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Evaluation of the effect of addition of polyethylene glycols of differing molecular weights on the mechanical strength of sodium chloride and sodium bicarbonate tablets

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Abstract

The effects of the addition of polyethylene glycols (PEGs) of differing molecular weights on the tensile strength of tablets made of sodium chloride or sodium bicarbonate were studied. The results indicated that fractures occurring during tablet strength testing tended to propagate around rather than through the sodium chloride and sodium bicarbonate particles. The addition of PEG to sodium chloride or sodium bicarbonate generally increased the tablet strength. In some cases, a synergistic effect was seen, i.e. the strength of the tablets made from the mixtures was higher than the strengths of the tablets made of the individual components. This was thought to be the result of an increased fracture surface area. When a PEG was added to a compound that had a high capacity for volume reduction (sodium chloride), the tensile strength of the compact reflected the ductility of the PEG but, when a compound with a lower capacity for volume reduction (sodium bicarbonate) was used, the tensile strength of the tablets reflected the tensile strength of the corresponding pure PEG tablet. The results also indicated that the bonding mechanisms of the compounds are likely to affect the tensile strength of the tablet obtained.

Keywords: Tablet; Axial tensile strength; Mixture; Bonding mechanism; Polyethylene glycol

1. Introduction

During the compaction of pharmaceutical powders, the particles are brought into closer proximity to each other, which reduces the porosity of the powder bed. This may facilitate the develop-

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ment of bonds between the powder particles, resulting in the formation of a compact with a certain tensile strength. To increase insufficiently low tablet strength a binder material may be added to the compound before compaction. In the case of direct compression, the binder material is generally added in the form of a powder and is referred to as a dry binder.

Dry binders often consist of ductile polymeric materials such as different types of cellulose and starch derivatives, but the binder properties of importance in obtaining an optimal increase in tablet tensile strength are not yet clearly understood. However, it seems likely that the effect of a certain binder is affected both by the properties of the binder and of the compound. It also seems possible that a dry binder and a compound may interact in different ways, implying that by carefully combining each individual compound with a suitable dry binder an optimal increase in tablet strength may be obtained.

Studies of dry binders and their properties, such as particle size, elasticity of the material and amount added, as well as properties connected to the compound, e.g. fragmentation propensity and bonding mechanisms have been reported (Nyström et al., 1982; Duberg and Nyström, 1985; Nyström and Glazer, 1985; Yu et al., 1989; Gren and Nyström, 1996). However, specific interactions between binders and compounds have rarely been reported.

The aim of this study was to investigate the effect of the addition of polyethylene glycols (PEGs) of differing molecular weights, corresponding to differences in mechanical and physicochemical properties, on the tensile strength of sodium chloride and sodium bicarbonate tablets. The aim was, thus, to gain further knowledge of the strength increasing mechanisms of a so called dry binder.

2. Materials and methods

2.1. Materials

2.1.1. Compounds

Two compounds were studied: sodium chloride (crystalline, puriss, Kebo Laboratories, Sweden) and sodium bicarbonate (crystalline, puriss Ph Eur., Kebo Laboratories, Sweden). Two size fractions of sodium chloride (125–180 and 355–500 μm) and one size fraction of sodium bicarbonate (125–180 μm) were prepared by dry sieving (Retsch, Germany).

2.1.2. Binders

PEGs of differing mean molecular weights were used as binders (PEG 3000, PEG 6000, PEG 10000 and PEG 20000, Kebo Laboratories, Sweden). Fine fractions of all the qualities of PEG were obtained using a pin disc mill (63C, Alpine, Germany) and an air classifier (100 MZR, Alpine, Germany), adjusted to produce a size fraction < 20 μm. The fine fractions obtained for the different PEG qualities were however not identical regarding the degree of fineness. Thus, the weight specific surface area of the different qualities of PEG differed. Consequently, the different qualities of PEG probably also differed in particle size.

Sodium chloride and sodium bicarbonate have both been classified as materials undergoing mainly plastic deformation when compressed (Duberg and Nyström, 1986). Differences in bonding mechanisms between the materials have however been reported (Nyström et al., 1993). In both materials, weak long range forces are considered to be the dominating bonding mechanism, but solid bridges are also believed to contribute to the strength of tablets made from sodium chloride (Karehill and Nyström, 1990; Nyström et al., 1993; Olsson et al., 1996). PEG is not normally used as a dry binder in direct compression but in this study it was chosen because of the range of molecular weights available and the subsequent variation in mechanical properties.

2.2. Methods

2.2.1. Apparent particle density

The apparent particle density (B.S. 2955, 1958) was measured with a helium pycnometer (AccuPyc 1330 Pycnometer, Micromeritics, USA). The densities of the pure compounds (Table 1), the pure binders (Table 2) and the ordered mixtures mentioned below were determined ($n = 3$).

Table 1
Characterisation of the compounds

Compound	Size fraction[a] (μm)	Apparent particle density[b] (g/cm^3)	External surface area[c] (cm^2/g)
Sodium chloride (I)	125–180	2.157 (0.0003)	210 (2)
Sodium chloride (II)	125–180	2.154 (0.0001)	192 (1)
Sodium chloride (I)	355–500	2.153 (0.0002)	69 (9)
Sodium chloride (II)	355–500	2.152 (0.0003)	79 (0)
Sodium bicarbonate	125–180	2.213 (0.0004)	327 (2)

The results are the mean value with the corresponding confidence interval for $p = 0.05$ in parentheses.
Batches I and II were sieved on different occasions.
[a] Obtained by dry sieving.
[b] Measured with a helium pycnometer (AccuPyc 1330 Pycnometer, Micromeritics, USA).
[c] Measured by Friedrich permeametry (Eriksson et al., 1990).

2.2.2. External surface area of the compounds

Friedrich permeametry, as described by Eriksson et al. (1990), was used to determine the external surface area of the sodium chloride and sodium bicarbonate particles ($n = 3$) (Table 1).

2.2.3. External surface area of the PEGs

Blaine permeametry was used to determine the external surface area of the PEGs. The apparatus and the equations used have been described earlier (Alderborn et al., 1985) ($n = 3$) (Table 2).

Table 2
Characterisation of the density and surface area of the different PEG qualities[a]

Molecular weight	Apparent particle density[b] (g/cm^3)	External surface area[c] (cm^2/g)
3000	1.222 (0.0002)	10170 (149)
6000	1.226 (0.0004)	6457 (54)
10 000 (I)	1.223 (0.0002)	5121 (25)
10 000 (II)	1.219 (0.0003)	6087 (17)
20 000 (I)	1.230 (0.0005)	3439 (83)
20 000 (II)	1.217 (0.0003)	3080 (25)

The results are the mean value with the corresponding confidence interval for $p = 0.05$ in parentheses.
Batches I and II were milled and air classified on different occasions.
[a] Obtained by using a pin disc mill (63C, Alpine, Germany) and an air classifier (100MZR, Alpine, Germany) adjusted to give size fractions <20 μm.
[b] Measured with a helium pycnometer (AccuPyc 1330 Pycnometer, Micromeritics, USA).
[c] Measured by Blaine permeametry (Alderborn et al., 1985).

2.2.4. Addition of PEG to the compounds

The different molecular weights of the fine PEG particles were mixed with the coarser sodium chloride or sodium bicarbonate particles in a Turbula mixer for 100 min. The relatively long mixing time was chosen to provide sufficient deagglomeration of the PEG particles (Nyström and Malmqvist, 1980).

The amount of PEG ($m_{(PEG)}$) added to a certain amount of compound ($m_{(compound)}$) to form each powder mixture, was chosen to correspond to the amount needed to approximately form a monoparticulate layer on the surface of the compound particles. This was estimated as described by Nyström et al. (1982),

$$m_{(PEG)} = \frac{R \cdot (m_{(compound)} \cdot Sw_{(compound)})}{Sw_{(PEG)}/4}$$

assuming that the coating capacity of a PEG particle corresponded to its projected surface area, i.e. one quarter of the external surface area of the PEG particle (Allen, 1997). $Sw_{(compound)}$ and $Sw_{(PEG)}$ denote the weight specific surface area of the compound and the PEG powder, respectively. The ratio between the projected surface area of the PEG and the external surface area of the compound was defined as the surface area ratio (R) (Nyström et al., 1982). The amount of PEG required to form a monoparticulate layer on the surface of the compound particles, i.e. resulting in a surface area ratio of unity ($R = 1$), was used in order to evaluate the effect of solid bridges on the tensile strength of the tablets.

Table 3
Amount of PEG (% w/w) to be added to the mixtures in order to achieve a surface area ratio of unity

	PEG 3000	PEG 6000	PEG 10 000	PEG 20 000
Sodium chloride (125–180 μm)	7.6	11.5	14.1	20.6
Sodium chloride (355–500 μm)	2.7	4.1	5.1	7.9
Sodium bicarbonate (125–180 μm)	11.3	16.8	17.7	29.8

When this concept is used the different mixtures will contain different amounts of PEG by weight (Table 3) because of differences in the surface areas of the compounds and the PEGs (Tables 1 and 2). In order to determine the effect of the amount (by weight) of PEG added on the results, the same amount (by weight) of PEG as that added to the sodium chloride 125–180 μm fraction was added to the sodium chloride 355–500 μm fraction and the same amount of PEG as that added to the sodium bicarbonate 125–180 μm fraction was added to the sodium chloride 125–180 μm fraction. In the mixtures containing sodium bicarbonate and PEG, the greatest amount of PEG was added when using PEG 20000 (Table 3). Therefore, mixtures were prepared of sodium bicarbonate and PEG which contained the same amount by weight of PEG 3000 or PEG 6000 as the mixture with PEG 20000. Due to a shortage of material, PEG 10000 was not included in this evaluation.

2.2.5. Compaction of the tablets

The powders were stored in a desiccator over saturated chrome trioxide in water (40% relative humidity) (Nyqvist, 1983) for at least two days before compaction. The tablets were compacted with 1.13 cm flat faced punches in an instrumented excenter press (30 rpm) (Korsch EK 0, Germany) at four different compaction loads (maximum upper punch pressure) of 50, 100, 200 and 300 MPa, unless otherwise stated. The powder for each tablet was weighed on an analytical balance and manually filled into the die. The compaction loads were adjusted by having a constant distance between the punches and varying the amount of powder in the die. The surfaces of the punches and the die were lubricated with magnesium stearate powder before each compaction. The tablets were made of pure compounds, pure PEGs and the ordered mixtures mentioned above. The mixtures prepared to evaluate the effect of differing amounts of PEG were compacted only at 300 MPa.

2.2.6. Measurement of the axial tensile strength of the tablets

The tablets were stored under the same conditions as the powders (40% relative humidity) for at least two days before the tablet strength was measured. The tablets were fixed between two adapters with an ethylcyanoacrylate adhesive (Loctite 480, Loctite, Sweden) and the axial fracture force was measured by pulling the tablet parallel to the direction of the applied force during the formation of the tablet, using a material tester (M30K, Lloyd Instruments, UK). The axial tensile strength was calculated using the equation described by Nyström et al. (1978). Axial tensile strength measurements were used since these will detect the weakest plane of the tablet. In general, no particulate trends regarding the location of the axial failure in the tablet was observed. The results shown are the mean of 3–12 tablets with 95% confidence intervals (Fig. 1a,b,c,d). The variation in the number of tablets was due to difficulties in obtaining an acceptable axial fracture.

2.2.7. Calculation of the tablet porosity

The porosity of the tablets was calculated from the apparent density of the material or ordered mixture and the dimensions and weight of the tablet, and is presented as the mean of 3–12 tablets with 95% confidence intervals (Figs. 2 and 3a,b,c). The tablets used were the same as in the axial tensile strength measurements.

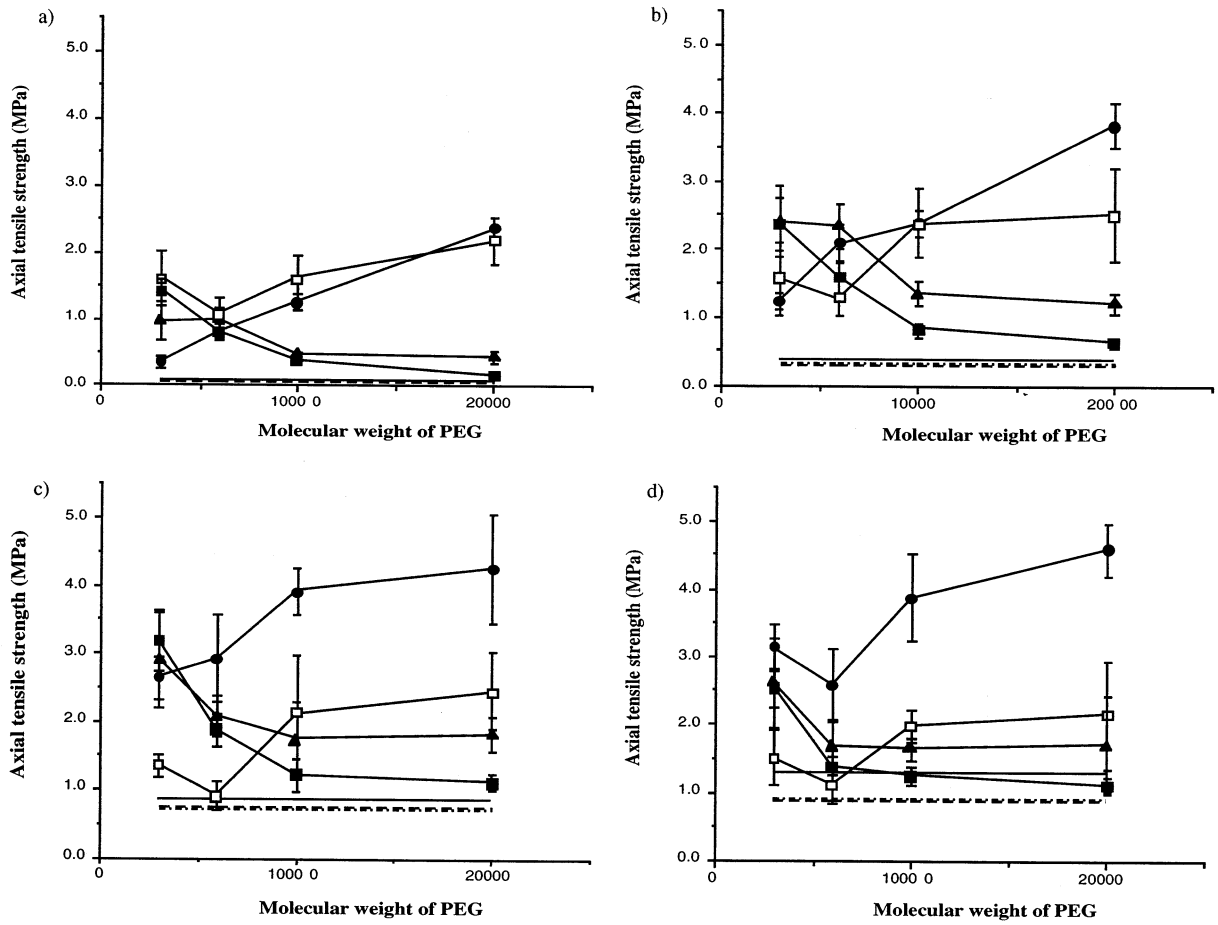

Fig. 1. Axial tensile strength of the tablets as a function of the molecular weight of PEG added to sodium chloride (125–180 μm) (▲), sodium chloride (355–500 μm) (■) and sodium bicarbonate (125–180 μm) (●). The axial tensile strength of the pure materials is also shown: polyethylene glycol (□), sodium chloride (125–180 μm) (- - -), sodium chloride (355–500 μm) (— — —) and sodium bicarbonate (125–180 μm) (— - —). The 95% confidence intervals are shown where they exceed the dimensions of the symbol. (a) Tablets compacted at 50 MPa, (b) tablets compacted at 100 MPa, (c) tablets compacted at 200 MPa and (d) tablets compacted at 300 MPa.

2.2.8. Characterisation of the deformability of PEG

The deformability of the PEGs was characterised using the Heckel equation (Table 4). The tablets were compressed at 200 MPa and the height of the tablets was recorded every ms during the compression cycle ($n = 2$). The values for tablet porosity during the compression cycle were calculated from the heights of the tablets and these values were used in the Heckel equation. The yield pressure of the materials was calculated from the reciprocal of the linear part of the Heckel plot, which in this case corresponded to a pressure range of 25–90 MPa. The correlation coefficient of the linear part was in all cases 0.999 or higher (Duberg and Nyström, 1986) (Table 4). Since the yield pressure was calculated from an in die Heckel plot it is considered to reflect the total deformation of the material, i.e. both elastic and plastic deformation (Duberg and Nyström, 1986; Paronen, 1986) and is thus referred to as the apparent yield pressure. Since negative values of the minimum porosity were obtained in some cases, the changes in porosity were subsequently expressed as changes in tablet height. Elastic re-

covery was then calculated as the relative difference between the minimum and maximum tablet height (Armstrong and Haines-Nutt, 1972) (Table 4).

3. Results

3.1. Tableting properties of PEGs of differing molecular weights

The tensile strength of pure PEG tablets generally increased with increasing molecular weight (Fig. 1a,b,c,d). Similar results have been presented earlier (Al-Angari et al., 1985; Blattner et al., 1986; Ching-Wei and Thau-Ming, 1995; Larhrib et al., 1997). The apparent yield pressure of PEG seemed to be relatively independent of molecular weight, while the elastic recovery results indicated more elastic behaviour for the higher molecular weight PEGs (Table 4), which may be explained by the fact that these molecules are larger. If the apparent yield pressure, calculated from the reciprocal of the linear part of an 'in-die-Heckel plot', is considered to reflect the total deformation of the material, i.e. both elastic and plastic deformation (Duberg and Nyström, 1986; Paronen, 1986), it seems reasonable to assume that the plastic deformation of PEG increases with decreasing molecular weight. Also, compaction of a low molecular weight PEG resulted in tablets with lower porosity than compaction of PEGs with a higher molecular weight (Fig. 2) (Al-Angari et al., 1985; Blattner et al., 1986; Ching-Wei and Thau-Ming, 1995; Larhrib et al., 1997).

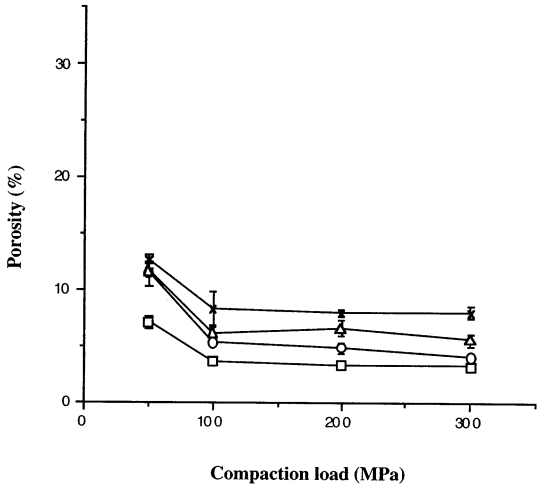

Fig. 2. Porosity of the tablets of pure PEGs of differing molecular weights as a function of the compaction pressure. PEG 3000 (□), PEG 6000 (○), PEG 10000 (△) and PEG 20000 (X). The 95% confidence intervals are shown where they exceed the dimensions of the symbol.

3.2. Properties of tablets consisting of mixtures of sodium chloride or sodium bicarbonate and PEGs of differing molecular weights. Surface area ratio 1

The tensile strength of pure sodium bicarbonate tablets was generally lower than that of the corresponding pure sodium chloride tablets (Fig. 1a,b,c,d). Also the tensile strength of the tablets of the 355–500 μm fraction of pure sodium chloride was generally lower than that of the tablets of the 125–180 μm fraction. The tensile strength of the pure PEG tablets was higher than that of the pure sodium bicarbonate or the pure sodium chloride tablets, irrespective of the molecular weight of the PEG (Fig. 1a,b,c,d).

When PEG was added to either of the two compounds, the tensile strength of the tablets increased (Fig. 1a,b,c,d). This increase was more pronounced with sodium bicarbonate and was greatest when the highest molecular weight of PEG (PEG 20000) was added. Conversely, the sodium chloride tablets showed the highest tensile strength when the PEG with the lowest molecular weight (PEG 3000) was added and the lowest tensile strength when the PEG with the highest molecular weight (PEG 20000) was added. At compaction loads above 100 MPa, the tensile strength of the tablets made of sodium bicarbonate and PEG was greater than the tensile strengths of the tablets made of each individual component, i.e. the tensile strength was even higher than that of the corresponding pure PEG tablet. This effect has earlier been seen in similar systems (Gren and Nyström, 1996), in other binary systems (Newton et al., 1977; Cook and Summers, 1985; Vromans and Lerk, 1988) and is

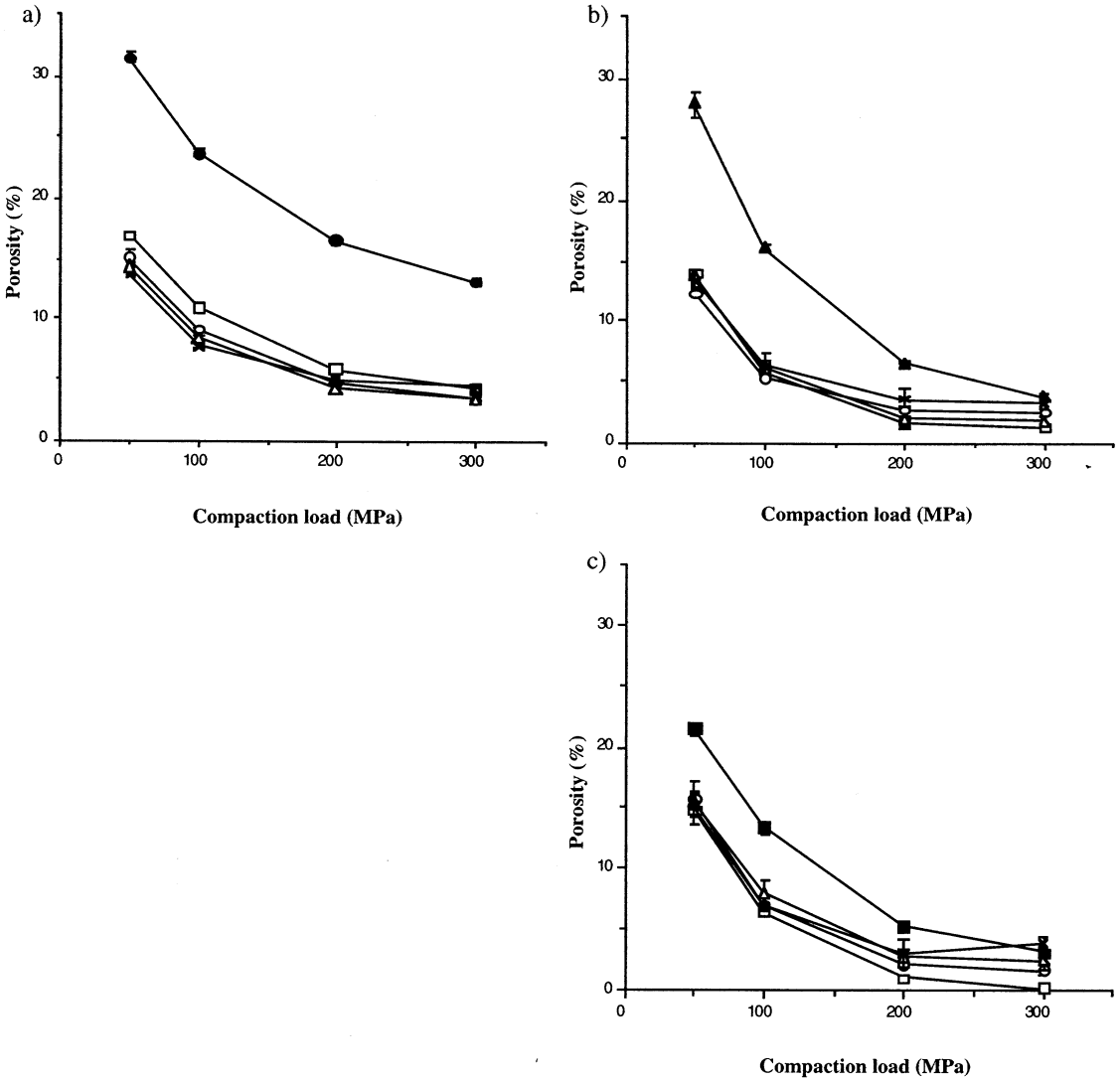

Fig. 3. Tablet porosity as a function of the compaction load. The 95% confidence intervals are shown where they exceed the dimensions of the symbol. (a) Pure sodium bicarbonate (125–180 μm) (●) and sodium bicarbonate (125–180 μm) mixed with PEGs: PEG 3000 (□), PEG 6000 (○), PEG 10000 (△) and PEG 20000 (x). (b) Pure sodium chloride (125–180 μm) (▲) and sodium chloride (125–180 μm) mixed with PEGs: PEG 3000 (□), PEG 6000 (○), PEG 10000 (△) and PEG 20000 (x). (c) Pure sodium chloride (355–500 μm) (■) and sodium chloride (355–500 μm) mixed with PEGs: PEG 3000 (□), PEG 6000 (○), PEG 10000 (△) and PEG 20000 (x).

in this paper referred to as a synergistic effect. This effect was also seen for sodium chloride tablets but only when the lowest molecular weights of PEG were added, i.e. PEG 3000 and PEG 6000.

The porosity of both the sodium bicarbonate tablets and sodium chloride tablets decreased when PEG was added. Generally the porosity of tablets containing sodium chloride was lower than the corresponding tablets containing sodium bicarbonate. For sodium bicarbonate there was also a tendency for a greater reduction in porosity on the addition of higher molecular weight PEGs, while the opposite was seen for sodium chloride tablets (Fig. 3a,b,c).

Table 4
Characterisation of the deformability of PEG

Molecular weight	Apparent yield pressure[a] (MPa)	Minimum tablet height (mm)	Maximum tablet height (mm)	Elastic recovery[b] (%)
3000	28.7 (1.5)	3.452 (0.006)	3.674 (0.020)	6.45
6000	36.5 (0.1)	3.452 (0.008)	3.718 (0.018)	7.70
10 000	32.3 (0.1)	3.461 (0.007)	3.786 (0.013)	9.40
20 000	24.5 (0.2)	3.449 (0.015)	3.862 (0.020)	12.0

The results are the mean value with the corresponding S.D. in parentheses.
[a] Obtained from the reciprocal of the linear part of an 'in-die-Heckel plot' (Duberg and Nyström, 1986), thus including both plastic and elastic deformation.
[b] Defined as the relative difference between the minimum and maximum tablet height.

3.3. Properties of tablets consisting of mixtures of sodium bicarbonate or sodium chloride and the same amount by weight of PEGs of differing molecular weights

When PEG 3000 or PEG 6000 were added to sodium bicarbonate in the same amounts by weight as PEG 20000 (Table 3), the tensile strength of the mixtures was not significantly different from that seen when the amount of PEG corresponding to a surface area ratio of unity was added (Fig. 4a). When PEG 3000, PEG 6000 or PEG 20000 was added to sodium chloride (125–180 μm) in the same amount by weight as to sodium bicarbonate, the tensile strength was significantly affected only when PEG 20000 was added (Fig. 4b). At this point the tensile strength was similar to that of the tablets consisting of sodium bicarbonate and PEG.

The tensile strength of the tablets made from the 125–180 and the 355–500 μm fractions of sodium chloride mixed with the various PEGs to obtain a surface area ratio of unity did not differ significantly from each other (Fig. 5). However, when the same amount of PEG (by weight) was added to sodium chloride (355–500 μm) as had been added to sodium chloride (125–180 μm) (Table 3), the profile of tensile strength versus molecular weight altered and became similar to that of sodium bicarbonate mixed with PEG (Fig. 5).

4. Discussion

4.1. The effects of addition of PEGs of differing molecular weights to sodium bicarbonate

The addition of PEG to sodium bicarbonate reduced the porosity of the compacts. This probably indicates that the PEGs were able to partly fill the pores between the sodium bicarbonate particles (Fig. 3a). At low compaction loads, the addition of a high molecular weight PEG (PEG 20000) tended to result in tablets with lower porosity than tablets with the addition of a low molecular weight PEG (PEG 3000). This may have been because the porosity of the pure sodium bicarbonate tablets was quite high at low compaction loads, so that the effects of the different amounts of PEG added (by weight) (Table 3) were more pronounced than at higher compaction loads.

The tensile strength of the sodium bicarbonate tablets was affected to a great extent by the properties of the particular PEG added (Fig. 1a,b,c,d). In fact the profile of the tensile strength of the tablets made of sodium bicarbonate and the various PEGs was remarkably similar to the corresponding profile of the pure PEG tablets. In other words the tensile strength of the tablets of the mixtures seemed to be determined partly by the tensile strength of the pure PEG. This observation may indicate that the main route for failure during strength testing of the

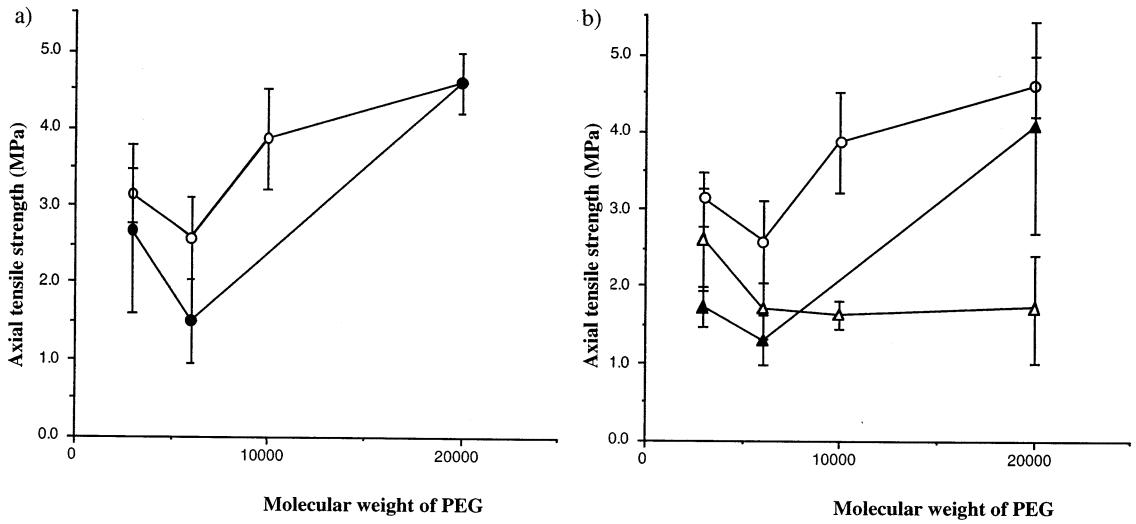

Fig. 4. Axial tensile strength of the tablets compacted at 300 MPa as a function of the molecular weight of PEG added in order to evaluate the effect of the amount of PEG in the mixtures. The 95% confidence intervals are shown where they exceed the dimensions of the symbol. (a) Sodium bicarbonate (125–180 μm) mixed with PEG (surface area ratio 1.0) (○) and sodium bicarbonate (125–180 μm) mixed with the same amount (by weight) of PEG as in the mixture containing PEG 20000 (●). (b) Sodium chloride (125–180 μm) mixed with PEG (surface area ratio 1.0) (△), sodium bicarbonate (125–180 μm) mixed with PEG (surface area ratio 1.0) (○) and sodium chloride (125–180 μm) mixed with the same amount (by weight) of PEG as in the mixture containing sodium bicarbonate (▲).

tablets consisting of sodium bicarbonate and PEG was not through the sodium bicarbonate particles but rather around them, i.e. through the interparticulate voids, which in this case were partly filled with PEG. This is presented in a qualitative tablet model (Fig. 6b).

In the literature, pharmaceutical compacts are often described as aggregates of particles where the bonds within a particle are stronger than the bonds between the particles (Nyström et al., 1993). As a consequence of this assumption, compacts would tend to fail around rather than through the particles (Shotton and Ganderton, 1961; Eriksson and Alderborn, 1995; Adolfsson and Nyström, 1996). This is probably what occurs with pure sodium bicarbonate tablets (Fig. 6a). The failure of a pure PEG tablet may be more difficult to describe in such general terms because of the high ductility and the low melting point of the PEGs (between 48 and 63°C (Wade and Weller, 1994)) (Fig. 6c).

The overall increase in tensile strength when PEG was added to sodium bicarbonate may, according to the qualitative tablet model (Fig. 6), be caused by two factors. Firstly, when a failure occurs in a pure sodium bicarbonate tablet it is likely to propagate mainly through the interparticulate voids, i.e. through an air phase (Fig. 6a). When PEG is present in the interparticulate voids, the porosity of the compact is reduced and the failure is likely to propagate through more solid material, i.e. the PEG phase (Fig. 6b). Consequently the fracture surface area and thus the tensile strength of the compact is increased. Secondly, if the fracture is likely to propagate mainly through the PEG phase rather than through the sodium bicarbonate crystals, the tensile strength will probably, to some extent, reflect the tensile strength of the corresponding pure PEG tablet, which has a higher tensile strength than a pure sodium bicarbonate tablet (Fig. 1a,b,c,d).

The discussion above implies that the increase in tensile strength with increasing molecular weight of PEG, in tablets made of sodium bicarbonate and PEG, was associated strongly with the increase in tensile strength of pure PEG tablets

with increasing molecular weight (Fig. 1a,b,c,d). However, it is possible that other factors may also contribute to this increase. For example, the amount of PEG added (by weight) to sodium bicarbonate increased with increasing molecular weight (Table 3) (which may be reflected as a greater reduction in porosity). However, the importance of this factor is most likely small, because when PEG 3000 or PEG 6000 were added to sodium bicarbonate in the same amounts by weight as PEG 20000 (Fig. 4a), the increased amount of PEG had little or no effect on the tensile strength of the compact.

An increase in compaction load probably brings the compound particles into closer proximity to each other. Since the fracture is likely to propagate around the sodium bicarbonate particles the fracture surface area consequently increases. This probably has a greater impact when coarse, rigid particles are present in the tablet, i.e.

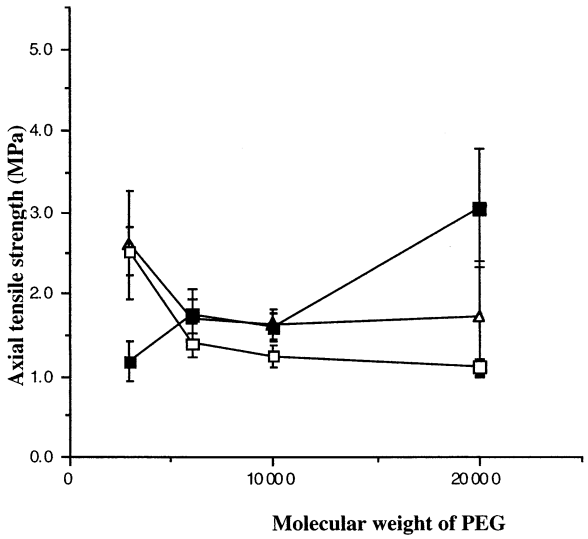

Fig. 5. Axial tensile strength of the tablets compacted at 300 MPa as a function of the molecular weight of PEG in order to evaluate the effect of the amount of PEG in the mixtures. The 95% confidence intervals are shown where they exceed the dimensions of the symbol. Sodium chloride (125–180 μm) mixed with PEG (surface area ratio 1.0) (△), sodium chloride (355–500 μm) mixed with PEG (surface area ratio 1.0) (□) and sodium chloride (355–500 μm) mixed with the same amount (by weight) of PEG as in the mixture containing sodium chloride (125–180 μm) (■).

this effect is not as pronounced in pure PEG tablets as in tablets containing sodium bicarbonate (Fig. 6a,b,c).

As discussed above, it may be assumed that the fracture propagates around the sodium bicarbonate particles and that the tensile strength of tablets of the mixtures is governed by the tensile strength of the materials in the pores between the sodium bicarbonate particles, i.e. PEG. The presence of coarse sodium bicarbonate particles is likely to increase the fracture surface area of the compact (Fig. 6b), compared to a compact consisting only of PEG (Fig. 6c). As a consequence the tensile strength of the compacts of the mixtures may in some cases be higher than that of the tablets of each single component (Gren and Nyström, 1996).

4.2. The effect of addition of PEGs of differing molecular weights to sodium chloride

When PEGs of differing molecular weights were added to sodium chloride (125–180 and 355–500 μm), the profile of the tensile strength was different from that seen with sodium bicarbonate. Firstly, the tensile strength was generally increased, but not to the same extent as with sodium bicarbonate. Secondly, in contrast to the situation with sodium bicarbonate, the tensile strength of the tablets containing a high molecular weight PEG (PEG 20000) was lower than that of tablets containing a low molecular weight PEG (PEG 3000). Thirdly, the synergistic increase in tensile strength was not as pronounced as with sodium bicarbonate and only occurred when PEG 3000 or PEG 6000 were added.

The overall increase in tensile strength when PEG was added to both size fractions of sodium chloride may probably be explained by the same factors as for sodium bicarbonate. Thus, the addition of PEG reduced the porosity and increased the fracture surface area of the compact (Fig. 3a,b,c) and the tensile strength of the pure PEG tablets was overall higher than the tensile strength of the pure sodium chloride tablets.

The profile of the tensile strength of the mixtures did not reflect the profile of the tensile

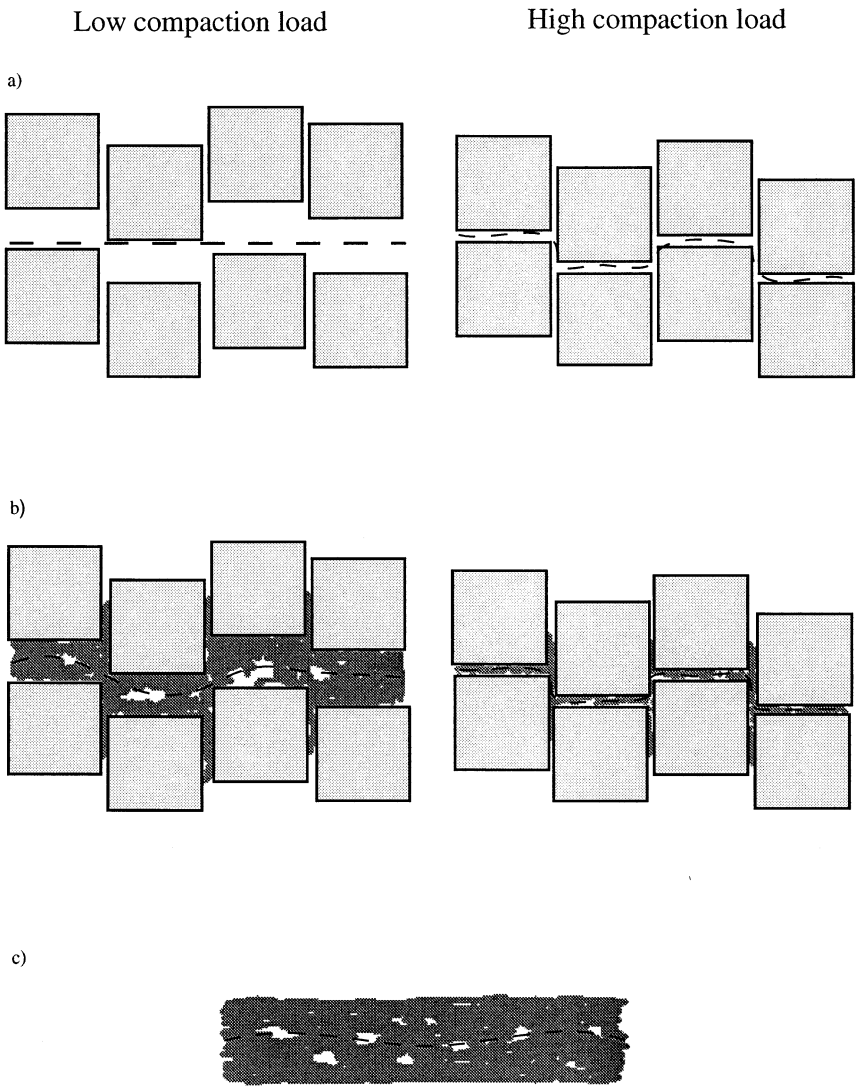

Fig. 6. A schematic picture describing the fracture surface of a tablet on a macroscopic level. The fracture is indicated by the dotted line. The light grey area represents the compound particles, the white area represents the air phase and the dark grey area represents the PEG component. (a) A tablet consisting of a single compound compacted at low or high compaction loads; (b) a tablet consisting of two components where the second component, PEG, is present in the voids between the compound particles, compacted at low or high compaction loads; and (c) a tablet made of pure PEG.

strength of the pure PEGs (Fig. 1a,b,c,d) to the same extent as seen with tablets made from sodium bicarbonate and PEG. This observation may partly be explained by the reported ability of sodium chloride to develop solid bridges (Führer, 1977; de Boer et al., 1978; Karehill and Nyström, 1990; Nyström et al., 1993; Olsson et al., 1996).

Solid bridges are together with weak long range forces (intermolecular forces) and mechanical interlocking the bonding mechanisms generally assumed to dominate in dry pharmaceutical compacts (Führer, 1977). Solid bridges are thought to consist of particle-to-particle contact at an atomic level. Weak long range forces, i.e. van der Waals forces, electrostatic forces and hydrogen bonds act between surfaces separated

by some distance. Mechanical interlocking can occur if the particles can hook or twist together during compaction. The different bonding mechanisms have been previously described in detail (Olsson et al., 1996).

It has been demonstrated previously that solid bridges are able to penetrate layers of magnesium stearate located around larger particles of sodium chloride (Nyström et al., 1993). It therefore seems reasonable to assume that solid bridges may be capable of penetrating the PEG layer and thus creating solid bridges between the sodium chloride particles. The fracture would thus be forced through both the solid bridges and the PEG phase. Solid bridges have been described as a continuous phase between two particles, where the molecules in the solid bridge are arranged in the same manner as the molecules inside each particle (Olsson et al., 1996). It therefore seems reasonable that a fracture through a solid bridge could be seen as propagating partly through the sodium chloride particles themselves, in accordance with Shotton and Ganderton (1961). Consequently, the tensile strength of the tablets made from the mixtures would in this case not only depend on the tensile strength of pure PEG but also on the nature of the solid sodium chloride bridges.

It has also been shown that the degree to which the solid bridges contribute to the tensile strength of a compact increases with increasing compaction load and increasing particle size (Adolfsson et al., 1997). In Fig. 1a,b,c,d it can be seen that the influence of PEG on the tensile strength of the tablets made from sodium chloride and PEG decreased with increasing compaction load and increasing sodium chloride particle size, i.e. it could be hypothesised that the influence of the solid bridges on the tensile strength of the tablets increased.

It can also be seen from the results that the tensile strength of tablets made from the mixtures decreased as the molecular weight of the added PEG increased. The sodium chloride tablets were generally less porous than the corresponding sodium bicarbonate tablets. Consequently, the particle size and the mechanical properties (plastic and elastic behaviour) of the binder (PEG) used to fill the voids in (and thus increase the tensile strength of) the tablet may be important considerations. Fig. 1a,b,c,d show, in contrast to the tablets made of sodium bicarbonate, that the tablets containing the finest, i.e. the particles with the largest external surface area (Table 2), and most plastic of the PEGs (PEG 3000) had the highest tensile strength, while those containing the coarser and more elastic PEG showed a lower tensile strength (Nyström et al., 1982). This effect may also have been enhanced by the increased amounts of the higher molecular weight PEGs.

For tablets made from sodium chloride and PEG a significant synergistic effect was only seen when PEG 3000 or PEG 6000 was added at compaction loads above 100 MPa. This is probably also caused by the more ductile nature of the low molecular weight PEGs, facilitating the reduction in porosity and thus increasing the fracture surface area (Fig. 6a,b,c).

4.3. Differences between the effects of addition of PEGs of differing molecular weights to sodium bicarbonate and sodium chloride

The overall increase in tensile strength when PEG was added to the sodium chloride tablets was generally less than for the corresponding sodium bicarbonate tablets. This is probably related to the smaller reduction in porosity seen with the sodium chloride tablets (Fig. 3a,b,c), which in turn was probably caused by the lower porosity of the pure sodium chloride tablets. The smaller amount of PEG added to sodium chloride than to sodium bicarbonate may also have been a factor (Table 3). However, when the same amount of PEG by weight was added to sodium chloride (125–180 μm) as to sodium bicarbonate (125–180 μm) the tensile strength of the tablets was not significantly affected for all PEG molecular weights except PEG 20000 (Fig. 4b). Thus, differences in the amount of PEG appear not to fully explain the differences in porosity and tensile strength between the tablets of sodium chloride and those of sodium bicarbonate.

When PEG 20000 was added to sodium chloride (125–180 μm) in the same amount as to sodium bicarbonate (125–180 μm), the tensile strength of the tablets increased to almost the same level as that of the corresponding sodium bicarbonate tablets. This may be because of the large amount of PEG 20000 that was added, and perhaps also the lower ductility and higher elasticity of the material may have prevented solid bridges from forming, so that the tensile strength was determined to a greater extent by pure PEG. This tendency can also be seen in Fig. 5 where PEG 20000 was added to sodium chloride (355–500 μm) in the same amount as to sodium chloride (125–180 μm).

5. Conclusions

When a relatively ductile, fine particulate material (such as polymeric binders) is added to a relatively rigid, coarse particulate compound (as are most pharmaceutical active ingredients) in the form of an ordered mixture, the fracture probably occurs around the coarse compound particles and through the interparticulate voids partly filled with the binder. The tensile strength of the resulting tablets seems to be governed by mechanical properties such as the mechanical strength and volume reduction ability of both the compound and the binder.

When a compound that produces tablets of low porosity is used, the plasticity and perhaps also the particle size of the binder material appears to affect the fracture surface area and thus the tensile strength of the tablets. In this study this was demonstrated for sodium chloride, where addition of PEG 3000, the most ductile additive tested, gave the lowest tablet porosity and the greatest improvement in tablet strength. When a compound that produces tablets of higher porosity is used (sodium bicarbonate) the volume reduction mechanism of the binder material is of less importance than the tensile strength of the binder, which seemed to determine the final tablet strength.

The bonding mechanism of the compound also seemed relevant to the tensile strength of the final tablet. When solid bridges are established between the compound particles, the tensile strength of the tablet appears less affected by the addition of a second component. However, when the amount of the second component exceeded a certain level, it was hypothesised that solid bridges could no longer be established, so that the tensile strength was governed to a greater extent by the tensile strength of the added material.

The tensile strength of a tablet consisting of a mixture of two components may in some cases exceed the tensile strength of each individual component. It is proposed that this phenomenon is caused by the increased fracture surface area resulting from lowered tablet porosity and by the longer distance that the fracture has to propagate.

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