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Moisture adsorption and tabletting. III. Effect on tablet strength-post compaction storage time profiles *

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Summary

The effect of air humidity on the post compaction changes in tensile strength of tablets of three test materials, saccharose, sodium chloride and dicalcium hydrogen phosphate dihydrate, was assessed during storage of the tablets for up to 168 h. For saccharose and sodium chloride also the changes in tablet permeametry surface area at storage times up to 24 h was measured. For tablets of saccharose and sodium chloride, the tablet strength increased generally during the storage. An increased air humidity increased both the rate and the degree of the increase in tablet strength, i.e., the storage time after which measurements of tablet data are performed is of importance when the compactibility of a material is evaluated. However, when tablets were stored at or above the critical relative humidity, the tablet strength decreased after a few hours storage. For tablets of dicalcium hydrogen phosphate dihydrate, the tablet strength did not vary with time or storage condition. For tablets of saccharose and sodium chloride, the surface area generally decreased with storage time and the effect was more pronounced with increased storage humidity. Hence, a relationship between the tablet strength and tablet surface area was found. Thus, the changes in tablet strength during storage are probably a result of a rearrangement of solid material within the tablet which is mediated or facilitated by sorbed water.

Introduction

Compaction of powders into coherent specimens requires the formation of interparticulate attractions between the particles during the compression phase. However, after ejection of the tablet from the die, the tablet strength can change (e.g., Rees and Shotton, 1970; Down and McMullen, 1985; Nyström and Karehill, 1986; Ahlneck and Alderborn, 1989a,b) which means that interparticulate attractions are formed or disturbed also during the post compaction storage phase.

In mechanistical studies on such post compaction strength changes, crystalline non-hygroscopic materials have normally been used. For

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such materials, an increase in tablet strength must theoretically be due to either a formation of solid bridges between particles or to an increase in the bonding surface area of intermolecular attraction forces. It seems that mainly three mechanistical explanations for the formation of such interparticulate attractions has been proposed in the literature:

(1) A continuing deformation of particles in the compact after the compaction (Rees and Shotton, 1970; Rue and Barkworth, 1980; El Gindy and Samaha, 1983; Nyström and Karehill, 1986; Karehill and Nyström, 1990b), i.e., what is often referred to as stress relaxation or stress relief. It seems reasonable that this continuing particle deformation can lead to an increased surface area for interparticulate attractions and a decreased interparticulate distance.

(2) A rearrangement of solid material at the particle surfaces within the tablet (Down and McMullen, 1985; Ahlneck and Alderborn, 1989a,b). This rearrangement can lead to either the formation of solid bridges between particles or to an increase in the bonding surface area of intermolecular attraction forces. It seems that this restructuring of solid material is mediated or facilitated by the presence of adsorbed water and that water can show this function although the point has not been reached where the state and thickness of the adsorbed water vapour allows a true dissolution of the solid material.

(3) A crystallization of dissolved material between neighbouring particles due to the movement of water within the tablet (Rees and Hersey, 1972; Hall and Rose, 1978; Ahlneck and Alderborn, 1989b). This explanation presupposes that adsorbed water condenses at particle surfaces (at or above the critical relative humidity) which makes a dissolution of solid material possible. The crystallization of dissolved material can lead to the formation of solid bridges between particles.

The second of the above described mechanisms was proposed as explanation for the post compaction increase in tensile strength (Ahlneck and Alderborn, 1989b) of tablets compacted of fine particulate qualities of two water soluble materials, saccharose and sodium chloride. It was also observed that the RH of the environment during the storage of the tablets gave larger differences in tensile strength of tablets of saccharose than tablets of sodium chloride after a storage period of 1 week. One suggested reason for this was a difference in the rate of changes in mechanical strength between compacts of the respective material. Thus, to further understand the post compaction changes in tablet strength due to adsorption of moisture, it is of interest to study the relationship between the mechanical strength and the post compaction storage time of the tablets. Although such relationships have been presented (e.g., Bhatia and Lordi, 1979; Lordi and Shiromani, 1983, 1984; Down and McMullen, 1985) they have not been widely reported in the literature, especially not changes in compact strength close to the time for compaction.

Experimental

Materials

(1) Sodium chloride (crystalline puriss., Kebo-Grave, Sweden) which is freely soluble in water and shows limited fragmentation during compression (Duberg and Nyström, 1982; Alderborn et al., 1985). A critical relative humidity (RH_0) of 75.3% has been reported (Van Campen et al., 1983).

(2) Saccharose (crystalline puriss., Kebo-Grave, Sweden) which is very soluble in water and fragments to a large extent during compression (Duberg and Nyström, 1982; Alderborn et al., 1985). RH_0-values of 84.3% (Van Campen et al., 1983) and 77.4% (Katalog Pharmazeutische Hilfstoffe, 1974) have been reported.

(3) Calcium hydrogen phosphate, dihydrate (CHP) (Calipharm, Albright and Wilson Ltd., Great Britain) which is regarded as practically insoluble and shows limited fragmentation during compaction (Ahlneck and Alderborn, 1989b).

Methods

Preparation of powders and tablets. For saccharose and sodium chloride, the size fraction of 40–60 μm was prepared by milling in a pin disc mill (Alpine 63C, Alpine AG, Germany) and classification with the aid of an air classifier (Alpine 100 MZR, Alpine AG, Germany). CHP was used without any pretreatment of the material. The particle size for CHP was estimated to be < 20 μm by the use of scanning electron microscopy.

The powders were stored for not less than 7 days before compaction: sodium chloride was prestored at 0% relative humidity (RH) while the other materials had to be stored at higher RH values (saccharose at 33% and CHP at 57%) to obtain an acceptable low friction between the powder and the die wall during the compaction.

Tablets were compacted with 1.13 cm flat-faced punches in an instrumented tablet press (Korsch EK O, Germany) at maximum upper punch pressures of 50 and 120 MPa (sodium chloride), 50 and 200 MPa (saccharose) and 50 MPa (CHP). The compression procedure has been described earlier (Ahlneck and Alderborn, 1989b). External lubrication was performed with a 1% magnesium stearate suspension in ethanol except for CHP for which a 5% suspension was used.

Characterization of tablets. Tablets were stored in desiccators at a low, an intermediate and a high RH at 21°C ±1°C. 33%, 57% and 75% RH was used for sodium chloride and 33%, 75% and 84% RH for saccharose. For CHP, storage was only carried out at 84% RH. The RH values in the desiccators were controlled by the use of saturated salt solutions (Nyqvist, 1983). To reduce the time for equilibration of the RH in the desiccators after contact with the atmosphere, the saturated salt solutions were gently stirred with a magnetic stirrer.

The diametral compression strength of the tablets was measured (Erweka TBH 28, Germany) directly after compaction ($t = 30$ s) and at regular time intervals up to 168 h (for CHP up to 240 h). The tensile strength of the tablets was thereafter calculated according to Fell and Newton (1970). The results are the means of ten determinations.

The permeametry surface area of saccharose and sodium chloride tablets, compacted by hand in the instrumented press at 50 MPa, was measured in the die with a Blaine apparatus. The procedure as well as the equations used for calculating the tablet surface area have been presented earlier (Alderborn et al., 1985). Tablets were stored up to 24 h and were used at the same storage humidities as described for tablet strength measurements. Each value presented is the result of one tablet.

Directly after compaction, three tablets were stored in desiccators with phosphorus pentoxide until the time for moisture uptake measurements and then stored in desiccators with the same RH values as described earlier. No weight gain of adsorbed moisture was monitored by the use of an analytical balance for the tablets stored at an RH below RH_0.

Results and Discussion

Changes in tablet strength during storage

The RH during storage of tablets had a marked effect on the post compaction changes in tensile strength of tablets of both saccharose (Fig. 1) and sodium chloride (Fig. 2). For saccharose tablets compacted at 50 MPa (Fig. 1a, b), storage at 33% RH gave a limited increase in tablet strength. At the intermediate RH (75%), the tablet strength initially increased markedly but with increased storage time the rate of increase was reduced and the tensile strength tended to reach a plateau. At the highest RH (84%), a dramatic increase in tensile strength was observed and the tablet strength is more than doubled within a few hours after the compaction. However, after more than 4 h of storage, the tablet strength was reduced markedly and the solid started to undergo deliquescence.

For sodium chloride tablets compacted at 50 MPa (Fig. 2a, b), the results were similar to the results for saccharose tablets. However, for sodium chloride tablets stored at 33% RH, there was a slow but marked increase in tablet strength throughout the storage period. After 1 week, a level close to the tablet strength measured at the intermediate RH (57%) was reached.

A comparison between the two materials shows that the tensile strength of the tablets immediately after compaction was slightly higher for sodium chloride than for saccharose. However, the absolute and the relative increase in tablet strength was more marked for tablets of sodium

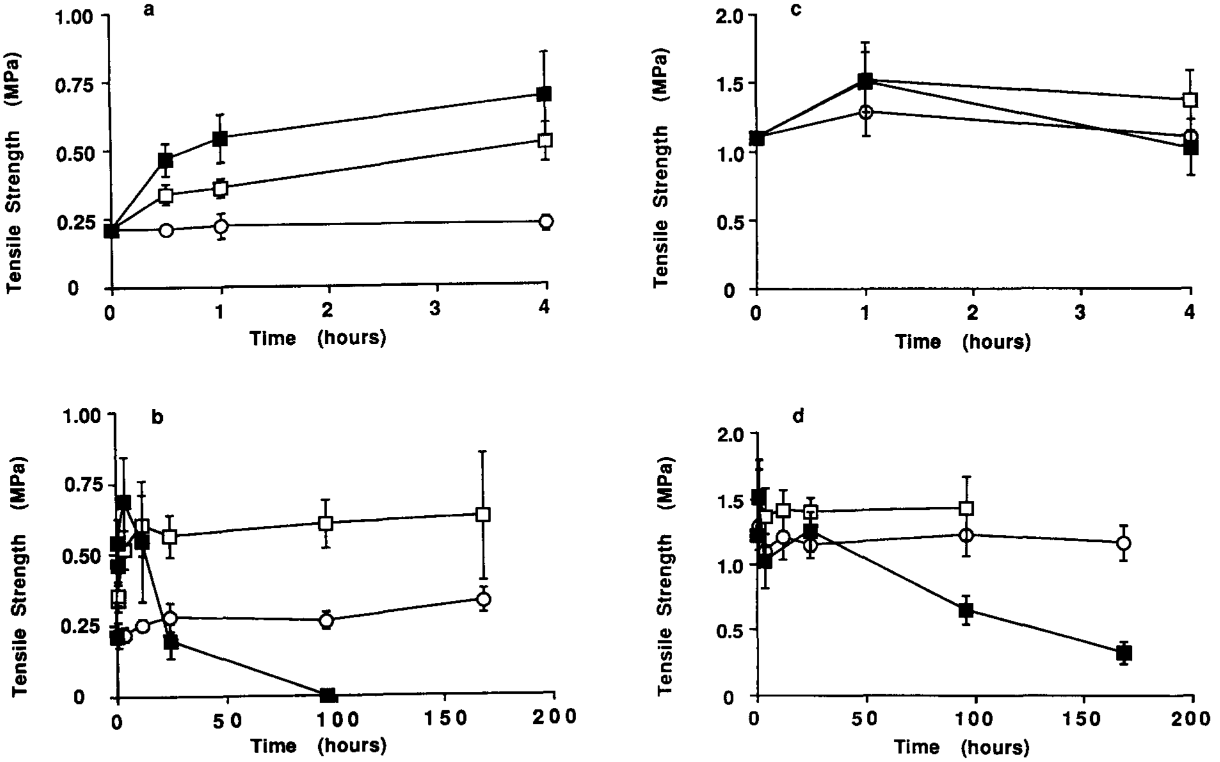

Fig. 1. Tensile strength of saccharose tablets, stored at three relative humidities, as a function of storage time. a. Tablets compacted at 50 MPa. Storage time 0–4 h. b. Tablets compacted at 50 MPa. Storage time 0–168 h. c. Tablets compacted at 200 MPa. Storage time 0–4 h. d. Tablets compacted at 200 MPa. Storage time 0–168 h. ○, 33% RH; □, 75% RH; ■, 84% RH. Bars represent 95% confidence limits of the mean calculated with the Student's *t* test.

chloride. At 75% RH, the tablet strength increased almost 5 times up to 1 h of storage before the reduction in tablet strength occurred.

For both materials, the results for tablets compacted at the higher pressure (Figs 1c, d and 2c, d) are consistent with the results for tablets compacted at 50 MPa although the relative changes in tablet strength are less. Hence, it seems as if differences in the mean size of the pores in the tablets are less important for the post compaction strength changes. However, it can be noticed that for tablets of saccharose, stored at the highest RH, the drop in tablet strength occurred earlier for tablets compacted at the higher pressure. The drop in tablet strength when tablets were stored at or above the RH_0 of the material, was probably due to the formation of a thick multimolecular layer of water at the particle surfaces, i.e., condensation of water in the tablet pores occurred. Thereby, the intensity of the intermolecular attraction forces between particle surfaces in the tablet was disturbed and hence, the tablet strength reduced (Ahlneck and Alderborn, 1989b; Karehill and Nyström, 1990a). It is possible that the reduction in size of the pores in the tablet when the compaction pressure was increased from 50 to 200 MPa, facilitated condensation of water in the pores.

The results for sucrose and sodium chloride demonstrate that the strength of a tablet, exposed to humid air, can change markedly during the storage. The results suggest that the strength increase follows a general pattern, i.e., a fast initial increase in tablet strength followed by a reduced strength increase and finally a leveling out of the profile. However, the shape of the tablet strength–post compaction storage time profile seems to be related to the RH of the

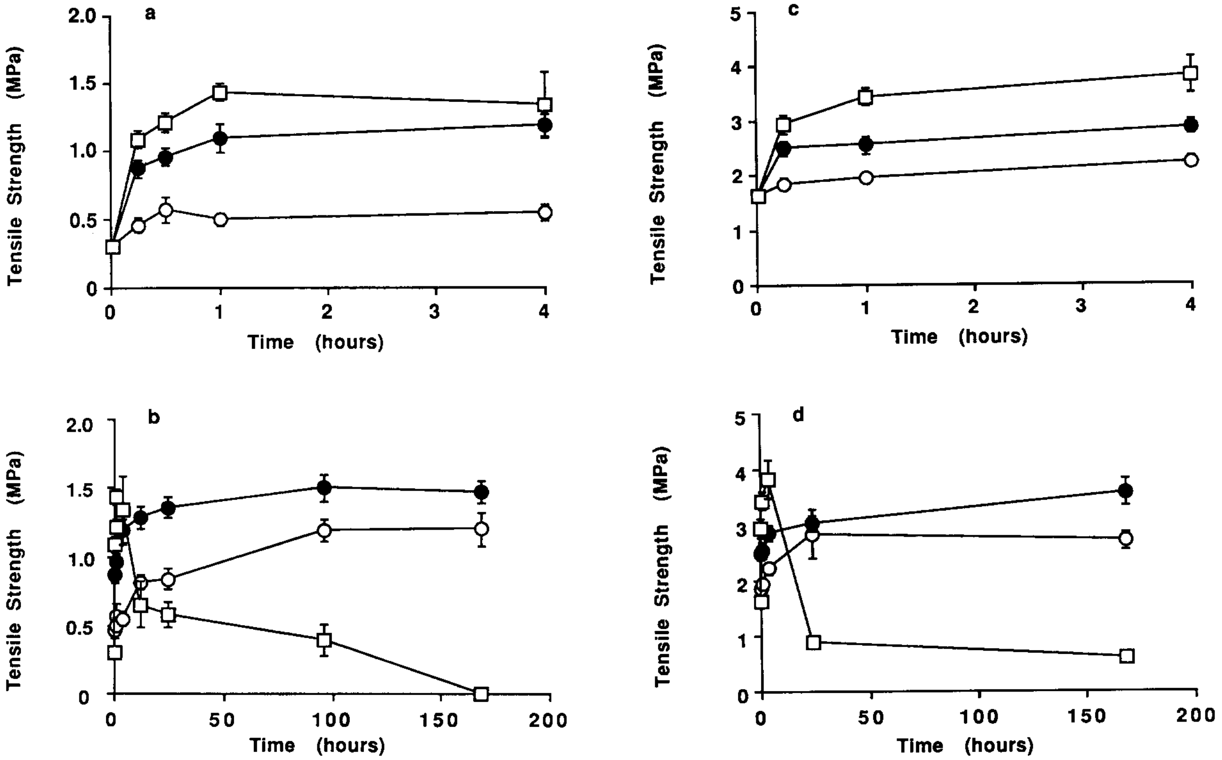

Fig. 2. Tensile strength of sodium chloride tablets, stored at three relative humidities, as a function of storage time. a. Tablets compacted at 50 MPa. Storage time 0–4 h. b. Tablets compacted at 50 MPa. Storage time 0–168 h. c. Tablets compacted at 120 MPa. Storage time 0–4 h. d. Tablets compacted at 120 MPa. Storage time 0–168 h. ○, 33% RH; ●, 57% RH; □, 75% RH. Bars represent 95% confidence limits of the mean calculated with the Student's *t* test.

storage environment, i.e., the curvature of the profile and thereby the time to reach the maximal tablet strength as well as the level of this maximal strength value. With a reduced RH of the environment, the curvature of the profile was less marked until a lower critical relative humidity level was reached where the tablet strength was constant and unaffected by the RH of the environment. When the RH of the storage environment was high, i.e., at or above the critical RH for the material, the tablet strength increased initially according to the general pattern but after a certain time period, the tablet strength decreased dramatically. Thus, the relationship between RH and tablet strength is related to a time factor, i.e., the storage time between compaction and strength analysis (Fig. 3a, b).

This general pattern of the tablet strength–storage time profile is similar to post compaction strength increase profiles presented earlier for, e.g., sodium chloride (Rees and Shotton, 1970; Rue and Barkworth, 1980; Nyström and Karehill, 1986). In such cases, a time-dependent particle deformation was proposed as mechanism for the observed increase in tablet strength.

To further study the importance of the RH of the storage environment for the tablet strength, tablets were compacted and stored for 1 week at 33% RH and then transferred to 75% RH (saccharose) or 57% RH (sodium chloride) for storage for another week (Fig. 4a, b). The tablet strength of the transferred tablets corresponded well to the strength of tablets stored only at the high RH values, i.e., it seems as if the change in tablet strength occurred independently of when the tablets were subjected to the final storage RH.

Tablets were also made of calcium hydrogen

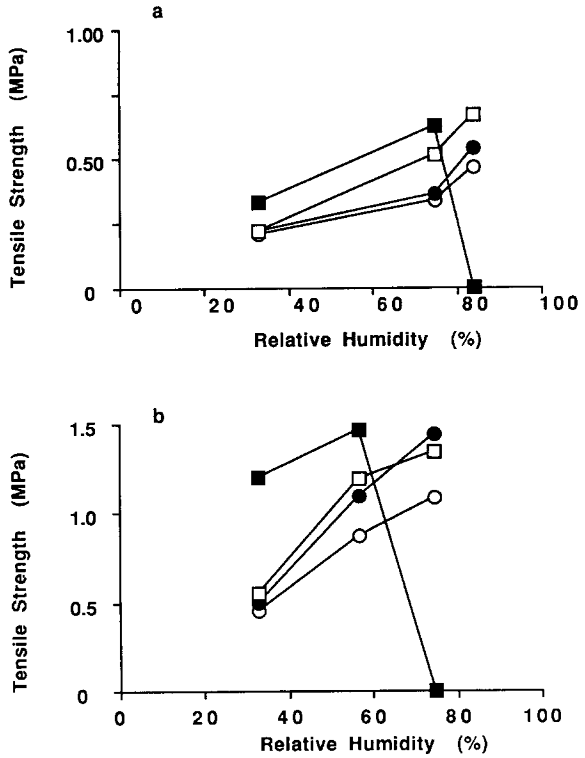

Fig. 3. a. Tensile strength of saccharose tablets, measured after four different storage times, as a function of storage relative humidity. ○, 30 min; ●, 60 min; □, 240 min; ■, 10080 min. b. Tensile strength of sodium chloride tablets, measured after four different storage times, as a function of storage relative humidity. ○, 15 min; ●, 60 min; □, 240 min; ■, 10080 min.

phosphate (CHP) at 50 MPa. The strength of the tablets was measured directly after compaction as well as after storage periods for up to 10 days at a storage RH of 84%. No significant change in tablet strength during the storage time was found at this storage environment. The tensile strength values were 0.343 MPa directly after compaction and between 0.313 MPa and 0.357 MPa throughout the whole measurement period. This finding suggests that the presence of water vapour at the surfaces or within the solid in combination with a specific interaction with the water and the solid is, at least for some materials, a prerequisite for a post compaction increase in tablet strength. Such an interaction or reactivity between water and solid might be related to water solubility. However, it is also possible that the reactivity with sorbed water is related to an activation of the solid material, e.g., mechanical activation during milling and compaction, which will be discussed further below. In this case, it cannot be excluded that CHP particles are in a much less activated state after the compaction than particles of the other materials, which have been subjected to milling.

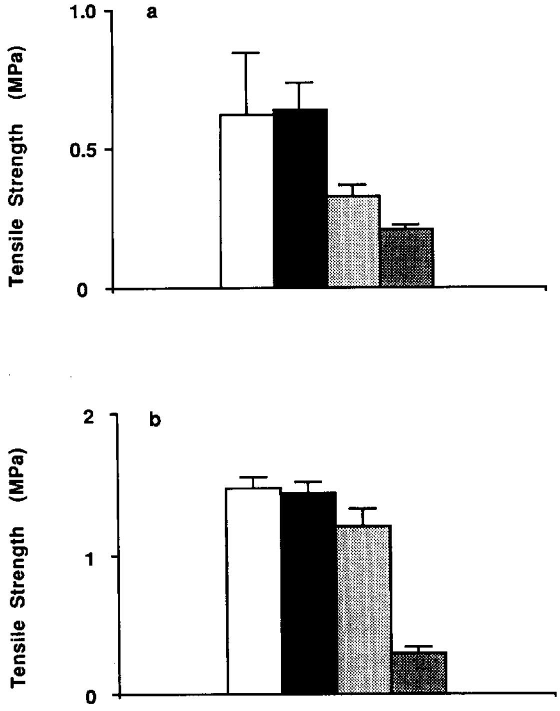

Fig. 4. a. Tensile strength of saccharose tablets, compacted at 50 MPa, after 7 days of storage at 75% RH. Tablets moved to 75% RH directly after compaction (open columns). Tablets stored at 33% RH for 7 days before transfer to 75% RH (closed columns). As reference values, the strength of tablets stored at 33% RH for 7 days (light grey columns) and the tablet strength immediately after compaction (dark grey columns) are included. b. Tensile strength of sodium chloride tablets, compacted at 50 MPa, after 7 days of storage at 57% RH. Tablets moved to 57% RH directly after compaction (open columns). Tablets stored at 33% RH for 7 days before transfer to 57% RH (closed columns). As reference values, the strength of tablets stored at 33% RH for 7 days (light grey columns) and the tablet strength immediately after compaction (dark grey columns) are included. Bars: see Fig. 2.

Changes in tablet surface area during storage

The tablet surface area–storage time profiles were also affected by the RH during storage of tablets of saccharose and sodium chloride (Ahlneck and Alderborn, 1989b). For saccharose tablets (Fig. 5a), a storage at 33% RH gave an almost constant surface area over the time period studied. At the intermediate level (75% RH), the surface area is clearly reduced with storage time, i.e., the pore structure of the tablet was opened up during storage which gave an increased tablet permeability and a reduced calculated tablet surface area. Initially the decrease in tablet surface area was most marked. At 84% RH, there was a fast initial reduction followed by a marked increase in tablet surface area. This latter observation is a result of condensation of water, which will block pores in the tablet and thereby markedly reduce the air permeability, i.e., the calculated surface area values cannot be related to the pore structure of the tablet.

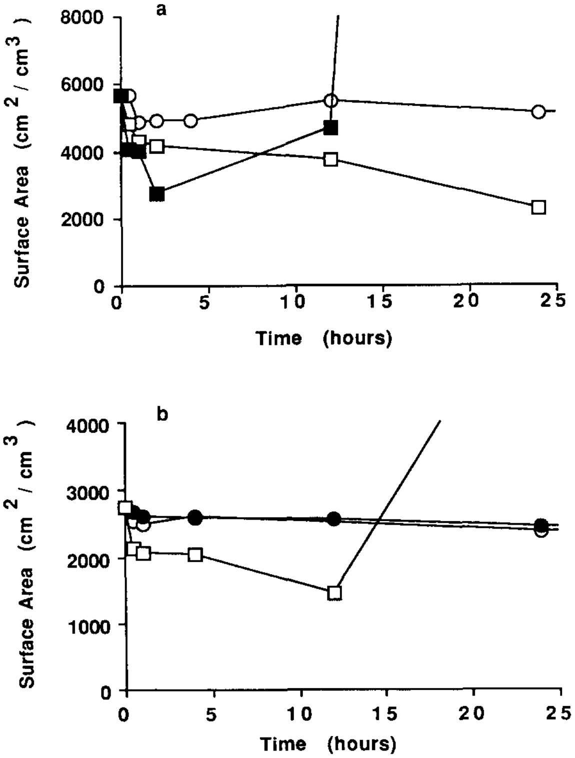

Fig. 5. a. Permeametry surface area of saccharose tablets, compacted at 50 MPa, as a function of storage time. ○, 33% RH; □, 75% RH; ■, 84% RH. b. Permeametry surface area of sodium chloride tablets, compacted at 50 MPa, as a function of storage time. ○, 33% RH; ●, 57% RH; □, 75% RH.

For sodium chloride (Fig. 5b), similar profiles as for saccharose were obtained. However, at 33% RH and 57% RH, the absolute decrease was comparatively small. However, due to the lower starting surface area for the sodium chloride tablets compared to the tablets of saccharose, the relative decrease in tablet surface area was similar for tablets of the two materials. A permeametry surface area unchanged with time has earlier been observed for tablets compacted of comparatively coarse particulate sodium chloride at intermediate RH values (Alderborn et al., 1985; Nyström and Karehill, 1986). The increase in surface area for tablets stored for more than 12 h is explained as a false value as described for saccharose.

For sodium chloride, the permeability of the tablets might be affected by the formation of a skin at the top surface of a tablet which means that such a skin can mask a change in the pore structure in the interior of the tablet. Such a skin has been observed for tablets compacted of a metal powder (Shotton et al., 1976). However, in this case the formation of a surface skin probably occurs to a limited extent because of the low compaction pressure used (Karehill et al., 1990a).

The general tendency for the surface area–storage time profiles seems to be a faster initial decrease in tablet surface area followed by a slower decrease, i.e., these profiles tend to be principally equal but inverted compared to the general tablet strength–storage time profiles discussed above.

Relationships between tablet strength and tablet surface area

In Fig. 6, the mechanical strength of saccharose and sodium chloride tablets are plotted as a function of the permeametry surface area of the tablets. For both materials, these tablet characteristics seem to be almost linearly related to each other although the slopes of the lines were different. Deviations from this relation were found when water condensed in the pores of the tablet (values for the latter tablets are not incorporated in the figure).

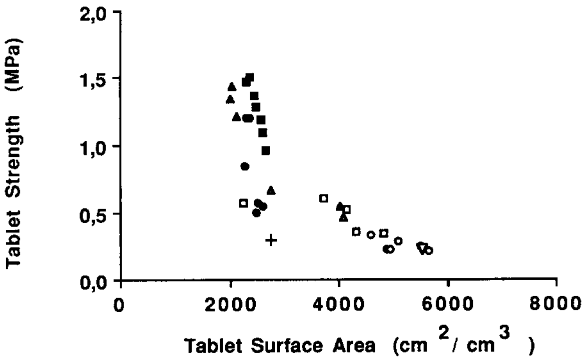

Fig. 6. Tensile strength as a function of permeametry surface area for saccharose and sodium chloride tablets compacted at 50 MPa. Saccharose: ▽, Immediately after compaction; ○, 33% RH; □, 75% RH; △, 84% RH. Sodium chloride: +, Immediately after compaction; ●, 33% RH; ■, 75% RH; ▲, 84% RH.

The reduction in surface area of the tablets during the storage probably means that the mean diameter of the pores increases. This indicates that there is a transport or movement of solid material within the tablet during the storage. The decrease in surface area is directly related to an increase in tablet strength, i.e., the movement of solid material results in such a rearrangement of the material that new interparticulate attractions are formed. This rearrangement of solid material seems to be mediated or facilitated by the uptake of water from the environment. It seems reasonable that the RH of the environment during storage of tablets affects both the rate and the amount of water uptake. Thus, both the rate and the total degree of movement of solid material and the subsequent formation of interparticulate attractions, is related to the amount of sorbed water.

It seems that two mechanisms for the rearrangement of solid material are possible. Firstly, the movement of solid material can be described as a process which reminds of molecular diffusion, i.e., there is a flow of molecules at the surface of the particles. It seems reasonable that there is an energetic drive behind this diffusion of molecules or ions within the tablet. Both a reduction in the surface area of the tablet and the formation of attractions or bonds between particles (Coffin-Beach and Hollenbeck, 1983) will reduce the energy of the system. This mechanism might be supported by observations (Kontny et al., 1987) that the specific surface area of sodium chloride powders reduced due to sorption of water.

As mentioned above, it has been suggested (Ahlneck and Zografi, 1990) that activation of the material is a prerequisite for a reactivity between water vapour and the solid. The proposed mechanism for this is that water molecules ‘dissolve’ in regions of disordered solid, created during mechanical processing such as milling and compaction. The water can then increase the free volume of the disordered solid, i.e., transform the solid from a glassy to a rubbery state. Hence, the mobility of solid molecules or ions can increase which will facilitate a diffusion of molecules and a ‘recrystallization’ of the material, i.e., a transformation from an amorphous to a crystalline state.

Secondly, it cannot be excluded that a deformation of the solid can occur due to the sorption of water. The water sorption might induce the formation of a shear plane and thereby a viscous flow of the material, e.g., by reducing the interactions between surfaces and particles or in a flaw in a particle.

It can be assumed that the surface area values are a measure of the amount of solid material which is rearranged within the tablet. A certain change in the pore structure of sodium chloride tablets gave a more marked increase in tablet strength, i.e., the slope of the tablet strength–tablet surface area line (Fig. 6) differed between saccharose and sodium chloride. Thus, it seems that for tablets of sodium chloride, the rearranged material will be more effectively used for the creation of new interparticulate attractions, either as solid bridges or as strong intermolecular attractions. This observation might be related to the bonding characteristics within the tablet formed during the compaction phase. In tablets of saccharose, the attraction forces between particles are probably mainly intermolecular attraction forces while for sodium chloride (Alderborn and Nyström, 1982; Karehill and Nyström, 1990a,b; Karehill et al., 1990b), a formation of solid bridges between particles in the tablets during the compaction phase is possible. Alternatively, local plastic flow may occur at points of interparticulate contact during the compaction which can result in particle surfaces in the formed tablet which locally are in very close proximity to each other. This will result in strong intermolecular attractions relative to the interactions in tablets of saccharose. In tablets of sodium chloride, the movement and the subsequent deposition of molecules might be more effective with respect to the creation of new interparticulate attractions during the post compaction storage phase.

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