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# Moisture adsorption and tableting. I. Effect on volume reduction properties and tablet strength for some crystalline materials

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## Summary

The presence of water in a powder mass is known to influence the behaviour of the powder during compaction as well as the mechanical strength of the tablets obtained. To study the influence of moisture content, 6 substances (sodium chloride, sodium bicarbonate, saccharose, lactose, acetylsalicylic acid, sodium citrate and Emcompress) were compressed in a range of RH (33–100%). The compression characteristics of the materials in terms of porosity–pressure displacement profiles and surface area–pressure profiles as well as the tablet strength by diametral compression were evaluated. The results showed that water adsorbed at particle surfaces has a very limited effect on the volume reduction behaviour of a particulate solid. The exception is when a fairly large amount of “condensed” water is present in the powder mass. In this case it seems that water can facilitate volume reduction, probably because water can reduce friction between particles and between powder and die wall. It was also found that the air humidity during storage markedly affected the tablet strength, showing both increases and decreases. Adsorbed water vapour increased the tensile strength for most of the tested materials at low and medium relative humidities. Condensation of water vapour at high relative humidities led to a decreased tablet strength in most cases.

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## Introduction

A common observation during the production of tablets is a variation in tablet strength associated with the presence of water in the powder mass. It is possible that sorbed water may affect the volume reduction of a powder mass as well as the interparticulate bonding in a tablet and it is as yet unclear to what extent these phenomena are affected by moisture uptake.

When a powder is brought into contact with moist air, the solid will normally sorb water. The affinity for sorbing water depends on solid/water interactions and thereby varies between materials. If absorption of water into the materials is excluded it seems that water can interact with the solid in two ways (Coelho and Harnby, 1978a; Van Campen et al., 1983; Zografi, 1988). In a fairly dry atmosphere, the water will be fairly tightly bound, as a non-freely movable layer of water, which sometimes is denoted *monolayer adsorbed moisture* (York, 1981) or *water vapour adsorption*. At most 2–3 layers of vapour will be adsorbed (Van Campen et al., 1980; Zografi, 1988). At higher RH, multilayer adsorption occurs and

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the water becomes more movable which is denoted *condensed water* (York, 1981), i.e. water becomes "solvent-like". When this occurs, molecules of the solid can dissolve in the water which might lead to deliquescence of the solid. The critical humidity ( $RH_0$ ) where this takes place is a characteristic of the solid and is the point above which the adsorbed water assumes the character of a bulk solution or condensate (Van Campen et al., 1983; Lordi and Shiromani, 1984). However, Zografi (1988) has pointed out that the model discussed is a simplification of the interaction between water in moist air and a solid.

The moisture content of the powder mass before compaction may influence the tablet strength indirectly by affecting the volume reduction of the powder mass during compression. Studies on the effect of moisture on volume reduction behaviour have been reported. Water has been suggested to act as a lubricant during compression and thereby reducing the *friction*, both interparticulate and between the particles and the die wall (Shotton and Rees, 1966; Armstrong and Haines-Nutt, 1974; Coelho and Harnby, 1978b). The compressibility of the powder mass and thereby the tablet strength can thus be influenced by water.

Increased moisture content has also been shown to give lower yield pressures and lower network during compaction (Ragnarsson and Sjögren, 1985). This was attributed to the assumption that water facilitates the *deformation* of particles in combination with reduced interparticulate friction. The former phenomenon is probably achieved primarily when water is absorbed into the particle structure.

Finally it has been suggested that moisture uptake can reduce particle *fragmentation* during compression (Armstrong and Haines-Nutt, 1974) which can have an effect on the tablet strength.

The moisture content of the powder mass can also directly affect the particle-particle interactions and thereby the tablet strength. Several different mechanisms have been discussed.

Recrystallization of dissolved material giving *solid bridges* has been proposed as a reason for increasing tablet strength for salts (Shotton and Rees, 1966; Rees and Hersey, 1972; Lordi and Shiromani, 1984; Down and McMullen, 1985) and

for compositions of many excipients (Nyqvist et al., 1981; Nyqvist and Lundgren, 1982). On the other hand, dissolution of solid bridges is claimed to give a reduction in compact strength (Rees and Hersey, 1972; Nyqvist et al., 1981; Nyqvist and Lundgren, 1982).

The formation of *liquid bridges* between particles can cause particles to adhere to each other (Rumpf, 1962). A liquid bridge will only be stable if its tendency to evaporate equals the tendency of water vapour to condensate on it (Rumpf, 1962; Coelho and Harnby, 1978a) which indicates that liquid bridges are not normally formed below the critical relative humidity. For porous solids, however, water may condense in pores at a RH lower than the critical humidity (Zografi, 1988), i.e. capillary condensation. The significance of liquid bridges for the compact strength in the case of compacts of fairly low porosity is still unclear.

It has been suggested that water vapour adsorption can have a negative effect on the interaction between particles which is due to *intermolecular forces* and thereby reduce the tablet strength (Herrman, 1971/72). However, the presence of water vapour films around particles has also been suggested as a means of affecting the tablet strength in a positive way. Firstly, it has been discussed that vapour adsorption layers can transmit molecular attraction forces if the layers touch or penetrate each other (Rumpf, 1962; Turner and Balasubramanian, 1974). Additionally, it has been argued that the vapour film can be seen as part of the particles and thereby reduce the interparticulate distances in a compact. This can increase the tensile strength of the tablet (Turner and Balasubramanian, 1974; Coelho and Harnby, 1978b).

Decreased tablet strength at elevated relative humidities have also been discussed. An increased moisture adsorption might lead to condensation and the formation of a water liquid film around particles. Such a water film can disturb intermolecular forces in a compact with a resultant decrease in compact strength (Lordi and Shiromani, 1983).

The aims of this paper are to study the role of adsorbed water for volume reduction properties during compression as well as on tensile strength

of tablets. The model materials chosen for the study are crystalline, unground substances which adsorb water onto crystal surfaces rather than absorb at the temperature and humidities chosen. They also represent a range of behaviour when compacted.

## Experimental

### Materials

Sodium chloride, 250–355  $\mu\text{m}$  (crystalline puriss, Kebo-Grave, Sweden) and sodium bicarbonate, 90–125  $\mu\text{m}$  (puriss, Kebo-Grave, Sweden) are materials which are considered to deform plastically during compaction (Duberg and Nyström, 1982; Alderborn et al., 1985b).

Saccharose, 355–500  $\mu\text{m}$  (crystalline puriss, Kebo-Grave, Sweden), acetylsalicylic acid (ASA), 355–500  $\mu\text{m}$  (Apoteksbolaget AB, Sweden), lactose, 150–180  $\mu\text{m}$  ( $\alpha$ -monohydrate, DMV, Netherlands), sodium citrate, 500–710  $\mu\text{m}$  (dihydrate, puriss, Kebo-Grave, Sweden) and Emcompress, 180–250  $\mu\text{m}$  (dicalcium phosphate dihydrate, E. Mendell Co., U.S.A.) were chosen as representative for materials which fragment to a large extent during compression (Duberg and Nyström, 1982, 1986; Alderborn et al., 1985b).

For each material the size fraction was prepared by dry-sieving (Retsch sieves, F.R.G.).

### Methods

*Storage of starting material.* The powders were stored in desiccators at constant relative humidities (RH) (33%, 57%, 75%, 84% and 100% RH) by use of saturated salt solutions (Nyqvist, 1983) at room temperature for not less than 15 days before compaction.

*Water uptake by sorption.* The water sorption for each material at each RH was determined gravimetrically ( $\pm 0.0001$  g) at 25°C ( $n = 3$ ).

*Compression of tablets.* Tablets were compressed with 1.13 cm flat-faced punches in an instrumented single-punch press (Korsch EK O, F.R.G.) at 150 MPa (maximum upper punch pressure) at 30 rpm. The distance between the punch faces at the lowest position of the upper punch was in all cases 3 mm at zero pressure. The

powder for each compact was individually weighed on an analytical balance and poured into the die. The compression procedure was carried out as fast as possible to minimize the period of time during which the material was at environmental RH (within 1 min). External lubrication with 1% magnesium stearate suspension in ethanol as well as compaction without lubrication were performed.

*Tablet porosity–pressure profiles.* For each material and storage condition (33–100% RH) 3 tablets were compressed as described above. The upper displacement and the compaction pressure was registered every 1 ms during a compression cycle as described earlier (Duberg and Nyström, 1986). After correction of punch deformation, porosity changes during a compression cycle were evaluated according to the Heckel equation (Duberg and Nyström, 1986). The Heckel plots are presented in 2 ways: firstly, by calculating the correlation coefficient of the profile with regression analysis in the pressure range 5–50 MPa; and secondly, by calculating the so-called yield pressure, i.e. the reciprocal of the slope value, in the compression range 40–140 MPa.

*Tablet surface area–pressure profiles.* For each material and storage condition (33–100% RH) approximately 8 tablets were compressed by hand in the instrumented press in the pressure range up to 50 MPa (except for sodium chloride and ASA tablets which were compressed up to a range of 125 MPa and 25 MPa, respectively). The air permeability of the tablets was measured immediately after compression, and from these data the tablet surface area was calculated according to the permeability equation. The compression procedure of the tablets as well as the equations used for calculating the tablet surface area have been presented earlier (Alderborn et al., 1985a).

*Tensile strength of tablets.* After compression, tablets were stored for 7 days before measurement of the radial tensile strength. (a) Tablets were stored in desiccators of the same RH as that at which the powder was stored before compaction. (b) Tablets compressed after pre-storage at a high RH (75%, 84% or 100%) were, after compression, directly transferred to desiccators of low RH (33% or 57%). (c) Tablets compressed after pre-storage at a low RH (33% or 57%) were after compression

directly transferred to desiccators of high RH (75%, 84% or 100%).

The diametral compression strength was measured (Erweka TBH 28, F.R.G.) on 6 tablets which had been compressed at 150 MPa for each material and storage condition. The tensile strength was then calculated according to Fell and Newton (1970). Only compacts compressed with external lubrication were stored for tensile strength measurements.

## Results and Discussion

### *Water uptake by sorption*

The materials generally showed a very small water uptake at low and medium RH (Table 1). At high RH, most materials showed a marked increase in water uptake. Exceptions are ASA and Emcompress for which only minor uptake of water is seen even at high RH. For materials that sorb water only at the particle surfaces, the increased moisture uptake at high RH is probably a result of condensation of water at the particle surfaces. For a soluble material this can, at a specific RH lead to deliquescence, e.g. as in the case of sodium chloride above 75% RH. The condensation of water tended to markedly increase the cohesiveness of the powders.

TABLE 1

*Water content of the tested materials obtained by gravimetry at various relative humidities at 25 °C*

Material	Water content in (%)				
	Relative humidity (%)				
	33	57	75	84	100
Sodium chloride	0.20	0.30	0.32	8.71	*
Sodium bicarbonate	< 0.1	< 0.1	0.29	0.26	18.3
Saccharose	< 0.1	0.25	0.38	0.83	*
Lactose	0.20	0.20	0.22	0.37	1.31
Sodium citrate	< 0.1	0.24	0.54	9.30	38.4
ASA	< 0.1	< 0.1	< 0.1	< 0.1	< 0.1
Emcompress	< 0.1	< 0.1	0.26	0.35	0.40

\* Deliquescence.

Sodium citrate shows a large increase in moisture sorption above 75% RH probably due to uptake of crystal water in combination with condensation of water at the particle surfaces. The appearance of the sodium citrate crystals were irreversibly changed by the location at 84% or higher RH. Values obtained above 75% RH are for this reason not included in the paper.

### *Volume reduction properties of materials*

#### *Tablet surface area–pressure profiles*

The tablet surface area by permeametry as a function of compaction pressure was measured for all materials and RH. It has earlier been suggested that at high pressures, i.e. above approximately 100 MPa, the tablet surface area obtained by this technique is an overestimated surface area (Alderborn, 1985). To avoid misinterpretations of experimental data obtained the pressure range up to 50 MPa was used for calculation of slope values from the surface area–pressure profiles (Fig. 1a–c). The large slope values of Emcompress, ASA and lactose, the medium slope values of saccharose and sodium citrate and the low values for sodium chloride and sodium bicarbonate are in agreement with earlier reports on the volume reduction mechanisms for these materials (Alderborn et al., 1985b; Duberg and Nyström, 1982).

For most materials there seems to be no change in slope value within the range of RH used, indicating that the degree of fragmentation during compression is not affected by the variations in amount of adsorbed moisture. Exceptions are ASA and saccharose. The slope values for ASA are steadily increasing with rising RH suggesting a slight increase in fragmentation with rising RH.

In the case of saccharose, a very large increase in slope values is found at 100% RH. This increase is suggested to be a result of a decrease in permeability due to a marked condensation of water in the pores in the tablet, i.e. the surface area deduced from the equation is a marked overestimated value.

#### *Tablet porosity–pressure profiles*

*Correlation coefficient (CC).* In Fig. 2a–c the CC has been plotted against RH. For the tablets

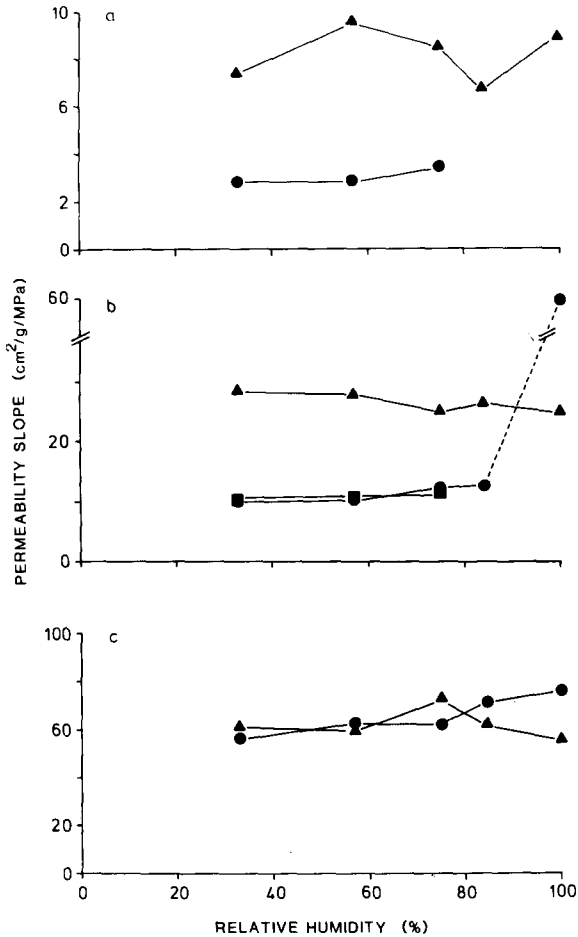


Fig. 1. Effect of relative humidity on absolute increase in tablet surface area with pressure (i.e. the slope from a plot of tablet permeametry surface area as a function of compaction pressure). a: ●, sodium chloride; ▲, sodium bicarbonate. b: ●, saccharose; ▲, lactose; ■, sodium citrate. c: ●, ASA; ▲, Emcompress.

compressed with a lubricated die only minor changes are found in CC below 84% RH (except for sodium chloride which deliquesces above 75% RH). In Table 2 the CC for tablets compressed with and without external lubrication are compared. For the 5 materials tested no differences in CC could be detected between the lubricated and unlubricated systems. This finding suggests that the CC solely reflects the interaction between the particles during the compression, i.e. the friction between the powder and the die wall is not affecting the CC. This is probably because the

stress transmission to the die wall is low at the range of compaction pressures used for the calculation of the CC. An exception is saccharose without lubrication at the lowest RH (33%) where a marked decrease in CC is found. This low CC is probably due to a comparatively high friction against the die wall for the system.

The CC is suggested to reflect the degree of fragmentation (Duberg and Nyström, 1986) during compression. The small decrease in CC observed for some materials might therefore indicate a slight increase in degree of fragmentation with

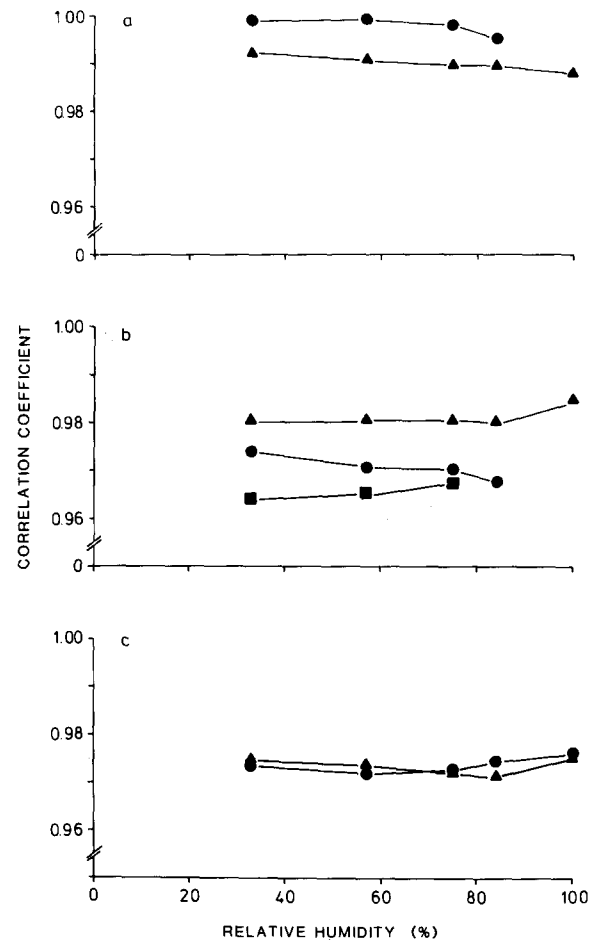


Fig. 2. Correlation coefficient, obtained from the Heckel plot, as a function of relative humidity. External lubrication performed. a: ●, sodium chloride; ▲, sodium bicarbonate. b: ●, saccharose; ▲, lactose; ■, sodium citrate. c: ●, ASA; ▲, Emcompress.

TABLE 2

Correlation coefficient for five of the studied materials with (+) and without (-) lubrication

In parentheses: S.D.s.

Material		Relatively humidity (%)				
		33	57	75	84	100
Sodium chloride	-	0.9983 (0.0003)	0.9984 (0.0003)	0.9981 (0.0004)	0.9952 (0.0004)	*
	+	0.9986 (0.0002)	0.9986 (0.0002)	0.9981 (0.0002)	0.9953 (0.0004)	*
Sodium bicarbonate	-	0.9895 (0.0007)	0.9892 (0.0002)	0.9890 (0.0002)	0.9874 (0.0007)	0.9874 (0.0001)
	+	0.9921 (0.0007)	0.9906 (0.0002)	0.9895 (0.0007)	0.9894 (0.0003)	0.9879 (0.0014)
Sodium citrate	-	0.9640 (0.0014)	0.9660 (0.0015)	0.9650 (0.0009)	-	-
	+	0.9639 (0.0014)	0.9652 (0.0018)	0.9675 (0.0021)	-	-
Saccharose	-	0.9453 (0.0230)	0.9737 (0.0039)	0.9735 (0.0006)	0.9726 (0.0011)	*
	+	0.9742 (0.0003)	0.9708 (0.0023)	0.9702 (0.0039)	0.9675 (0.0026)	*
Emcompress	-	0.9707 (0.0005)	0.9717 (0.0011)	0.9694 (0.0010)	0.9705 (0.0012)	0.9766 (0.0047)
	+	0.9745 (0.0012)	0.9735 (0.0010)	0.9720 (0.0008)	0.9713 (0.0006)	0.9752 (0.0009)

\* Deliquescence.

increasing RH. However, York (1978) has suggested that the deviation from linearity during the early compression phase is attributed to particle slippage and rearrangement in the die. The slight change in CC can therefore also be due to changes in the ability of the particles to rearrange in the die during the volume reduction.

The results indicate therefore that there are no or only minor changes in volume reduction behaviour of the materials due to sorbed moisture in the early compression phase.

*Yield pressure value ( $P_y$ ).* In Fig. 3a-c the  $P_y$ s are plotted against RH. The values obtained with

the lubricated die show no evident difference in  $P_y$  with increasing RH. An exception is sodium chloride at 84% RH where a small drop in  $P_y$  could be noticed.

Table 3 shows the  $P_y$  values for lubricated and unlubricated tablets for 5 materials. For these materials the  $P_y$ -values are higher for the unlubricated tablets than for the lubricated, with larger differences at low RH and less or none at higher RH. This suggests that the  $P_y$  is markedly affected by the friction against the die wall. The finding also suggests that water may act as a lubricant against the die wall during compression. It has

TABLE 3

Yield pressure for five of the studied materials with (+) and without (-) lubrication

In parentheses: standard deviation

Material		Relatively humidity (%)				
		33	57	75	84	100
Sodium chloride	-	169 (1.1)	166 (1.5)	164 (1.1)	115 (2.2)	*
	+	152 (0.7)	152 (0.7)	151 (1.5)	113 (2.5)	*
Sodium bicarbonate	-	238 (5.6)	211 (5.1)	231 (0.6)	222 (1.7)	179 (1.5)
	+	178 (0.0)	177 (3.5)	188 (1.0)	175 (1.0)	170 (5.0)
Sodium citrate	-	260 (3.1)	238 (2.3)	232 (2.0)	-	-
	+	233 (2.3)	244 (4.0)	216 (3.0)	-	-
Saccharose	-	211 (4.2)	209 (5.7)	209 (2.3)	199 (5.6)	*
	+	141 (0.7)	149 (2.5)	163 (3.8)	167 (0.0)	*
Emcompress	-	289 (2.5)	300 (3.1)	296 (0.7)	305 (14)	265 (6.7)
	+	276 (4.0)	266 (1.7)	272 (6.1)	277 (2.1)	275 (5.7)

\* Deliquescence.

also been pointed out earlier that the  $P_y$  seems to be dependent on experimental conditions such as degree and type of lubrication of punches and dies (York, 1979). However, this lubricating effect seems to occur only at the highest RH, i.e. probably when water was beginning to condensate on the particle surfaces.

This indicates that the volume reduction behaviour in the secondary compression phase is normally not affected by the change in amount of adsorbed water. However, when a large amount of water is present, it seems that water can act as a lubricant and reduce the friction between particles on one hand and between particles and die wall on the other. The compression of the powder is thereby facilitated. This is probably the reason for the drop in  $P_y$  at 84% RH for sodium chloride (Fig. 3a).

#### Tensile strength of tablets

For most materials the tensile strength increased with increasing RH (Fig. 4a-c). For sodium chloride, sodium bicarbonate and saccharose the tensile strength reaches a maximum at an intermediate RH and then decreases while for lactose and sodium citrate, the strength increased throughout the whole range of RH used. For sodium chloride, a similar relation between tablet strength and humidity as described here has also been presented earlier (Lordi and Shiramani, 1983; Down and McMullen, 1985). For ASA no significant ( $P < 0.05$ ) change in tensile strength was found throughout the range of RH used. For Emcompress finally, there was no significant change in tablet strength at the lower humidities but the strength decreased at the highest RH used.

The values of the porosity of the tablets are presented in Table 4. Generally the porosity seemed not to change with RH except at the highest humidity when the porosity for most materials decreased. This is probably due to an increase in weight of the tablets due to the uptake of water.

In an attempt to study if these changes in tablet strength are due to changes in the volume reduction behaviour during compression, tablets were compressed after pre-storage of the powder at one

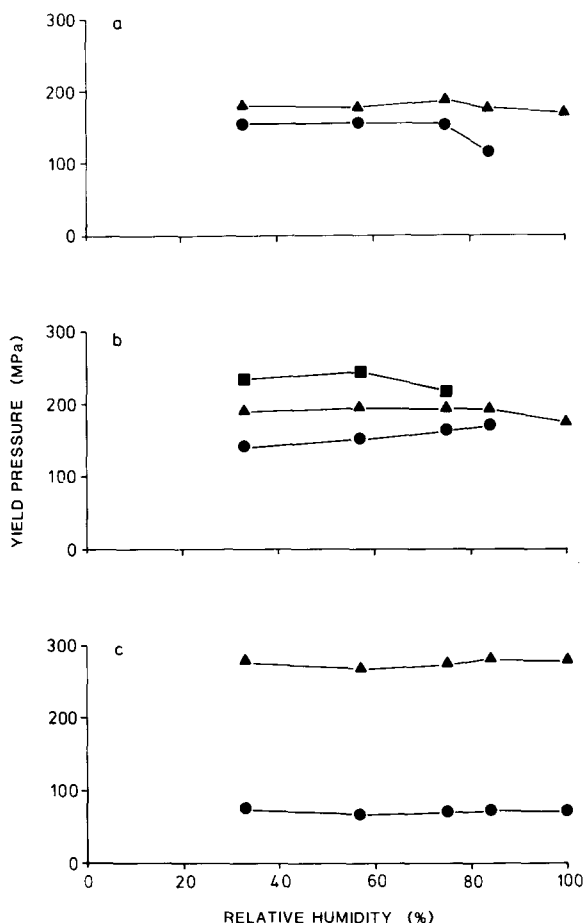


Fig. 3. Yield pressure, obtained from the Heckel plot, as a function of relative humidity. External lubrication performed. a: ●, sodium chloride; ▲, sodium bicarbonate. b: ●, saccharose; ▲, lactose; ■, sodium citrate. c: ●, ASA; ▲, Emcompress.

RH and were thereafter directly transferred and stored for 7 days at another RH before strength measurement (Table 5). Storage conditions of 33% and 84% RH were chosen as low and high RH, respectively, except for sodium chloride and sodium citrate where 75% was chosen as the high RH and for Emcompress where 57% and 100% RH were chosen as low and high RH, respectively.

For sodium chloride, the transfer of tablets from the low to the high RH led to a decrease in tensile strength (Table 5) which is due to the commencement of deliquescence of the sodium chloride. However, when tablets compressed with

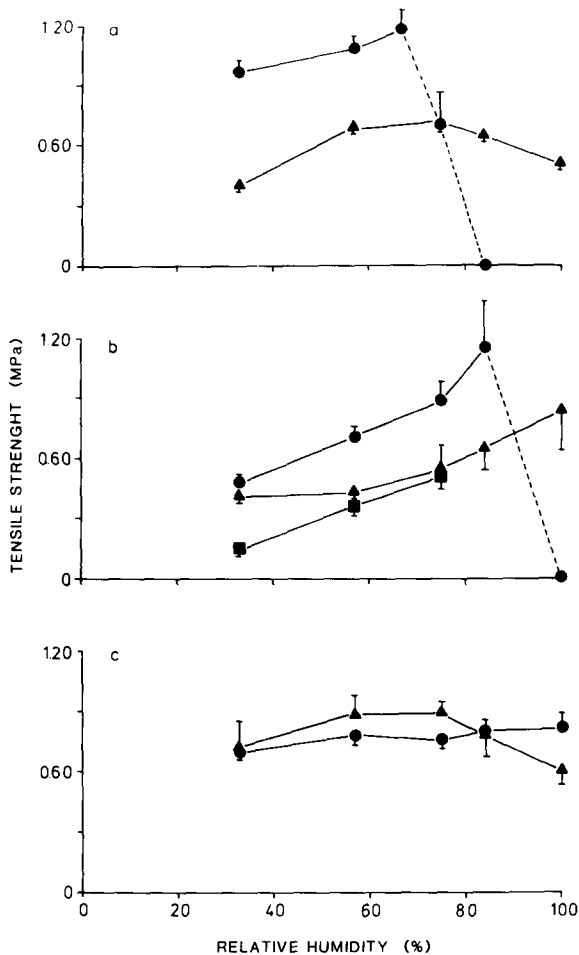


Fig. 4. Tensile strength of tablets as a function of relative humidity. Bars indicate S.D. a: ●, sodium chloride; ▲, sodium bicarbonate. b: ●, saccharose; ▲, lactose; ■, sodium citrate. c: ●, ASA; ▲, Emcompress.

the material pre-stored at 75% RH were transferred to 33%, the tensile strength increased. This can be explained by crystallization of a saturated solution, formed by the dissolution of sodium chloride in condensed water in the tablet. This conclusion suggests that solid bridges can be an important bonding mechanism between particles in a tablet in these cases.

For the fragmenting materials, saccharose, lactose, sodium citrate and Emcompress, the transfer in storage conditions showed that the tensile strength was merely dependent on the RH

during the storage of the tablets, i.e. the tensile strengths of tablets at a specific RH were the same regardless of the precompression storage RH.

For sodium bicarbonate the picture was different. The tensile strength increased when the storage conditions were changed from 33% to 84% RH, but did not reach the values of the tensile strength of tablets made and measured for tensile strength at 84% RH. Tablets made with 84% RH precompression stored material retained its tensile strength when the tablets were stored at the lower RH. In an attempt to examine this finding further, new tablets were made and storage was allowed for 7 and 30 days (Table 6). The tablets made of material pre-stored at 33% and then transferred to 84% seem to obtain the same tensile strength as tablets made of 84% RH precompression-stored material but the increase in tensile strength was proceeding much slower than for the other materials. No change in tensile strength is obtained by changing the storage RH from 84% to 33%.

It is suggested that for sodium bicarbonate the uptake and loss of water is much slower than for the other materials, but that the material in principle behaves like the other materials. Alternatively, sodium bicarbonate might in some way react with the water and the water taken up is not solely physically adsorbed at the particle surface.

To summarize, the observations concerning the effect of subjecting tablets to changing RH on storage supports the earlier conclusion that the

TABLE 4

*Porosity data at the time for strength measurement, for tablets compacted with external lubrication*

Materials	Porosity (%)				
	Relatively humidity (%):				
	33	57	75	84	100
Sodium chloride	11.2	11.8	11.2	*	*
Sodium bicarbonate	18.0	17.5	17.3	17.3	8.5
Saccharose	18.6	17.2	17.4	16.8	*
Lactose	21.7	23.0	22.2	22.8	17.3
Sodium citrate	23.0	17.3	20.3	-	-
ASA	4.91	4.70	5.18	5.25	5.84
Emcompress	25.3	22.6	23.8	25.5	21.4

\* Deliquescence.



TABLE 5

Effect on tablet strength when changing storage condition from a low to a high relative humidity or vice versa

In parentheses: standard deviation

Material	Relative humidity	Tensile strength (MPa)			
		{ Before compression: Low After compression: Low	Low High	High Low	High High
Sodium chloride *		0.96 (0.11)	0.62 (0.06)	1.2 (0.07)	0.68 (0.03)
Sodium bicarbonate **		0.40 (0.02)	0.50 (0.07)	0.65 (0.07)	0.65 (0.05)
Sodium citrate *		0.14 (0.03)	0.42 (0.09)	0.17 (0.02)	0.49 (0.05)
Saccharose **		0.48 (0.06)	1.0 (0.24)	0.53 (0.02)	0.88 (0.12)
Lactose **		0.42 (0.09)	0.63 (0.05)	0.36 (0.03)	0.65 (0.12)
ASA **		0.70 (0.02)	0.83 (0.11)	0.76 (0.09)	0.80 (0.04)
Emcompress ***		1.1 (0.06)	0.29 (0.02)	1.1 (0.10)	0.27 (0.01)

\* 33% RH – 75% RH; \*\* 33% RH – 84% RH; \*\*\* 57% RH – 100% RH.

volume reduction properties are not affected by moisture adsorbed on the surfaces of particles. It seems reasonable that a change in tablet strength due to some change in the volume reduction behaviour of the material at one RH should not lead to the same tablet strength as for tablets compressed at another RH and then transferred to the final RH.

The fairly dramatic effect of changes in tablet strength with RH therefore suggests that the moisture content during the storage time governs the tensile strength of tablets for these materials. This can be explained by the assumption that the interaction between particles in a compact is affected by adsorbed water at the particle surfaces and that the thickness and state of this water is of importance.

The assumption is based on a hypothesis that a tablet can be described as an aggregate of small, separated particles. This model is based on reports (Aldbörn, 1985; Nyström and Karehill, 1986; Aldbörn and Glazer, in preparation) which indicate that the surface area of solid bridges in a pharmaceutical compact is small. Both intermolecular forces between separate particles and the existence of solid bridges should then be of significance for the tablet strength, and the interaction between particle surfaces in the tablet and water is thereby important.

As an explanation of the *increased tensile strength* with increasing RH, we suggest that the adsorbed water vapour of a water-soluble material aids the dissolution of molecules at particle surfaces below the  $RH_0$  (Kontny et al., 1987).

TABLE 6

Tensile strength for sodium bicarbonate tablets when changing storage conditions and storage time

In parentheses: standard deviation.

Relative humidity (%)	Tensile strength (MPa)					
	{ Before compression: 33 After compression: 33	33	33	84	84%	84%
Time:	7 days	7 days	30 days	7 days	7 days	30 days
	0.31 (0.04)	0.41 (0.04)	0.48 (0.05)	0.54 (0.05)	0.50 (0.03)	0.54 (0.02)

This may lead to changes in the surface structure of the particles and also to the establishment of solid bridges by crystallization (Hall and Rose, 1978). With increasing RH, but still below  $RH_0$ , such changes will more readily occur. This mechanism can explain the results for ASA which has a relatively low solubility and for dicalcium phosphate which is practically insoluble in water. For these materials, the tensile strength was not affected by changes in RH (except for dicalcium phosphate at very high RH). No or only minor differences in tensile strength were found with increasing RH, i.e. adsorbed water vapour neither increases nor decreases the tablet strength for a substance of low solubility.

Another possible source of this increased tensile strength is that moisture adsorbed as water vapour can be seen as part of the particles. Aqueous adsorption layers of less than 3.0 nm have been claimed to be in a vapour phase and not freely movable (Rumpf, 1962; Turner and Balasubramanian, 1974; Coelho and Harnby, 1978a). Adsorbed water vapour may thereby contribute in two ways to the bonding of particles in a compact: (a) by reduction of the interparticulate surface distance by "enlargement" of the particles which could increase the effect of intermolecular attraction forces; and (b) a contribution to the tensile strength occurs due to the vapour films actually touching each other and thereby forming water vapour bridges.

The decrease in tensile strength above a maximum tensile strength RH-value that appeared for most materials, can be explained by the fact that water condenses at the particle surfaces at high RH. For water-soluble materials, such as sodium chloride and saccharose, deliquescence occurs above this critical relative humidity. For materials not undergoing deliquescence, condensed water can be considered to disturb intermolecular attraction forces and hence the tensile strength will decrease.

## References

Alderborn, G., Studies on direct compression of tablets. XV. An evaluation of the surface area obtained by permeametry

- measurements of tablets. *Acta Pharm. Suec.*, 22 (1985) 177-184.
- Alderborn, G., Duberg, M. and Nyström, C., Studies on direct compression of tablets. X. Measurement of tablet surface area by permeametry. *Powder Technol.*, 41 (1985a) 49-56.
- Alderborn, G., Pasanen, K. and Nyström, C., Studies on direct compression of tablets. XI. Characterization of particle fragmentation during compaction by permeametry measurements of tablets. *Int. J. Pharm.* 23 (1985b) 79-86.
- Alderborn, G. and Glazer, M., Studies on direct compression of tablets. XVIII. Surface areas and particles size distribution of compressed sodium chloride. In preparation.
- Armstrong, N.A. and Haines-Nutt, R.F., Surface area changes of lubricated powder systems. *Proc. 1st Int. Conf. Compaction Consol. Part. Matter 1972, Brighton*, Powder Advisory Centre, London, (1974) pp. 161-164.
- Coelho, M.C. and Harnby, N., The effect of humidity on the form of water retention in a powder. *Powder Technol.*, 20 (1978a) 197-200.
- Coelho, M.C. and Harnby, N., Moisture bonding in powders. *Powder Technol.*, 20 (1978b) 201-205.
- Down, G.R.B. and McMullen, J.N., The effect of interparticulate friction and moisture on the crushing strength of sodium chloride compacts. *Powder Technol.*, 42 (1985) 169-174.
- Duberg, M. and Nyström, C., Studies on direct compression of tablets. VI. Evaluation of methods for the estimation of particle fragmentation during compaction. *Acta Pharm. Suec.*, 19 (1982) 421-436.
- Duberg, M. and Nyström, C., Studies on direct compression of tablets. XVII. Porosity-pressure curves for the characterization of volume reduction mechanisms in powder compression. *Powder Technol.*, 46 (1986) 67-75.
- Fell, J.T. and Newton, J.M., Determination of tablet strength by the diametral-compression test. *J. Pharm. Sci.*, 59 (1970) 688-691.
- Hall, P.G. and Rose, M.A., Adsorption of water vapour on ammonium iodide and ammonium chloride. *J. Phys. Chem.*, 82 (1978) 1521-1525.
- Herrman, W., The effect of water vapour on the shear strength of briquettes. *Powder Technol.*, 5 (1971/72) 25-30.
- Kontny, M.J., Grandolfi, G.P. and Zografi, G., Water vapor sorption of water-soluble substances: studies of crystalline solids below their critical relative humidities. *Pharm. Res.*, 4 (1978) 104-112.
- Lordi, N. and Shiromani, P., Use of sorption isotherms to study the effect of moisture on the hardness of aged compacts. *Drug. Dev. Ind. Pharm.*, 9 (1983) 1399-1416.
- Lordi, N. and Shiromani, P., Mechanisms of hardness of aged compacts. *Drug. Dev. Ind. Pharm.*, 10 (1984) 729-752.
- Nyqvist, H., Saturated salt solutions for maintaining specified relative humidities. *Int. J. Pharm. Technol. Prod. Manuf.*, 4 (1983) 47-48.
- Nyqvist, H., Nicklasson, M. and Lundgren, P., Studies on the physical properties of tablets and tablet excipients III. Water sorption and its effect on hardness and disintegration. *Acta Pharm. Suec.*, 18 (1981) 305-314.

- Nyqvist, H. and Lundgren, P., Studies on the physical properties of tablets and tablet excipients. VI. The application of accelerating tests conditions to the study of water sorption and change in hardness. *Acta Pharm. Suec.*, 19 (1982) 401-412.
- Nyström, C. and Karehill, P.G., Studies on direct compression on tablets. XVI. The use of surface area measurements of the evaluation of bonding surface area in compressed powders. *Powder Technol.*, 47 (1986) 201-209.
- Ragnarsson, G. and Sjögren, J., Force-displacement measurements in tableting. *J. Pharm. Pharmacol.*, 37 (1985) 145-150.
- Rees, J.E. and Hersey, J.A., The strength of compacts containing moisture. *Pharm. Acta Helv.*, 45 (1972) 235-243.
- Rumpf, H., The strength of granules and agglomerates. In Knepper W.A. (Ed.), *Agglomeration*, Interscience-Wiley, New York, 1962 pp. 379-418.
- Shotton, E. and Rees, J.E., The compaction properties of sodium chloride in the presence of moisture. *J. Pharm. Pharmacol.*, 18 (1966) 160S-167S.
- Turner, G.A. and Balasubramanian, M., Investigations of the contributions to the tensile strength of weak particulate masses. *Powder Technol.*, 10 (1974) 121-127.
- Van Campen, L., Zografi, G. and Carstensen, J.T., An approach to the evaluation of hygroscopicity for pharmaceutical solids. *Int. J. Pharm.*, 5 (1980) 1-18
- Van Campen, L., Amidon, G.L. and Zografi, G., Moisture sorption kinetics for water-soluble substances. I. Theoretical considerations of heat transport control. *J. Pharm. Sci.*, 72 (1983) 1381-1388.
- York, P., Particle slippage and rearrangement during compression of pharmaceutical powders. *J. Pharm. Pharmacol.*, 30 (1978) 6-10.
- York, P., A consideration of experimental variables in the analysis of powder compaction behaviour. *J. Pharm. Pharmacol.* 31 (1979) 244-246.
- York, P., Analysis of moisture sorption hysteresis in hard gelatin capsules, maize starch, and maize starch: drug powder mixtures. *J. Pharmacol. Pharmacol.*, 33 (1981) 269-273.
- Zografi, G., States of water associated with solids. *Drug. Dev. Ind. Pharm.*, 14 (1988) 1905-1926.