	Solubility for sodium chloride at 25 °C [a] (mg/l)
Vacuum	1.00	–	–	–
n-Hexane	1.89	Merck	> 99	9×10^{-42}
Cyclohexane	2.02	Merck	99	1×10^{-38}
Carbon tetrachloride	2.24	Merck	> 99.5	1×10^{-38}
Trichloroethylene	3.40	Merck	> 99.5	7×10^{-21}
Chloroform	4.81	Merck	99.5	3×10^{-13}
Methyl acetate	6.68	Merck	> 99	5×10^{-8}
Pyridine	12.30	Merck	> 99.5	5×10^{-2}
Acetone	20.70	Kebo-Grave	99.5	4×10^{1}
Alcohol	24.30	Merck	99.5	2×10^{2}
Methanol	32.60	Merck	> 99	3×10^{3}

[a] Approximate values calculated according to (Israelachvili, 1985c).

Sodium chloride (cubic crystalline, puris, Kebo-Grave, Sweden) was fractionated by dry sieving to obtain the fraction of 250–355 μm. From this fraction a size fraction (< 63 μm) was prepared by milling the material in an Alpine 63 C. These fractions are henceforth denoted as coarse and fine sodium chloride, respectively.

Avicel® PH 101 (FMC, U.S.A.) was used as supplied.

Lactose (coarse powder, Swedish Sugar Co. was fractionated by dry sieving to obtain the 150–180 μm fraction and the quality Lactose 350 mesh (Die Melkindustrie Veghel) was used as supplied. These fractions are designated as coarse and fine lactose, respectively, in the subsequent text.

The primary characteristics of the materials are listed in Table 1.

Liquids Liquids with different dielectric constants were chosen for the study. Details of the dielectric constant, supplier and purity of the different liquids are presented in Table 2. The approximate solubilities of sodium chloride, the most aqueous-soluble substance in this study, in the various liquids are also listed in Table 2. These values were calculated according to $e^{-\text{constant}/e}$ where e is the dielectric constant of the liquid (Israelachvili, 1985c). A high solubility increases the risk of solid bridges and surface properties of the compact changing due to dissolution. This risk is difficult to grade and evaluate. However, it is our opinion that for liquids with a dielectric constant below 10–20 the solubility is limited and subsequently does not significantly affect the bonding properties of the tested materials.

Methods

Compaction of test specimen Tablets were compressed in a specially designed apparatus manufactured from steel (Fig. 1). After manual filling of the die, each compact was prepared by compression in a hydraulic press to 150 MPa over 10 s.

Compaction under ambient conditions An amount of powder sufficient to give a compact height of approx. 0.3 cm at 150 mPa pressure was used. The maximum compression loads were within ±3% of the mean values presented. The die was not lubricated prior to compaction. Before any compact characterization the specimens were

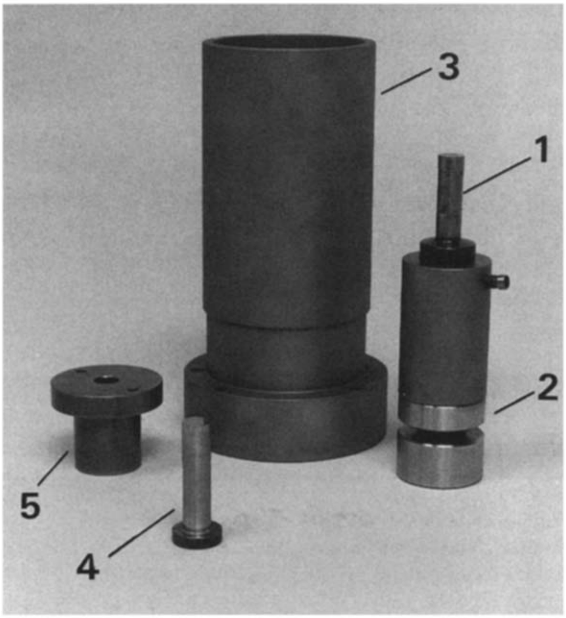

Fig. 1. Tablet compression apparatus: (1) upper punch, (2) load cell, (3) compression chamber, (4) lower punch and (5) die.

stored for at least 2 days. In this study the term ambient conditions corresponds to a temperature of 20 °C and a relative humidity (RH) of 40–50%.

Compaction in liquids The liquids used in this study were preconditioned with the solid material prior to compaction to obtain a saturated solution. The apparatus described above (Fig. 1) was filled with liquid to the top of the die. Excess liquid was then removed from the die with a pipette making it possible to add the powder in dry form. An amount of powder sufficient to give a compact height of approx. 0.3 cm at 150 MPa pressure was poured into the die. Liquid was then added to the apparatus to completely wet the powder mass. After 1 min the upper punch was inserted in the die and the compression chamber was mounted in the hydraulic press. The upper punch pressure was then raised to 150 MPa over 10 s. This procedure resulted in two effects. Firstly, the liquid was able to leave the tablets when the load increased without disturbing the consolidation of the compact and, secondly, the time for plastic flow in the tablet was increased. Ejection of the tablet from the die was performed in the liquid by turning the die and applying pressure with the hydraulic press on the lower punch. The compact was not exposed to air during the compression and ejection phase, since the compression chamber was completely filled with liquid. After ejection the tablets were removed and stored in the saturated liquid for 24 h before measurement of the tensile strength. The compaction procedure described was carried out in a ventilated safety box.

This procedure, which involved preparation of the compacts by compression in the liquids, proved to be more reliable than first making the tablets under ambient conditions and then soaking them in the liquids. Wetting of the tablets proved to be a major problem for liquids with low dielectric constants when using the soaking technique. It can be assumed that the ability to wet the powder completely is of crucial importance for the interaction between the liquid and the bonding forces inside the compact (Rumpf, 1962).

Both methods gave an increased capping tendency with increases in the dielectric constant of the liquids. Capping was observed when the fine lactose compacts were compressed in liquids with dielectric constants which gave radial tensile strength values near zero. This is probably due to a lowering of the bonding strength in the compact down to a level where even small elastic tendencies can rupture the weak bonds formed during compaction.

The soaking procedure caused capping for Avicel® PH 101 in methanol probably due to a

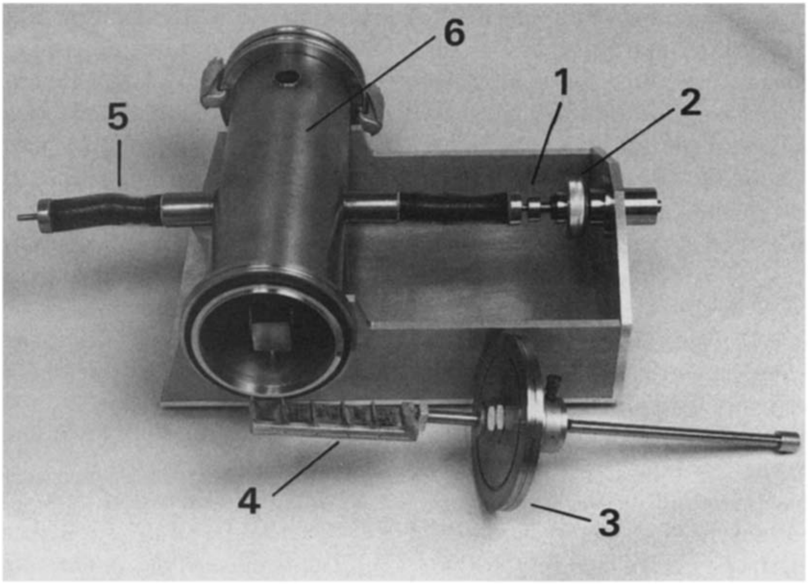

Fig. 2. Vacuum tensile strength tester: (1) load cell, (2) traction wheel, (3) end plate, (4) magazine, (5) bellow and (6) tube.

non-homogeneous distribution of the liquid and swelling of the cellulose in the compact during soaking. It is known that swelling for all types of cellulose materials generally increases with increasing dielectric constant of the liquid (Stamm, 1964). Thus, in this study all compacts were prepared by suspending the powders in the liquids, prior to compression.

Characterization of compact strength under ambient conditions A Heberlein diametral compression test apparatus (TBH 28, ERWEKA, F.R.G.) was used for all materials except Avicel® PH 101. The compact strength of Avicel® PH 101 was measured in a material tester (Overload dynamics, Overdyn, The Netherlands). Since all compacts showed approximately normal tensile failure, the radial tensile strength was calculated according to Fell and Newton (1970). Results presented are mean values of ten determinations.

Characterization of compact strength in vacuum A vacuum tensile strength tester was constructed for this experiment (Fig. 2). The tester was constructed from a tube of stainless steel with two movable vacuum-proof end plates. On each side of the tube two bellows were attached via vacuum-proof welding. Inside the bellows the tablet crushing device moved freely with a minimum of frictional loss, to transmit the force to the tablets in the tester. The force was manually transmitted to the crushing device by a traction wheel and measured with a piezoelectric crystal attached to the bellows. The tester was able to hold five compacts, stored in a sliding magazine. Prior to each measurement the tablets were degassed for 24 h or longer at a relative humidity (RH) of 40–50% to a pressure less than 10^{-4} mmHg. For each material, ten tablets were measured in vacuum and ten in air in the apparatus. The radial tensile strength was then calculated as described above.

Characterization of compact strength in liquids To evaluate the compact strength in liquids a material tester (Overload Dynamics, Overdyn) was used. A compact was taken from the jar where it had been stored in the test liquid and put into a cup filled with the same liquid on the tester. This procedure is important in that the creation of solid-liquid-gas interfaces, which are responsible for capillary forces and liquid bridges that may increase the tensile strength of the compact (Rumpf, 1958, 1962), is thus avoided. The radial tensile strength was evaluated, after crushing the tablets in the liquid, using calculations according to Fell and Newton (1970). Results presented are mean values of ten determinations.

Surface area of powders A Blaine permeameter was used to measure the specific surface area for a weighed amount of powder. The apparatus and calculations are described elsewhere (Alderborn et al., 1985). For the coarse fractions of sodium chloride and lactose, a powder plug with a diameter of 9.86 mm and a height of 100 mm was used. The calculation of surface area was then based on the assumption of a pure viscous gas flow through the plug. Results presented are mean values of three determinations.

Surface area of tablets compressed under ambient conditions A weighed amount of powder was put into a specially constructed die which was sealed with a plate according to Alderborn et al. (1985). The die and plate were placed on the table of the hydraulic press and the powder was compressed by slowly raising the pressure on the upper punch to 75 and 150 MPa over 10 s. After compaction and at least 1 h of storage under ambient conditions, the die containing the compact was connected to a Blaine permeameter. The compact surface area was calculated as described earlier (Alderborn et al., 1985), using terms for both viscous and molecular flow. Results presented are mean values of three determinations.

Surface area of tablets compressed in liquids The same die and compaction technique as described above was used for the tablets compressed in liquids. After compaction, the die, still containing the compact, was stored at 30 °C in a static-bed dryer for 5 h. All compacts were stored in ambient air for at least 12 h before the die was attached to the Blaine permeameter and measured in the same way as the compacts compressed under ambient conditions. Results presented are mean values of three determinations.

Results and Discussion

Effect of vacuum on compact strength

The values determined for the radial tensile strength of the different materials tested, under

TABLE 3

Radial tensile strength measured under ambient conditions and in vacuum of compacts prepared at 150 MPa

Material (−)	Tensile strength (MPa) [a]		Increase in tensile strength (MPa)
	Ambient	Vacuum	
Avicel PH 101	6.37 (0.81)	8.08 (0.73)	1.71
Sodium chloride coarse	1.01 (0.13)	1.28 (0.20)	0.27
fine	4.13 (0.56)	5.00 (0.56)	0.87
Lactose coarse	0.73 (0.08)	0.80 (0.10)	0.07
fine	1.03 (0.22)	1.40 (0.21)	0.37

[a] Standard deviations are given in parentheses.

both ambient conditions and in vacuum, are presented in Table 3. In this study, the compact strength in vacuum increased significantly ($P < 0.01$) for Avicel® PH 101, both coarse and fine sodium chloride and fine lactose. Coarse lactose showed only a minor increase in tensile strength. Avicel® PH 101 showed the greatest differential strength increase followed by the fine fractions of sodium chloride and lactose. These materials have a high surface area in common. All compacts returned to their initial strength values when the tablets were exposed to air after being degassed at high vacuum.

The increased compact strength for the investigated materials in vacuum could be due to several different mechanisms. One possible mechanism is the removal of contaminating films present on the material surfaces which reduce bonding with intermolecular forces (Rees and Hersey, 1972). Another interpretation is that solid bridges are formed due to recrystallization of soluble materials from an adsorbed surface film when this is removed from the compact (Shotton and Rees, 1966). However, this explanation is less likely because the compact strength of all of the investigated materials increased independently of their solubility. Avicel® PH 101, which is practically insoluble in water, showed the greatest differential strength increase of all the investigated compounds while the readily soluble sodium chloride fractions increased much less.

Dollimore and Heal (1961) have studied the tensile strength changes when water is adsorbed on degassed silica compacts and found a decrease corresponding to the surface coverage of water. Removal of condensed material from the compacts may have the opposite effect, i.e., it may increase the interparticulate attraction forces in the compact. Bonding with solid bridges is probably unaffected by the removal of an adsorbed surface film from the compact. This suggests that the strength increase in vacuum is primarily caused by increased surface interactions due to removal of adsorbed water vapor and surface contamination which act as a filter to reduce bonding with intermolecular forces in the compact. With a completely cleaned surface, the radial tensile strength value reached a maximum, corresponding to a dielectric constant of unity, i.e. maximal interaction between surfaces in close contact.

Effect of liquids with different dielectric constants on compact strength

The surface areas for compacts compressed in air and in *n*-hexane are listed in Table 1. Avicel® PH 101 and coarse and fine lactose showed a minute increase in compact surface area when compacted in *n*-hexane compared to air. Coarse and fine sodium chloride showed a minor decrease in compact surface area for compacts compressed in the same way. These results show that the presence of a liquid did not significantly affect the fragmentation tendency for the investigated materials.

The radial tensile strengths for tablets compressed in liquids with different dielectric constants are shown in Fig. 3. Tensile strength for tablets compressed and measured both under ambient conditions and in vacuum are associated with a dielectric constant of unity. Since the tensile strength of compacts prepared in air can be regarded as a starting point before transfer takes

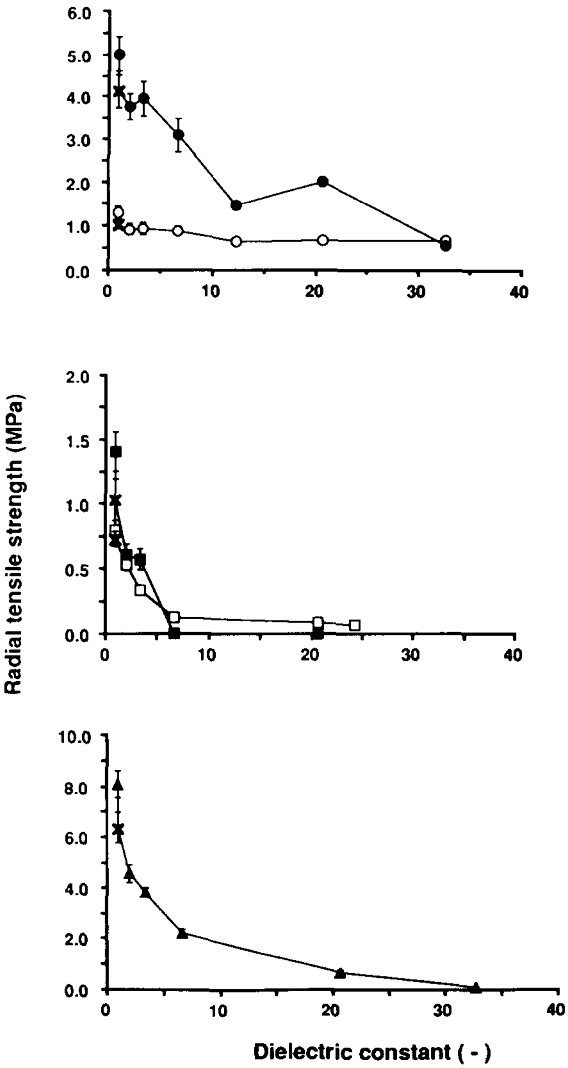

Fig. 3. Effect of the dielectric constant of the test liquid on the compact strength: (○) sodium chloride coarse; (●), sodium chloride fine; (□) lactose coarse; (■) lactose fine; (▲) Avicel® PH 101. All compacts compressed at 150 MPa. Error bars represent confidence intervals of the mean for 95% probability. For some of the results, the precision is better than can be denoted in figure. Compact strength in ambient surroundings is indicated by ×.

place to a vacuum or a liquid environment, the compact strength measured under ambient conditions is denoted by a different symbol (×) in the figures. In Fig. 4 the remaining strengths for all materials are compared to their radial tensile strengths in vacuum.

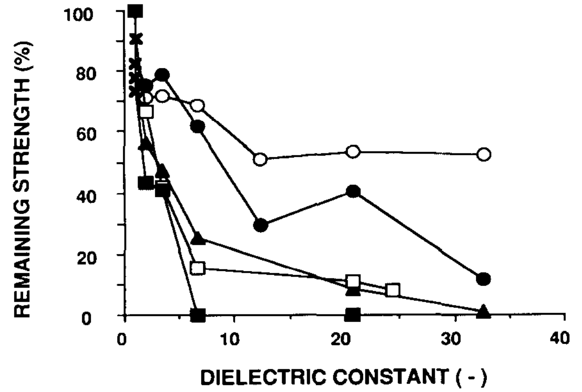

Fig. 4. The remaining compact strength in liquids compared with the radial tensile strength in vacuum. Symbols as in Fig. 3.

Sodium chloride

The fine fraction of sodium chloride (Fig. 3) decreased in radial tensile strength with increasing dielectric constant in the interval tested. This decrease is probably caused by the blunting of intermolecular forces by the liquid. Since bonding with intermolecular forces according to Shirvinski et al. (1984) is at a minimum for a dielectric constant of 10–20, the compact strength in this interval will be due to bonding with solid bridges or mechanical interlocking. The fact that no stable plateau is formed can perhaps be explained by a limited tendency for the many but weak solid bridges formed by this fine particulate quality of sodium chloride to dissolve in the liquid, compared with the few but strong solid bridges formed by the coarse fraction.

A stable plateau was reached in the test interval for the coarse sodium chloride after an initial decrease. It seems, therefore, that the effect of dissolution was less for the coarse than for the fine sodium chloride fraction.

The formation of a plateau has earlier been suggested to be typical for a material bonding with at least two different bond types, e.g. solid bridges and intermolecular forces (Nyström and Karehill, 1986; Karehill et al., 1989). Bonding with intermolecular forces could then be very sensitive to surface changes, while the other mechanisms (e.g. solid bridges and/or mechanical interlocking) could be established even in the presence of a lubricant film or a liquid between the surfaces. When a stable plateau is obtained, the compact strength in the ideal case will be determined by solid bridges or mechanical interlocking alone. There is some similarity in the results obtained with liquids and the results previously published concerning small amounts of magnesium stearate for these sodium chloride fractions (Nyström and Karehill, 1986; Karehill et al., 1989). The difference in absolute value of the plateaus, between the studies, is probably caused by the different compaction methods. In the magnesium stearate studies an instrumented single-punch press (Korsch EkO, F.R.G.) was used to prepare the compacts. Due to the long consolidation time in a hydraulic press, approx. 500-times longer than in a single-punch press, more plastic flow in the compacts can be expected (Sheikh-Salem and Fell, 1982).

Nevertheless, the present results confirm that bonding by solid bridges is a contributory mechanism besides bonding with intermolecular forces for both sized fractions of sodium chloride. Bonding with mechanical interlocking is less likely for the two sodium chloride fractions because of their low tendency to hook or twist together during compaction.

Lactose

For the fine fraction of Lactose (Fig. 3), no coherent compacts were formed when the liquid dielectric constant exceeded approx. 7, indicating that intermolecular forces are the dominating bonding mechanism for this fraction.

It was also expected that the solubility of lactose would increase with increased dielectric constant (Israelachvili, 1985c). However, it is our belief that the solubility is limited for liquids with dielectric constants up to approx. 10–20 and there will be no significant effect on the bonding mechanisms of lactose. The coarse lactose compact strength (Fig. 3) showed a leveling off and formed a plateau, indicating the existence of more than one bonding mechanism. Although lactose is described as a brittle material, the participation of plastic flow in the densification process has been reported (Butcher et al., 1974). It seems possible, therefore, that solid bridges contribute to the radial tensile strength of this material although bonding with mechanical interlocking cannot be excluded.

Avicel® PH 101

Avicel® PH 101 (Fig. 3) showed a continuous decrease in tablet strength down to zero with increasing dielectric constant. Cellulose consists of microfibrils with hydrogen bonds linking neighboring cellulose chains. Liquids that penetrate this structure cause swelling that disrupts the cellulose-cellulose bonds in proportion to the dielectric constant of the liquid (Stamm, 1964). The compact strength will, therefore, decrease proportionally with an increase in the dielectric constant of the liquid. This indicates bonding with intermolecular forces to be the dominating bonding mechanism for this material. The relative changes in residual strength in Fig. 4 seem to differ for Avicel® PH 101 and coarse lactose compared to the fine lactose fraction. All three materials appear in the initial phase (up to a dielectric constant of approx. 4) to be equally influenced by an increase in the dielectric constant of the liquid. This indicates that the same bonding mechanism (i.e. intermolecular forces) has been affected in all three materials. With a dielectric constant of approx. 7, when the compact strength for fine lactose is zero, a different kind of bonding mechanism seems to be dominating for Avicel® PH 101 and coarse lactose. This bonding mechanism could be either bonding with solid bridges, mechanical interlocking or a combination of both. Avicel® PH 101 is insoluble and does not melt in the contact points during compression. The formation of solid bridges in such a material is unlikely. A possible explanation is that mechanical interlocking is responsible for the residual strength of Avicel® PH 101 at a dielectric constant above 7. The compact strength of Avicel® PH 101 decreased slowly from this point down to zero with increasing dielectric constant. This may be caused by a structurally oriented effect due to swelling of the irregularly formed grains, producing increased entanglement (Stamm, 1964; Khan et al., 1988).

It seems evident that, for Avicel® PH 101, as described earlier for coarse lactose, there is at least one other bonding mechanism besides intermolecular forces. It cannot be excluded that mechanical interlocking plays an important role in determining the compact strength for this material.

Conclusions

The different bonding mechanisms responsible for compact strength in pharmaceutical tablets can be studied by performing strength measurements in liquids as well as vacuum. The use of a vacuum, corresponding to the maximum interaction of a clean surface bonding with intermolecular forces, increased the compact strength for all materials tested. The results also showed that the radial tensile strength decreased with increasing dielectric constant of the liquids, which acted as filters to reduce bonding with intermolecular forces. Bonding with solid bridges and mechanical interlocking is probably less sensitive to an increase in the dielectric constant compared to bonding with intermolecular forces. Our results support the view that most pharmaceutical tablets can be regarded as agglomerates of discrete primary particles that are attracted to each other predominantly by intermolecular forces. For one of the investigated materials, coarse sodium chloride, bonding with solid bridges had a substantial effect. This is in agreement with previously established results (Nyström and Karehill 1986; Karehill et al., 1989). However, it is important to point out that the absolute values obtained are dependent upon factors such as tablet dimensions, fragmentation propensity, compaction pressure and compaction rate.

Nevertheless, measurement of compact strength in liquids with different dielectric constants can represent a method for gaining deeper insights into the bonding mechanisms of pharmaceutical materials.

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