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The effect of pre-compaction processing and storage conditions on powder and compaction properties of some crystalline materials

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Abstract

The effect of humidity during the pre-compaction storage of milled activated materials on the powder and compact properties was studied. Test materials were sodium chloride, sucrose, dicalcium hydrogen phosphate (CHP) and acetylsalicylic acid (ASA). Storage of the milled powders at 0% RH before compaction affected neither the powder characteristics nor the tablet strength of the materials. Storage at high RH before compaction affected the powder and tablet surface areas as well as reducing the tablet strength for sodium chloride. Crystallisation of the solid materials' activated surfaces occurred before compaction, i.e., a deactivation of the milled material, mediated by the presence of water vapour at the particle surfaces. For sucrose, a reduction in powder surface area on pre-compaction storage at high RH did not lead to changes in tablet strength. This was attributed to its fragmenting behaviour during compaction creating new bonding surfaces. Storage of sodium chloride and sucrose compacts increased the tablet strength except at 0% RH, suggesting the existence of a lower critical RH, below which the compacts appeared to be physically stable. The pre-compaction powder storage at high RH, reduced the post-compaction strength increase for sodium chloride compacts. ASA and CHP being less water soluble were not affected by RH on pre-compaction storage of the milled powders.

Key words: Activation; Deactivation; Glass transition temperature; Lower critical relative humidity; Storage effect; Tablet tensile strength; Surface area

1. Introduction

In the formulation of solid dosage forms, the use of crystalline forms of drugs is normally favoured due to their improved physical and chemical stability compared to amorphous forms. However, crystals are never totally perfect in their structure and defects or imperfections can act as reactive sites. Special interest has been focused on the solid state structure of the surface of particles since disordered particle surfaces, i.e., activated surfaces, might affect the physico-chemical properties, such as solubility (Florence and Salole, 1976), chemical stability (Waltersson and

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Lundgren, 1985) and the process performance of a powder.

It has been suggested that mechanical processing (e.g. milling, mixing and compaction) can activate particle surfaces or localised regions of that surface, the so-called 'frictional hot spots' (Kornblum and Sciarrone, 1964; Hersey and Krycer, 1980). Disordered solid surfaces seem to be prone to change their structure and approach an ordered structure with time (Hüttenrauch et al., 1985; Kontny et al., 1987). This change can be described as a deactivation or crystallisation of the material, probably associated with a reduction in surface energy, enabling the activated surface regions of the particles to resume a more thermodynamically stable, lower energy state. The initiation of such a process depends on whether the molecules of the solid exhibit a sufficient molecular mobility (Ahlneck and Zografi, 1990) which is caused by an increase in temperature (Danjo and Otsuka, 1988) and/or the presence of water vapour in the material (Ahlneck and Alderborn, 1989b; Alderborn and Ahlneck, 1991). It has been shown that moisture can be absorbed into an amorphous structure and upon crystallisation be released from the material (Makower and Dye, 1956). The use of sorption of water into amorphous surface regions has also been used for the assessment of the degree of disorder in solid materials (Saleki-Gerhardt et al., 1994; Sebhatu et al., 1994).

It has been proposed that the solid state structure of particle surfaces can affect the potential of particles to form interparticulate bonds during compaction (Hüttenrauch, 1978), as well as changes in compact strength during storage (Mitchell and Down, 1984; Down and McMullen, 1985; Ahlneck and Alderborn, 1989a,b; Alderborn and Ahlneck, 1991). Especially with respect to the mechanical instability of the compacts, a disordered solid state structure at particle surfaces has been suggested as a prerequisite for bond formation during storage of compacts. Thus, storage of milled particles in humid atmospheres before tabletting might affect both the compactability of the powders, as well as the changes in compact strength occurring during the storage of compacts. There is a limited knowledge of how storage conditions of processed materials affect their behaviour in the production of pharmaceutical preparations. The objective of this paper was, therefore, to determine whether conditions during storage of a milled material prior to compaction affect its technical and compaction properties.

2. Materials and methods

2.1. Materials

2.1.1. Sodium chloride

Sodium chloride (crystalline puriss, Kebo-Grave, Sweden) is freely water soluble and shows limited fragmentation during compression (Duberg and Nyström, 1982; Alderborn et al., 1985). An RH_0 of 75.3% at 25°C has been reported (Van Campen et al., 1983). RH_0 is the critical relative humidity above which the adsorbed water assumes the character of a bulk solution or condensate.

2.1.2. Sucrose

Sucrose (crystalline puriss, Kebo-Grave, Sweden) is a very water soluble material that fragments extensively during compression (Duberg and Nyström, 1982; Alderborn et al., 1985). RH_0 values of 84.3% at 25°C (Van Campen et al., 1983) and 77.4% (Katalog Pharmazeutische Hilfstoffe, 1974) have been reported.

2.1.3. Calcium hydrogen phosphate dihydrate

Calcium hydrogen phosphate dihydrate (CHP) (Emcompress, E. Mendell and Co., U.S.A.) is a practically water insoluble material. Small particles of CHP show limited fragmentation during compaction (Ahlneck and Alderborn, 1989b).

2.1.4. Acetylsalisylic acid

Acetylsalisylic acid (ASA) (Apoteksbolaget AB, Sweden) is a slightly water soluble material that fragments to a large extent during compression (Duberg and Nyström, 1982, 1986; Alderborn et al., 1985).

2.2. Methods

2.2.1. Preparation of powders

The size fraction of 40–60 μm was prepared for all powders by milling coarse crystals, prestored in desiccators for 7 days at about 0% RH (P_2O_5), using a pin disc mill (Alpine 63C, Alpine AG, Germany) followed by size classification with an air classifier (Alpine 100MZR, Alpine AG, Germany).

A fraction of each material was used immediately after milling and size classification. The rest of the powders were spread in petri dishes and stored for 7 days at room temperature in desiccators at constant RH. These were 0% RH, 33% RH and a high RH below RH_0 (57% RH for sodium chloride, 75% RH for sucrose and 84% RH for ASA and CHP) obtained by the use of P_2O_5 or saturated salt solutions (Nyqvist, 1983).

During storage, sucrose particles stored at 75% RH formed a cake in the petri dish. To make it possible to handle this powder, it was necessary to break down the aggregates by gentle crushing with a spoon. It was considered unacceptable to apply higher stresses to the powder during deaggregation due to the risk of comminuting the original particles (and hence producing new disordered particles surfaces). An identical procedure for preparing the powder for surface area analysis and for powder compaction was used.

2.2.2. Powder surface area

The surface area was determined by air permeametry using a Blaine apparatus (Ton Industries, Germany) for all materials, immediately after milling and size classification and after 7 and 30 days storage at the RH described above. The weight specific surface area corrected for slip flow was calculated as described earlier (Alderborn et al., 1985) ($n = 3$).

For sodium chloride and sucrose, the powder surface area was also determined by photometry. The inclusion of photometry was made to investigate whether the change in permeametry surface area was due to changes in particle surface area or in degree of agglomeration. At least four different amounts of sodium chloride and sucrose powders, stored at 0% and higher RH, were each suspended in saturated solutions of 95% ethanol or in methyl acetate, and the volume made up to 50 ml. The samples of each material and concentration were measured in an EEL photometer (Evans Electroselenium, U.K.). The surface area was calculated using the correction for the extinction coefficient proposed by Rose and Sullivan (1959). Following the initial readings, the samples were subjected to ultrasonic treatment in a water-bath (Bransonic 220, 50 KHz, U.S.A.) for 1, 3, 5, 7, 9, 11 and 15 min. The surface area was calculated after each treatment.

2.2.3. Thermogravimetric analysis (TGA)

TGA was performed for selected samples of sucrose and CHP after milling and storage for 7 days at various RH values using a Perkin Elmer TGA 7 (Perkin Elmer, U.S.A.).

2.2.4. Scanning electron microscopy

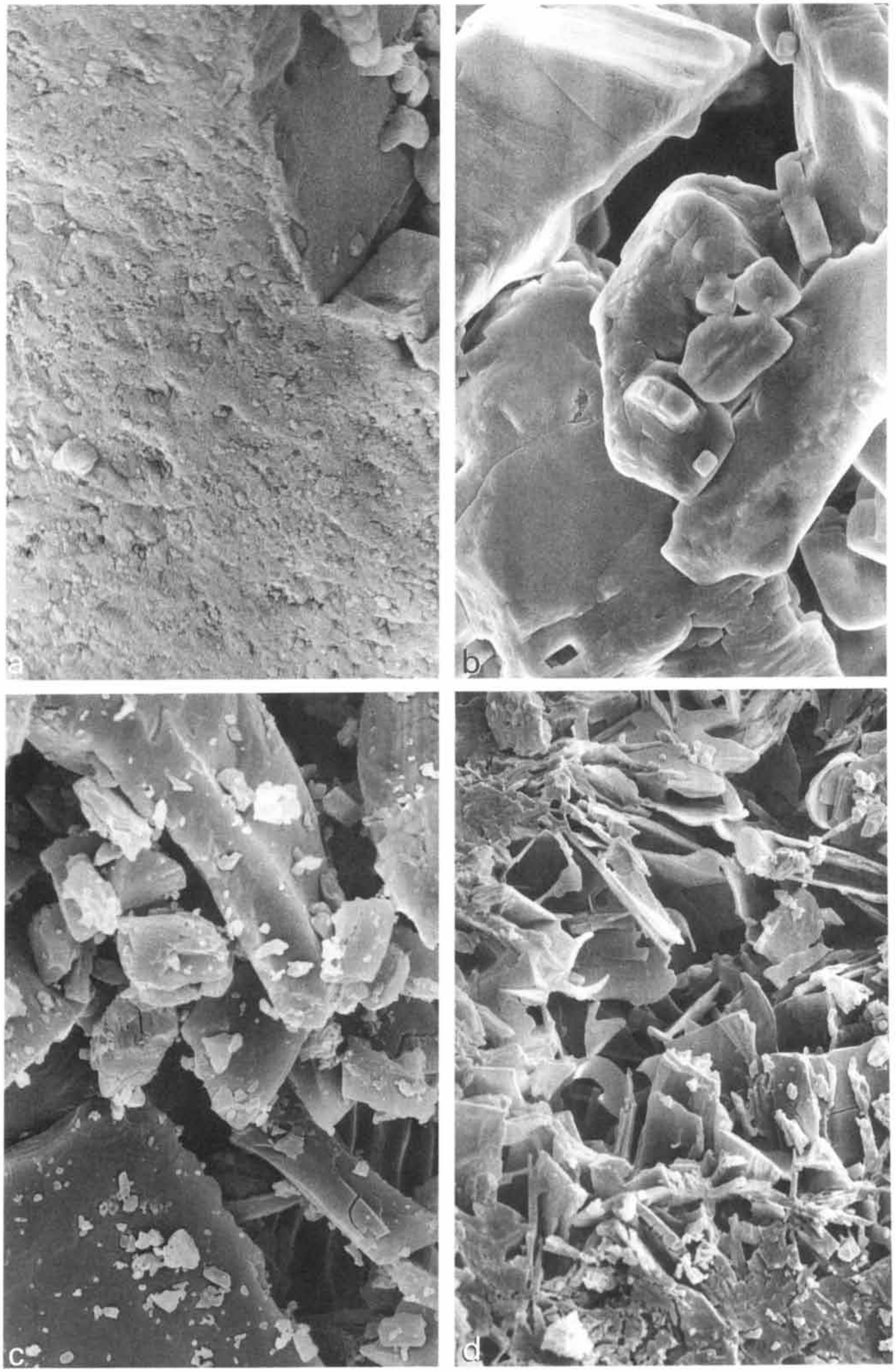
Samples of sodium chloride powders stored at 0 and 57% RH and sucrose powders stored at at 0 and 75% RH were sputter-coated with a thin layer of gold and examined under a scanning electron microscope (JEOL JSM T330, Japan) using secondary electron imaging with an accelerating voltage of 10 kV.

2.2.5. Compression of tablets

Tablets were compressed in an instrumented single punch tablet press (Korsch EK O, Germany) at a maximum upper punch pressure of 50 MPa. Flat faced punches with a diameter of 1.13 cm were used with a distance of 3 mm between the punch faces at the lowest position of the upper punch at zero pressure. The powder for each compact was individually weighed on an analytical balance and poured into the die. External lubrication was performed using a 1% magnesium stearate suspension in ethanol.

2.2.6. Storage and characterisation of the compacts

Some tablets were characterised immediately after compaction (within 1 min). The rest of the compacts were stored for 4 h or 7 days at room temperature at 0%, 33% and either at 57% (sodium chloride), 75% (sucrose) or 84% RH (ASA and CHP), before characterisation.


a
b
c
d

The diametral compression strength was measured (Erweka TBH, Germany) for compacts of each material and storage condition ($n = 10$). The weight and height were recorded. The tensile strength was calculated according to Fell and Newton (1970).

The air permeametry surface area, of tablets compacted by hand in the instrumented press at 50 MPa, except for ASA which was compacted at 12 MPa, was measured in the die immediately after compaction with a Blaine apparatus ($n = 3$). The procedure and the equations used for calculating the tablet surface area have been presented earlier (Alderborn et al., 1985).

3. Results and discussion

3.1. Powder properties

Storage of sodium chloride and sucrose powders at 0% RH did not affect the character of the powder, as assessed by visual and optical microscopic examination. However, after storage at 33% RH, aggregates could be seen. Storage at the highest RH produced a marked aggregation of the particles, especially for sucrose particles where a cake was formed in the petri dish. It seems that milled particles of sodium chloride and sucrose are prone to form aggregates spontaneously during storage. The presence of water vapour within the material, obtained in this case by sorption from the humid storage environment, seems to be a prerequisite for the initiation of such a process. This suggests that a combination of a disordered particle surface structure, as a result of the milling procedure, and the presence of sorbed moisture in the material, induce sufficient mobility of the ions/molecules to initiate crystallisation at the particle surface of the solid material, i.e., a transformation of the surface from a disordered (amorphous) structure to an ordered (crystalline) structure (Kontny et al., 1987; Ahlneck and Zografi, 1990).

Table 1
Thermogravimetric analysis of moisture content (% w/w) of sucrose and dicalcium hydrogen phosphate (CHP) powders

Material	Storage condition (% RH)			
	No storage	0	33	High
CHP (as supplied)	5.24	5.02	–	–
CHP (milled)	–	4.33	4.19	4.44 [a]
Sucrose (milled)	–	0.16	0.17	0.06 [b]

[a] 84% RH.
[b] 75% RH.

Thermogravimetric analysis of the milled sucrose following storage for days at various RH (Table 1) showed that the powders stored at 0 and 33% RH have a higher moisture content than that stored at 75% RH. This finding supports the view that crystallisation of activated surface regions of sucrose particles does occur during storage, with a subsequent release of the sorbed moisture. The relatively small loss of moisture during storage suggests that only the surface layer of sucrose particles was affected by the milling process.

The existence of a deactivation process at the particles' surface is further supported by the photomicrographs (Fig. 1). Sodium chloride particles stored at 0% RH possessed a rough, matt surface (Fig. 1a) while those stored at 57% RH possessed a smoother, more brilliant surface (Fig. 1b), suggesting that the surfaces of particles stored at 0% RH were disordered, while those stored at 57% RH were more crystalline. Following the storage of sucrose particles at 0% RH, individual particles can be distinguished (Fig. 1c) while after storage at 75% RH, a cake was formed by a massive network of particles (Fig. 1d) with the loss of particle individuality.

This indicates that the deactivation of the material can lead to the formation of strong interparticulate bonds parallel to and caused by, the deactivation, with spontaneous aggregate formation. The most extreme aggregation is the formation of a strong cake. It seems reasonable to

Fig. 1. Scanning electron microscopic photographs of: (a) sodium chloride powder stored at 0% RH; (b) sodium chloride powder stored at 57% RH; (c) sucrose powder stored at 0% RH; (d) sucrose powder stored at 75% RH.

Table 2
Permeametry surface area and porosity for sodium chloride (40–60 μm) powders and tablets compacted at 50 MPa

	RH (%)	Surface area (cm^2/g)		Porosity (%)
Powders, not prestored	–	2038	(63.0)	44.7
Powders stored for 7 days at	0	1638	(155)	43.7
	33	1747	(142)	42.3
	57	1243	(54.0)	42.3
Powders stored for 30 days at	0	1475	(212)	45.0
	33	1694	(53.0)	44.1
	57	1306	(36.3)	43.8
Tablets made from powders not prestored	–	2082	(47.1)	28.0
Tablets made from powders prestored for 7 days	0	1854	(229)	31.4
	33	1739	(47.1)	30.7
	57	1315	(45.5)	32.7
Tablets made from powders prestored for 30 days	0	1817	(20.0)	29.8
	33	1739	(44.0)	30.1
	57	1359	(20.4)	30.9

Standard deviations are given in parentheses.

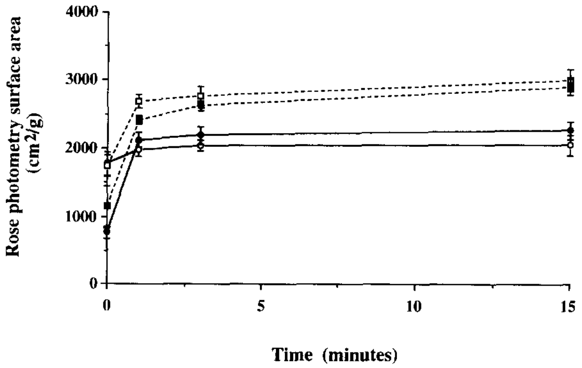


Fig. 2. Rose photometry surface area for sodium chloride and sucrose powders as a function of ultra-sonification time (bars represent the standard deviation). (○) Sodium chloride powder stored at 0% RH; (●) sodium chloride powder stored at 57% RH; (□) sucrose powder stored at 0% RH; (■) sucrose powder stored at 75% RH.

suggest that the mechanism behind this interparticulate bond formation process is similar to that of the bond formation processes occuring in compacts of these materials during storage (Ahlneck and Alderborn, 1989b; Alderborn and Ahlneck, 1991).

The properties of the powders were also characterized by air permeametry and photometry surface areas. Sodium chloride powder showed no clear pattern in the relationship between permeametry surface area and the storage conditions (Table 2). However, a slight decrease in surface areas for the powders stored at the highest RH was noted. The photometry measurements (Fig. 2) clearly demonstrated a reduction in the initial surface area for the powder stored at 57% RH compared to that stored at 0% RH, the surface area values being obtained without sonification of the samples. However, an increased sonification time resulted in an equal surface area for both samples. These results support the existence of aggregates in the powder stored at the high RH, formed as a result of a surface crystallisation process. Nevertheless, these aggregates can be broken down by sonification. It also indicated that the size of the original particles was not changed during storage.

For sucrose powders, storage at 0 and 33% RH did not affect the surface area (Table 3) while storage at 75% RH led to a marked reduction in surface area. This was also supported by the photometry measurements (Fig. 2).

For ASA and CHP, storage did not seem to affect the character of the powders, i.e., no aggre-

Table 3
Permeametry surface area and porosity for sucrose (40–60 μm) powders and tablets compacted at 50 MPa

	RH (%)	Surface area (cm^2/g)		Porosity (%)
Powders, not prestored	–	3048	(165)	45.5
Powders stored for 7 days at	0	3032	(61.6)	44.0
	33	3003	(23.6)	45.4
	75	801	(191)	41.2
Powders stored for 30 days at	0	3091	(21.1)	44.6
	33	2620	(206)	47.1
	75	932 [a]		43.2
Tablets made from powders not prestored	–	4854	(517)	28.6
Tablets made from powders prestored for 7 days	0	4517	(302)	28.2
	33	4263	(132)	29.5
	75	2429	(50.2)	29.4
Tablets made from powders prestored for 30 days	0	4760	(319)	28.5
	33	4327	(377)	30.6
	75	–		

Standard deviations are given in parentheses.
[a] Only one sample.

gation or caking took place. It appears that these materials were either not affected by the milling process and thereby not activated in the first place, or were not deactivated under the storage conditions used, or the deactivation process was not manifested as an aggregation of particles. Thermogravimetric analysis (Table 1) showed that milling of CHP led to a reduction in the moisture content, probably due to loss of crystal water (Carstensen, 1988), indicating that the milling process had an effect on the solid state structure of the material. It is thus suggested that milling of particles produced a similar disordering of the particle surfaces of CHP and probably also for ASA as for the other materials. The lack of spontaneous aggregation during storage of ASA and CHP suggested that the mobility of the molecules might not be sufficient to result in a bond formation process and the spontaneous crystallisation of surface material during storage is thereby inhibited. If this is valid, it is reasonable to suggest that solubility of the material is of importance for the interaction of water with an activated material.

3.2. Compact properties determined immediately after compaction

For compacts of sodium chloride, the specific surface area was generally similar to that of the powder before compression (Table 2), supporting the view that the particles fragment to a limited extent during compression. The surface area of the compacts of the different powders were similar except for compacts of the powder stored at the highest RH where a decrease in tablet surface areas was observed. Firstly, these compacts seemed to exibit a more open pore structure which might be because some of the aggregates formed during powder storage retained their integrity to some extent during the compression phase. If so, the separation distance between aggregates in the compact will be larger than that between individual particles and thus, a more

Table 4
Tablet strength of sodium chloride, sucrose, acetylsalicylic acid (ASA) and dicalcium hydrogen phosphate (CHP) tablets as a function of storage conditions

Material	Powder storage RH (%)	Initial tablet strength (MPa)	Post-compaction tablet strength (MPa) Tablet storage RH (%)					
			0		33		High [d]	
			4 h	168 h	4 h	168 h	4 h	168 h
Sodium chloride	[c]	0.493	0.638	0.577	0.775	1.09	1.31	1.45
	0	0.418 [b]	0.422 [b]	0.373 [a]	0.698	0.986	1.40	1.46
	33	0.293 [a]	–	–	0.656	0.885	1.27	1.33
	57	0.279	–	–	–	–	0.923	0.976
Sucrose	[c]	0.453	0.448	0.448	0.460	0.513	0.678	0.995 [a]
	0	0.413	0.433	0.425	0.475	0.520	0.639	0.959 [a]
	33	0.428	–	–	0.461	0.504	0.721 [a]	1.13
	75	0.397	–	–	–	–	0.716 [a]	0.845
ASA	[c]	0.400	0.607 [a]	0.867 [a]	0.616 [a]	0.929 [a]	0.730	1.05
	0	0.406	0.548	0.783	0.617 [a]	0.765 [a]	0,626 [a]	0.836
	33	0.385 [a]	–	–	0.565	0.783	0.632 [a]	0.897
	84	0.372	–	–	–	–	0.677	0.897
CHP	[c]	0.231 [a]	0.299 [a]	0.291	0.286	0.293	0.276	0.233
	0	0.222	0.255	0.273	0.209	0.175	0.103 [a]	0.103 [a]
	33	0.270	–	–	0.278 [a]	0.306	0.294	0.232
	84	0.242	–	–	–	–	0.236	0.194

The relative standard deviation is 0–10% if not otherwise stated; [a] relative standard deviation 10–20%; [b] relative standard deviation 20–30%; [c] no pre-compaction storage of powder; [d] sodium chloride 57%, sucrose 75%, ASA and CHP 84%.

open compact pore structure will result. Secondly, the difference in the solid structure of the surfaces might affect their compression behaviour, reflected as changes in the tablet pore structure. Thirdly, the deactivation process might have changed the particle geometry in such a way as to produce compacts of more open pore structure.

For sucrose, the formation of compacts involved a marked increased in the surface area of the particles due to the excessive particle fragmentation during compaction (Table 3). Also, a reduction in tablet surface area was achieved only for powders stored at the highest RH. The same explanations as for sodium chloride are probably applicable here.

For ASA and CHP, the compact surface areas were generally similar and independent of the powder storage conditions before compaction (results not shown).

The initial tensile strength of compacts of sodium chloride was not significantly ($p < 0.05$) affected by the pre-storage of the powder at 0% RH for 1 week (Table 4). However, there is a tendency that storage of powders at 33 and 57% RH before compaction reduced the strength of the compact formed. The tensile strength values determined after storage of the compacts revealed that only the compacts of the powder pre-stored at the highest RH were of lower strength values. A possible explanation of the reduction in compact strength measured directly after compaction is that the binding potentials of the surfaces are reduced as a result of the deactivation process during the powder pre-storage, as discussed above. However, since the reduction in compact strength coincided with the presence of aggregates in the powder before compression, this might also contribute to the reduction in the compact strength.

The tensile strength of sucrose compacts was not affected by pre-storage at any studied RH, except for a slight tendency to a decreased tensile strength of compacts produced from the powder stored at the highest RH (Table 4). Although sucrose powder is deactivated by the sorbed water vapour, as indicated by the reduction in powder surface area when stored at high RH, it did not show changes in compact strength. This is most likely due to the fact that sucrose fragments excessively during compaction, creating new surfaces which are unaffected by the earlier storage conditions.

For ASA and CHP, the variation in the pre-compaction storage conditions did not appear to affect the compactability of the powders (Table 4).

3.3. *Compact properties determined after storage of compacts*

The tablet strength increased with the post-compaction storage time for both sodium chloride and sucrose at intermediate and high RH (Table 4; Fig. 3a,b) which is consistent with earlier findings (Ahlneck and Alderborn, 1991). The increase in compact strength occurred mainly within the first 4 h of storage. However, only a minor change, if any, in the post-compaction tablet strength was noticed when the tablets were stored at 0% RH. The small increase in tablet strength for sodium chloride compacts stored at this RH during the first 4 h of storage could be due to a minute restructuring of the compacts, initiated by small amounts of water vapour present in the material, after milling.

For sodium chloride tablets, an equal increase in tablet strength was achieved after storage, independent of the pre-compaction storage condition of the powder (Table 4; Fig. 3a), except for the powder pre-stored at 57% RH, for which the increase in compact strength was lower in absolute terms. This might be due to the reduced fraction of disordered regions remaining at the particle surfaces following the deactivation of the material during pre-compaction storage. Nevertheless, this sample showed a fairly marked increase in tablet strength during the storage of the compacts. This could be explained as being due to the 'fresh' particle surface activation that took place as a result of interparticulate friction during compaction.

Also for sucrose, an increased RH during storage of compacts increased the compact strength (Table 4; Fig. 3b). Again the pre-compaction storage of the powder had a limited effect on the

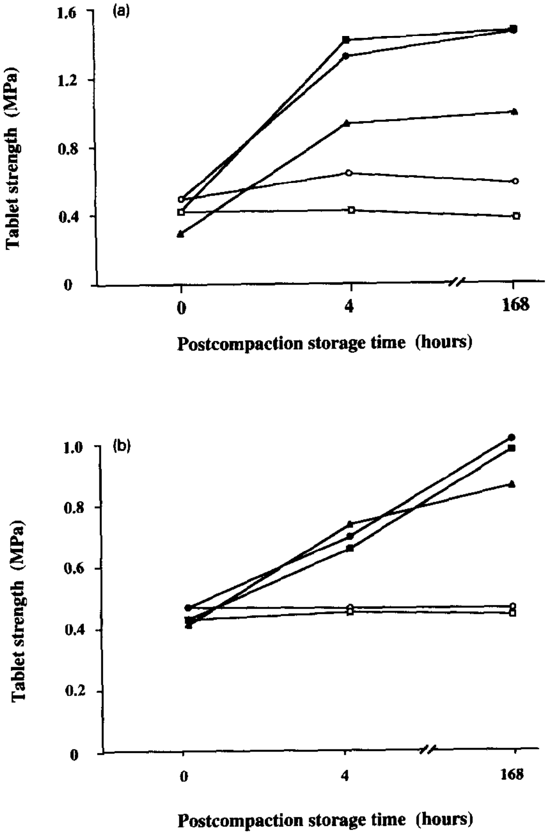


Fig. 3. Tablet strength as a function of the post-compaction storage time. (a) Sodium chloride tablets. (○) No prestorage performed - post-compaction condition 0% RH; (●) no prestorage performed - post-compaction condition 57% RH; (□) prestorage condition 0% RH, 1 week - post-compaction condition 0% RH; (■) prestorage condition 0% RH, 1 week - post-compaction condition 57% RH; (▲) prestorage condition 57% RH, 1 week - post-compaction condition 57% RH. (b) Sucrose tablets. (○) No prestorage performed - post-compaction condition 0% RH; (●) no prestorage performed - post-compaction condition 75% RH; (□) prestorage condition 0% RH, 1 week - post-compaction condition 0% RH; (■) prestorage condition 0% RH, 1 week - post-compaction condition 75% RH.

changes in tablet strength during storage. The change in the post-compaction tablet strength obtained was similar to that for sodium chloride. This seems reasonable since sucrose particles fragment to a large extent during compaction, and a significant fraction of the tablet particle surfaces is created during the formation of the compact.

The results obtained in this study indicate that the increase in tablet strength during the post-compaction storage is a water vapour mediated phenomenon, when the temperature is kept constant. A lower critical relative humidity appears to exist for the substances, below which no changes in the physical properties of the compact occur. This observation is consistent with the behaviour of the material during storage of the milled powder. The molecular mobility of solid material below the lower critical relative humidity is too low for changes to occur despite the presence of defects or disordered material at particle surfaces. Above this RH, the mobility is high enough to produce favourable conditions for crystallisation of the disordered particle surface to occur. The lower critical relative humidity is probably related to both the temperature and moisture content, which suggests that it can be related to the glass transition temperature (T_g).

CHP compacts showed some variability in the results obtained, but generally the compact strength seemed unchanged during storage of the compacts at the various RH (Table 4). This might be due to the fact that CHP is a practically water insoluble material.

ASA demonstrated an increase in the post-compaction tablet strength with time almost independent of the storage RH (Table 4; Fig. 4). This indicates that the storage RH has only a minor effect, if any, on the mechanism by which ASA tablets increase their strength after compaction. This finding supports previously published data (Mitchell and Down, 1984) where crystallisation of ASA occurred very rapidly at 25°C even at 0% RH. The difference between ASA and sucrose, for which the tablet strength increase is RH dependent, might be that sucrose in the dry state has a T_g above room temperature (Elamin et al., 1993), while ASA has a T_g below 0°C (−30°C; Fukuoka et al., 1989). Therefore, the disordered material in ASA tablets is in a rubbery state even at 0% RH and the mobility of ASA molecules is high enough to allow crystallisation. For sucrose, it is the presence of moisture that suppresses the T_g of the material to a temperature at or below room temperature (Ahlneck and Zografi, 1990). Thereby, transition from a glassy to a rubbery

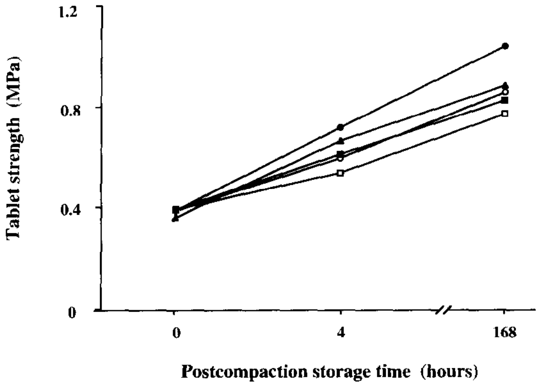


Fig. 4. Tablet strength of acetylsalicylic acid (ASA) tablets as a function of the post-compaction storage time. (○) No prestorage performed – post-compaction condition 0% RH; (●) no prestorage performed – post-compaction condition 84% RH; (□) prestorage condition 0% RH, 1 week – post-compaction condition 0% RH; (■) prestorage condition 0% RH, 1 week – post-compaction condition 84% RH; (▲) prestorage condition 84% RH, 1 week – post-compaction condition 84% RH.

state can only take place at medium/high RH. When the material is in the amorphous rubbery state conditions for crystallisation are set up. It is also possible, however, that the post-compaction strength increase for compacts of ASA is caused by visco-elastic deformation of particles, as suggested for the changes in tensile strength during storage of compacts prepared from coarse sodium chloride particles (Eriksson and Alderborn, 1994). The lack of spontaneous aggregation of ASA particles during storage of the powder before compaction thus might indicate that the post-compaction tablet strength increase for ASA compacts is caused by a visco-elastic particle deformation.

4. Conclusions

Energy-rich processing operations that cause friction and/or fracture of crystalline solids produce particle surfaces exhibiting a solid state structure different from the crystalline structure of the bulk of the particle, i.e., a disordered (amorphous) solid surface is produced. The disordered particle surfaces are thermodynamically unstable, and under favourable temperature and humidity conditions, the solid material surface will approach an ordered structure, i.e., it will crystallise. However, the activation energy can be so high that crystallisation will not occur, or will take place so slowly that crystallisation will not be observed within a certain time scale.

The amount of water sorbed by the solid material seems to be a critical factor for the material at the surface, to reach a sufficient potential to react, which is suggested in this paper to be associated with the T_g of the amorphous fraction of the solid and hence its transition from a glassy to a rubbery state, followed by its eventual spontaneous crystallisation.

It also appears that a spontaneous aggregation of particles does occur parallel to such surface crystallisation, due to the formation of interparticulate bonds. The observed changes in the powder following milling and storage might drastically affect its technical and processing properties, such as powder mixing, powder flow and die filling.

It has been suggested that the activation of a surface affects the interparticulate bond formation processes, both during compaction and storage of compacts. The ability of solid materials to change the character of their surfaces during storage emphasises the question of the relationship between the conditions during storage of the milled materials and their compaction properties.

The results obtained indicated generally that the storage conditions had a limited effect on the strength of the compact as a result of the compaction process. The reasons are probably, firstly, that some of the studied materials were physically stable during storage prior to compaction (possibly due to a low potential to sorb water from the environment) and secondly, that the particles of some of the materials fragmented markedly during compaction. In the latter case, only a fraction of the surface area of the compact corresponds to the surface area of the particles before compaction. However, especially for sodium chloride, an effect of powder storage on the interparticulate bond formation during compaction was noticed. This suggested that the pre-compaction storage conditions are critical particularly for materials which firstly show a marked tendency to crystallise during powder storage and which secondly compress by deformation rather than by fragmentation. Alternatively, they possess a marked tendency to develop solid bridges between particles during compaction (Down and McMullen, 1985; Karehill and Nyström, 1990). Since sodium chloride probably differs from sucrose in both these latter aspects, their relative importance cannot be estimated.

Concerning the changes in tablet strength occurring during storage, it was concluded, that a lower critical relative humidity might exist for certain materials, below which the compact is physically stable. However, the powder storage conditions before preparation of compacts seemed to have only a limited effect on the post-compaction strength changes, even for materials prone to crystallise readily when exposed to humid atmospheres. A possible explanation is that the particle surfaces might be activated during compression due to interparticulate friction.

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