The effect of original particle size and tablet porosity on the increase in tensile strength during storage of sodium chloride tablets in a dry atmosphere

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Abstract

Compacts were formed of three particle size fractions of sodium chloride (425–500, 90–150 and 20–40 μm) at a series of applied pressures. The tensile strength of the compacts was determined directly after compaction and after storage of the compacts in dry air for different periods of time. For compacts formed of the two coarser particles, the compact strength increased during storage and a reduced compact porosity increased the magnitude but decreased the rate of the strength increase. Compacts formed of the smallest particles were mechanically stable during storage irrespective of applied pressure and compact porosity. By stress relaxation measurements it was shown that particles of all three sizes were prone to deform viscous or visco-elastically. However, both porosity-pressure relationships and stress relaxation measurements indicated that particle deformation due to an external applied stress became difficult at low tablet porosities (approx. 5%). Thus, there were differences in the dependence of particle size and compact porosity, between stress relaxation and tablet strength instability. This indicates that time dependent particle deformation is not responsible for the increase in tensile strength of sodium chloride tablets stored in a dry atmosphere.

1. Introduction

A number of studies in the literature (Rees and Shotton, 1970; Rees and Rue, 1978; Bhatia and Lordi, 1979; Rue and Barkworth, 1980; Sheikh-Salem and Fell, 1981; Down and Mc-Mullen, 1985; Ahlneck and Alderborn, 1989; Karehill and Nyström, 1990; Alderborn and Ahl-neck, 1991; Elamin et al., 1994; Eriksson and Alderborn, 1994) have demonstrated the existence of changes in mechanical strength of tablets after compaction, i.e., a mechanical instability of tablets. Our interpretation of this observation is that the interparticulate bond structure in a compact can change although no external force is applied to the compact. However, there is a lack of knowledge concerning the physical processes

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responsible for such changes in interparticulate bond structure, as well as concerning the importance of material and compaction process factors in relationship to the changes in tablet bond structure. A knowledge of these questions is important during preformulation and formulation of drugs, in order to predict problems with mechanical instability of compacts.

By studying the changes in mechanical strength of sodium chloride tablets compacted of particles of different dimensions and mechanical treatments (Eriksson and Alderborn, 1994), two different mechanisms – denoted α and β – were found to cause an increase in mechanical strength of the compacts during storage. The β-type post compaction increase in tablet strength (obtained for compacts prepared of coarse particulate sodium chloride) was characterised by the following features: Firstly, the total magnitude of increase in tensile strength was independent of the humidity of the storage environment. However, the presence of moisture at the particle surfaces resulted in a slower increase in tensile strength during storage. Secondly, the tablet strength increase during storage was not accompanied by a measurable change in tablet pore structure.

For this mechanical instability behaviour of the compacts, i.e., the β-mechanism, it was suggested that a time-dependent, i.e., a viscous or a visco-elastic, deformation of the particles after compaction could be responsible for the change in interparticulate bond structure. This could be described as the classical interpretation of tensile strength instability of tablets (e.g., Rees and Shotton, 1970; Rees and Rue, 1978; Karehill and Nyström, 1990). However, the effect of relative humidity during storage on the time period, which elapsed before maximum increase in tablet strength was achieved (Eriksson and Alderborn, 1994), was difficult to explain with the time-dependent particle deformation theory. Thus, it was suggested that time-dependent particle deformation might fail to explain mechanistically the β-type post compaction tablet strength increase.

One approach to the assessment of time-dependent deformation of particles is to determine the stress relaxation of a compact while an external stress is applied to the compact. Thus, a comparison between stress relaxation behaviour, and tablet strength increase behaviour might contribute to establish if time-dependent particle deformation is responsible for the β-type instability in tensile strength of sodium chloride compacts. Thus, the aim of this paper was to investigate the effect of compaction pressure and compact porosity on post-compaction changes in tensile strength of sodium chloride compacts, stored in a dry atmosphere, and on stress relaxation of compacted sodium chloride particles under external mechanical stress. The outcome of the study might be a better mechanistical understanding of a post-compaction tablet strength increase according to the β-mechanism. Moreover, to our knowledge, no systematic investigation on the relationship between tablet porosity and mechanical instability of sodium chloride compacts exists in the literature. The outcome of this study might also be a contribution to the establishment of factors which affect a post-compaction tablet strength increase according to the β-mechanism.

2. Materials and methods

2.1. Preparation of powders

Three size fractions of sodium chloride (crystalline puriss., Kebo, Sweden) were prepared in the following way:

The size fractions 425–500 and 90–150 μm were prepared by dry sieving of the raw material with ordinary laboratory sieves. The size fraction 20–40 μm was prepared by milling the raw material in a mortar mill (Retsch KM1, Germany) followed by air classification (Alpine 100 MZR, Alpine AG, Germany). All powders were stored at 0% relative humidity (desiccators with phosphorus pentoxide) and room temperature, for not less than 7 days before compaction.

2.2. Compaction and determination of tablet tensile strength

Compacts were prepared in an instrumented single-punch tablet machine (Korsch EK 0, Germany), equipped with 1.13 cm flat-faced punches,

at a series of maximum upper punch pressures (see Tables 1–3). The compaction was performed under ambient conditions (20–50% relative humidity). The distance between the punch faces at the lowest position of the upper punch was in all cases 3.0 mm at zero pressure, i.e., the different compaction pressures were controlled by varying the amount of powder filled into the die. The powder for each compact was individually weighed on an analytical balance and manually poured into the die. The motor of the machine was then started when the upper punch was at its highest position and the motor was stopped and the flywheel manually arrested directly after the compression process and the compact was finally removed from the die table. The weight and the height of the tablets were measured before determination of the diametral compression strength and used for the calculation of tablet porosity.

To obtain relatively high compaction pressures, tablets were also formed in a hydraulic press (Apex, Sweden), equipped with 1.13 cm flat-faced punches, of the coarsest and finest sodium chloride particles up to the maximum upper punch pressures representing the limit for the experimental procedure (see Tables 1 and 3). The compaction pressure was controlled by varying the amount of powder filled into the die. The powder for each compact was individually weighed on an analytical balance and manually poured into the die. The upper punch was placed in the die and the compression was performed by manually raising the pressure over a period of 10 s. After compaction the tablet was manually forced out of the die over a period of 10 s. Finally, the weight and the height of the tablets were measured before determination of the diametral compression strength.

In all cases, external lubrication of the die wall with 1% w/w magnesium stearate suspension in ethanol was performed before each compaction.

The diametral compression strength of the tablets (Holland C50, U.K. or Lloyd M 30 K, Lloyd Instrument Ltd, U.K.) was measured immediately after compaction ($t = 30$–40 s) or after storage of the tablets in mini dessicators at 0% relative humidity. Storage times of 15, 60 and 10 080 min (7 days) were used.

In all cases, the tensile strength of the compacts was calculated according to Fell and Newton (1970). The results presented are the mean of five determinations.

2.3. Stress relaxation of compacts under external stress

As a measure of the ability of the particles to deform time dependently, stress-relaxation measurements of compacts were performed. Powders were compressed in a material testing machine (Lloyd M 30 K, Lloyd Instrument Ltd, U.K.) at maximum applied pressures of 75, 150, and 275 MPa for size fractions 20–40 and 425–500 μm and maximum applied pressures of 50, 100 and 275 MPa for size fraction 90–150 μm at a compression speed of 4 mm/min. The stress-relaxation measurements was performed under ambient conditions (20–50% relative humidity). When the maximum pressure was reached, the machine was stopped and the distance between the punches was kept constant for a period of 20 min. During this time, the reduction in force on the upper punch was monitored. The stress relaxation curves is presented as the force decay/unit mass material as a function of time. The stress-relaxation of the rig as such, i.e., when the punch tips were in contact, was also recorded and the results presented are compensated for the stress-relaxation of the rig. The powder for each compact was individually weighed on an analytical balance and manually poured into the die. The amount of powder for each compact was the same as for the preparation of compacts in the tablet press and the hydraulic press. External lubrication with 1% w/w magnesium stearate suspension in ethanol was performed before each compression. The results presented are the mean of three determinations.

3. Results and discussion

3.1. Compressibility and compactability of particles

The compressibility and compactability of the coarsest and finest particles were assessed based

on the relationships between applied pressure, tablet strength and tablet porosity. It should be noted that the two tablet presses, using markedly different times for compression, were used during the preparation of compacts to obtain a wide range of tablet porosities.

Generally, the finer particles gave compacts of a higher porosity than the coarse particles (Tables 1 and 3). For compacts of fine particles, an

Table 1
Porosity and tensile strength for tablets compacted of sodium chloride size fraction 425–500 μm (results for all compaction pressures after storage of the tablets at 0% relative humidity for different storage times)

Compaction pressure (MPa)	Storage time (min)	Porosity (%)	Tensile strength (MPa) [c]
75 [a]	0	16.0	0.10 (0.04)
	15	18.6	0.28 (0.11)
	60	17.2	0.27 (0.07)
	10 080	18.3	0.33 (0.04)
100 [a]	0	13.9	0.31 (0.06)
	15	15.1	0.54 (0.04)
	60	14.3	0.61 (0.02)
	10 080	15.3	0.49 (0.06)
150 [a]	0	10.5	0.61 (0.04)
	15	10.7	1.00 (0.07)
	60	10.6	1.01 (0.06)
	10 080	10.0	1.11 (0.04)
200 [a]	0	8.44	0.85 (0.03)
	15	7.15	1.30 (0.12)
	60	7.56	1.68 (0.10)
	10 080	6.68	1.57 (0.09)
200 [b]	0	6.30	1.18 (0.03)
	15	6.12	1.37 (0.08)
	60	6.64	1.84 (0.15)
	10 080	6.37	2.44 (0.22)
295 [a]	0	3.72	1.47 (0.07)
	15	4.33	1.57 (0.05)
	60	4.55	1.87 (0.14)
	10 080	3.87	2.19 (0.06)
400 [b]	0	4.89	1.42 (0.09)
	15	6.16	1.56 (0.07)
	60	4.62	1.64 (0.13)
	10 080	4.48	3.01 (0.27)
600 [b]	0	5.73	1.47 (0.10)
	15	4.73	1.57 (0.11)
	60	6.24	1.56 (0.11)
	10 080	3.91	2.62 (0.15)

[a] Tablets compacted in the instrumented single-punch press.
[b] Tablets compacted in the hydraulic press.
[c] Standard deviations in parentheses.

exponential tablet porosity-applied pressure relationship seemed to exist over the whole range of porosities obtained. However, for compacts of the coarse particles, an exponential relationship was obtained in the range down to a porosity of approx. 5% (corresponding to a pressure of approx. 300 MPa). Thereafter, an increased compaction pressure, i.e., up to 600 MPa, seemed not to affect the porosity any further. Thus, at this critical porosity, the particles within the compact became difficult to deform, at least in the direction governed by the applied force, which is reflected as a biphasic relationship between tablet porosity and applied pressure. There was a tendency for the hydraulic press to give compacts of a lower porosity than the single-punch press at equivalent pressure, i.e., 200 MPa (Tables 1 and 3). A possible explanation is a slightly higher degree of time-dependent deformation of the particles during the compression phase due to the slower rate of compression.

The fine particles generally formed compacts of higher tensile strength compared to the coarse particles (Eriksson and Alderborn, 1994). For both size fractions, the tensile strength was related to the tablet porosity in a non-linear way. At equivalent applied pressure, the hydraulic press tended to give compacts of a higher tensile strength than the single-punch press (Tables 1 and 3). However, in relation to the tablet porosity (Fig. 1), there seemed to be no difference in tablet strength depending on the press used. It appears that the time of compression had only a limited effect on the formation of interparticulate bonds during compaction although the degree of deformation of the particles can be affected by the compression time.

3.2. Effect of compact porosity on post-compaction changes in tensile strength

The humidity of the storage atmosphere has earlier been recognised as a factor that affects the mechanism which is responsible for a post-compaction change in tensile strength of sodium chloride compacts (Eriksson and Alderborn, 1994). In the present paper, compacts were stored only in a dry atmosphere in order to avoid a

change in the interparticulate bond structure by mechanism α.

For compacts prepared from 425–500 μm particles, the tablet strength increased during the storage period (Table 1), which is consistent with the earlier findings (Eriksson and Alderborn, 1994). However, the character of the tensile strength-storage time relationship was affected by the compact porosity in two ways: Firstly, the time period which must elapse before the maximum tensile strength is reached seemed to be dependent on the compact porosity. Thus, for higher porosities, a plateau was reached for the tensile strength values after 15–60 min storage time, while for the lower porosities, the tensile strength continued to increase also after 60 min storage. Secondly, the general tendency was that the degree of tensile strength change increased as the compact porosity decreased. However, for compacts prepared by the single-punch press, the degree of tensile strength change was similar for compacts of the two lowest porosities. The most marked tensile strength increase was obtained for the compacts prepared by the hydraulic press, which was similar for all three pressures used. It seems that the time for compression can affect the degree of tensile strength increase during storage.

These effects of compact porosity on the character of the tablet strength-storage time relation-

Fig. 2. Tensile strength difference (i.e., the difference between the tensile strength measured after storage and measured directly after compaction) as a function of tablet porosity. The tablets were compacted of sodium chloride size fraction 425–500 μm. ($\square$) Tensile strength difference between 0 and 15 min storage times. ($\blacksquare$) Tensile strength difference between 0 and 7 days storage times.

ship are illustrated in Fig. 2. The difference in tensile strength after storage of the compact for 15 min or 7 days and the tensile strength measured immediately after compaction is given as a function of compact porosity. For compacts stored for 15 min, a peak in the tablet strength difference-tablet porosity profile is observed at a porosity of approx. 10%. For compacts stored for 7 days, the peak has disappeared and the tablet strength difference increases continuously with a reduced tablet porosity. The consequence is that in the upper range of tablet porosities, the results obtained at 15 min and 7 days coincide, while in the lower range, they diverge.

For compacts prepared of the 90–150 μm particles at the lowest pressure (Table 2), the tensile strength remained constant during the storage period. Thereafter, a reduced porosity gave mechanically unstable compacts with an increased degree of tensile strength change with a decreased tablet porosity.

For compacts prepared from the 20–40 μm particles (Table 3), the tensile strength was generally unchanged during the storage period, which is consistent with previous results (Elamin et al., 1994; Eriksson and Alderborn, 1994). Thus, with respect to the storage conditions used in this
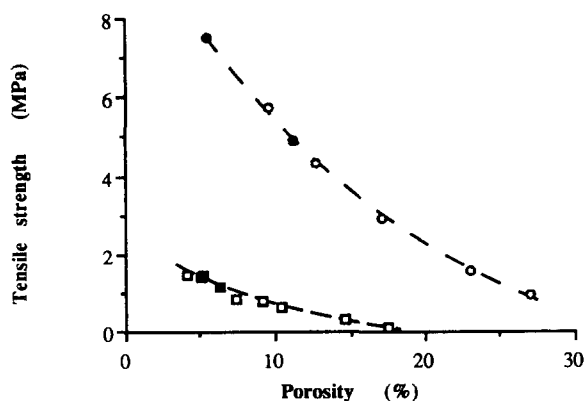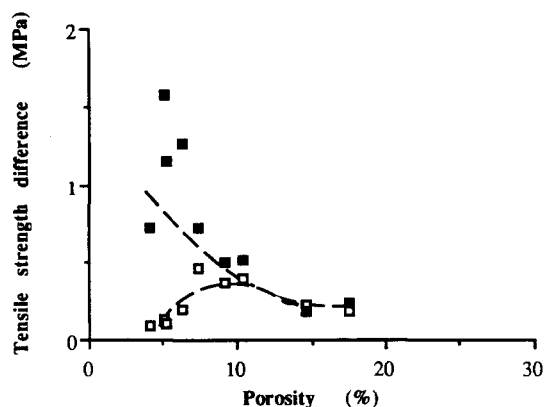

Fig. 1. Tensile strength of sodium chloride tablets as a function of tablet porosity. The tablets were compacted in the instrumented single-punch press (open symbols) and in the hydraulic press (closed symbols). The tablets were compacted of size fractions ($\square$,$\blacksquare$) 425–500 μm and ($\bigcirc$,$\bullet$) 20–40 μm.

Table 2
Porosity and tensile strength for tablets compacted of sodium chloride size fraction 90–150 μm (results for all compaction pressures after storage of the tablets at 0% relative humidity for different storage times)

Compaction pressure (MPa)	Storage time (min)	Porosity (%)	Tensile strength (MPa) [b]
50 [a]	0	27.8	0.09 (0.02)
	10080	28.0	0.11 (0.01)
100 [a]	0	18.2	0.43 (0.04)
	10080	17.7	0.55 (0.03)
200 [a]	0	9.42	1.25 (0.07)
	10080	9.20	1.62 (0.06)
275 [a]	0	5.63	1.83 (0.02)
	10080	5.93	2.43 (0.08)

[a] Tablets compacted in the instrumented single-punch press.
[b] Standard deviations in parentheses.

Table 3
Porosity and tensile strength for tablets compacted of sodium chloride size fraction 20–40 μm (results for all compaction pressures after storage of the tablets at 0% relative humidity for different storage times)

Compaction pressure (MPa)	Storage time (min)	Porosity (%)	Tensile strength (MPa) [c]
75 [a]	0	27.3	0.94 (0.15)
	15	26.7	0.92 (0.08)
	60	26.8	1.07 (0.14)
100 [a]	0	22.5	1.57 (0.10)
	15	22.8	1.66 (0.09)
	60	23.5	1.63 (0.22)
150 [a]	0	17.4	2.90 (0.18)
	15	17.3	3.26 (0.15)
	60	16.7	3.12 (0.14)
200 [a]	0	13.3	4.36 (0.19)
	15	12.8	4.46 (0.21)
	60	13.2	4.24 (0.23)
	10080	11.5	4.79 (0.31)
200 [b]	0	10.8	4.90 (0.32)
	15	11.5	5.28 (0.38)
	60	11.2	5.24 (0.28)
275 [a]	0	10.2	5.75 (0.18)
	15	8.74	5.60 (0.16)
	60	9.95	5.82 (0.19)
400 [b]	0	5.56	7.51 (0.10)
	15	5.35	7.69 (0.37)
	60	5.00	7.45 (0.59)
	10080	5.89	6.35 (0.22)

[a] Tablets compacted in the instrumented single-punch press.
[b] Tablets compacted in the hydraulic press.
[c] Standard deviations in parentheses.

paper, compacts prepared of the smallest particles can generally be described as mechanically stable, in contrast to compacts prepared of the coarser particles.

It should finally be noted that there was generally no change in tablet porosity during storage of the compact. Thus, the observed post compaction increase in tensile strength of compacts prepared from the two coarser qualities of sodium chloride is not accompanied by a measurable change in the dimensions of the compact.

The results obtained in this study show that for one specific material, a storage-related tensile strength increase can be dependent on both the original particle size and on the porosity of the compact formed. Compacts of fine sodium chloride, stored in a dry atmosphere, were mechanically stable irrespective of the applied pressure and thus tablet porosity, while compacts of coarser particles demonstrated post compaction changes in tensile strength of which the magnitude and rate were dependent on the tablet porosity.

3.3. Effect of compact porosity on stress-relaxation of compacts

The ability of the sodium chloride particles to deform viscous or visco-elastically was assessed by stress relaxation measurements of compacts. Compacts of all three size fractions used in this study possessed a marked stress relaxation during the measuring period (Fig. 3). The force decay was accompanied by a small reduction in tablet porosity and an increase in tablet strength. It seems reasonable that the force decay on the upper punch is a direct reflection of the reduction in volume of the compact. It is suggested that the degree of stress relaxation is a measure of the degree of densification of the compact while kept under static conditions, which is probably a reflection of the degree of time-dependent deformation of the particles within the compact.

The stress-relaxation process was followed for a time period of 20 min (Fig. 3). Generally, the stress relaxation of the compacts did not cease within this time period although a marked flattening of the curves was obtained and the rate of stress relaxation was generally low at the end of

the loading period. However, it can be noted that for compacts prepared of 425–500 and 90–150 μm particles at the highest applied pressure, the stress relaxation seemed nearly completed within the time period. It seems that a reduced compact porosity tended to decrease the time period over which the particles in the compact deformed. The degree of stress relaxation was similar for all three particle size fractions indicating that the propensity of the particles to deform time dependently was similar between and thus independent of original particle size. There was also a tendency for all particle sizes that compaction at the highest applied pressures, corresponding to the lowest porosities, reduced the degree of stress relaxation of the compacts (Fig. 4). A similar observation has earlier been reported on the stress relaxation behaviour (Esezobo and Pilpel, 1987) and on the creep behaviour (Rees and Tsardaka, 1993) of compacts. It thus appears that a low porosity of the compact constitutes a restriction against a deformation of the particles within the compact under static loading. This is also supported by the fact that densification of compacts under dynamic loading became difficult at low compact porosities (Table 1).

3.4. Discussion regarding process responsible for post-compaction tablet strength increase denoted mechanism β

The post-compaction changes in tensile strength of compacts denoted the β-mechanism seemed to be characterised by the following features:

(i) The increase in tensile strength after compaction was dependent on original particle size.

(ii) The increase in tensile strength can be completed within 15 min, but can also occur for time periods longer than 60 min. The time period over which the tablet strength changed increased with a decreased compact porosity.

(iii) A reduced compact porosity increased the magnitude of the post-compaction increase in tensile strength.

The stress-relaxation behaviour of the compacts seemed to be characterised by the following

features:

(i) The ability of the sodium chloride compacts to possess stress relaxation was independent of particle size.

(ii) The rate of stress-relaxation was low after 20 min of loading. There was also a tendency for a reduced compact porosity to reduce the time over which the compact possessed stress relaxation.

(iii) Low porosities of the compacts, as a consequence of higher applied stresses, reduced the degree of the stress relaxation of the compacts.

The traditional way of explaining the post compaction tablet strength increase observed for sodium chloride tablets is a time-dependent particle deformation (e.g., Rees and Shotton, 1970; Rees and Rue, 1978; Karehill and Nyström, 1990). However, the inconsistency in the obtained results between stress relaxation and tablet strength instability with respect to the effect of original particle size and compact porosity questions the relevance of the time-dependent deformation of the particles as the major process responsible for the strength increase of sodium chloride compacts. However, this conclusion might be questioned from the starting-point that an analogy between deformation properties of particles during stress-relaxation and during storage of compacts cannot be made, i.e., during stress relaxation analysis an external stress is applied to the compact in contrast to a situation where the compact is stored.

The suggestion, put forward in this paper, that time-dependent deformation of particles fails to explain the β-type post compaction tensile strength increase of sodium chloride tablets requires an alternative physical explanation for the mechanical instability. One possible suggestion here is (Eriksson and Alderborn, 1994) that a temperature reduction of the compact after compaction can be the cause of the observed tensile strength increase. Such a temperature reduction might affect both the bonding force of interparticulate bonds as well as the mechanical properties of the particles in the compact, i.e., a change in temperature of the compact might affect the assessed tensile strength independently of the

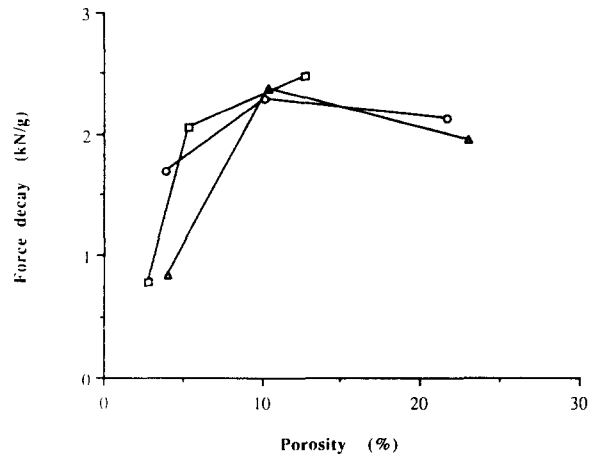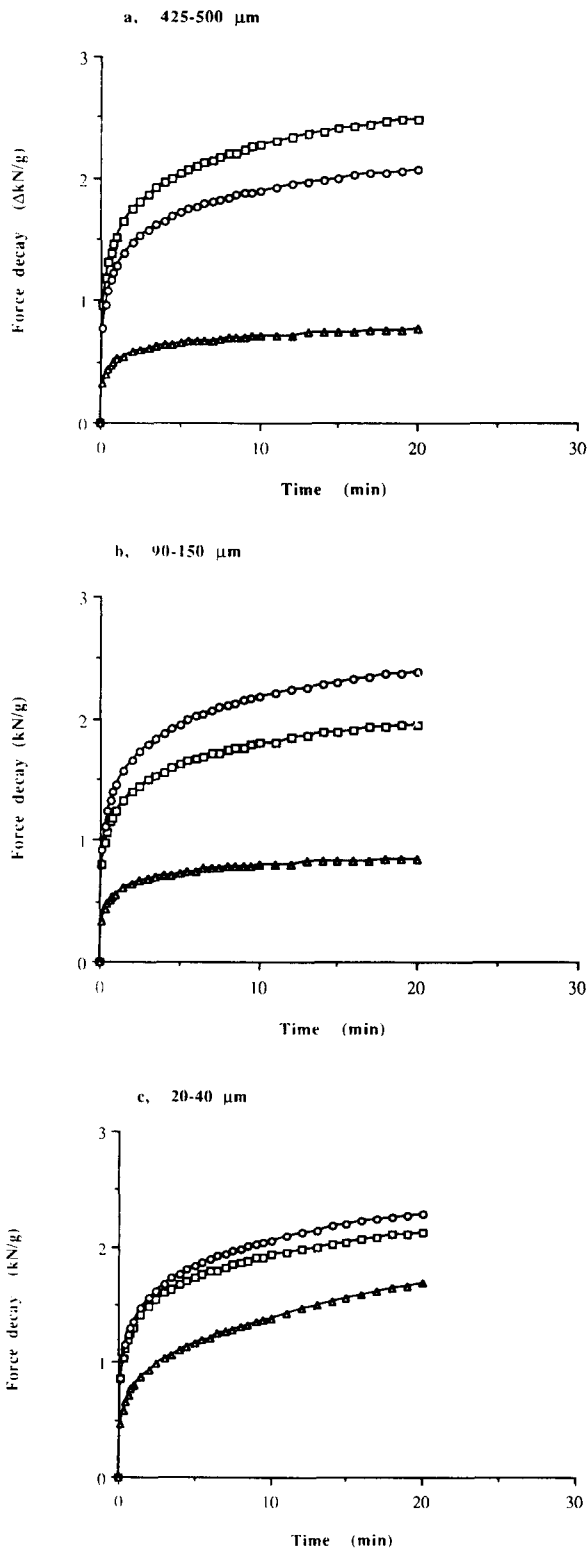a, 425-500 μm

b, 90-150 μm

c, 20-40 μm

Fig. 4. Force decay on the upper punch, per unit mass material, after 20 min of stress relaxation as a function of tablet porosity. Tablets compacted of sodium chloride size fraction (○) 20–40 μm, (△) 90–150 μm, (□) 425–500 μm.

mechanics of the fracture when a tablet fails in tension due to diametral compression. An increased strength of the tablet due to a temperature reduction of the specimen requires that the cooling process occurs over a relatively long time period, i.e., in many cases above 60 min. A compaction induced increase in temperature of a solid system has been reported, e.g., by infrared imaging of compacts (Bechard and Down, 1992; Ketolainen et al., 1993). The decrease in compact temperature with time after compaction has not been studied in detail but Bechard and Down (1992) demonstrated a fast, non-linear decrease in compact temperature with time for compacts of a direct compactable powder mixture over a time period of 4 min. However, at the end of this time period, a plateau in the temperature-time profiles was not reached and the temperature of the tablets was still above normal room temperature. It cannot thus be excluded that the cooling process may occur over a time period considerable longer than a few minutes. It should also be

Fig. 3. Force decay, per unit mass material, on the load cell as a function of time, for tablets compacted of sodium chloride. The force decay on the upper punch was monitored at maximum applied pressures of: (a) (□) 75, (○) 150 and (△) 275 MPa; (b) (□) 50, (○) 100 and (△) 275 MPa; (c) (□) 75, (○) 150 and (△) 275 MPa.

mentioned that Bechard and Down (1992) used a force of compaction of 15 kN which in this study corresponds to a pressure of 150 MPa. Tablets formed at this pressure seemed to stabilise mechanically within a time period of 15 min (Table 1).

4. Conclusions

Compacts formed of sodium chloride particles can be mechanically unstable and two types of instability behaviour have been identified, α and β (Eriksson and Alderborn, 1994). The β-type is characterised by the fact that a tablet strength increase during storage occurs over a relatively short period of time in connection with the compaction process and that the magnitude of this increase is independent of the humidity as long as this humidity is below the critical relative humidity for sodium chloride. In this paper, it has been shown that the magnitude and the rate of this β-type increase in tablet strength are also dependent on the original particle size and the compact porosity or the stress applied to the particles when compacted.

The results presented in this paper do not provide sufficient information to resolve the question of which physical process causes the post compaction tablet strength increase. However, this paper has shown that there are differences in the dependence of particle size and compact porosity between stress relaxation and tablet strength instability. This lack of consistency between stress relaxation and mechanical instability behaviour of the compacts questions the relevance of the assumption that a viscous or visco-elastic deformation is responsible for the tensile strength increase in a dry atmosphere.

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