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European Journal of Pharmaceutics and Biopharmaceutics 52 (2001) 237–247

European Journal of Pharmaceutics and Biopharmaceutics

www.elsevier.com/locate/ejphabio

Research paper

The use of mercury porosimetry in assessing the effect of different binders on the pore structure and bonding properties of tablets

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Received 15 December 2000; accepted in revised form 23 April 2001

Abstract

This study investigated the effect of binders with different deformability characteristics on the pore structure of tablets composed of binary mixtures. The pore structure was evaluated using mercury porosimetry. The pore size distribution in tablets of both individual components and binary mixtures indicated that the pores in pure binder tablets appeared not to exist to the same degree in composed tablets and were therefore unlikely to substantially contribute to the pore structure. It is therefore suggested that, because the binder undergoes extensive deformation and shearing during compaction, it will exist as relatively small lumps or aggregates or even primary particles that are located between the compound particles. Most of the pores in the binary tablets studied were thus found between particles of the compound and the binder phase. The most deformable binder, polyethylene glycol 3000, had the greatest effect on pore structure, reflected in the greatest increase in tablet strength. An attempt was also made to use mercury porosimetry data to qualitatively assess the effect of a binder on the dominating bond types in a tablet. The results indicated that addition of a binder caused a decrease in the probability of forming solid bridges.

Keywords: Tablet strength; Binder; Pore size distribution; Deformability; Interparticulate bonds; Mercury porosimetry

1. Introduction

When a powder is compressed, the amount of air in the powder bed is reduced and the particles are moved into closer proximity to each other, allowing bonds between the particles to form. The pore structure of the resulting tablet, expressed in terms of porosity and pore size distribution, affects tablet properties such as tensile strength and disintegration time. However, the relationship between tensile strength and pore structure appears to be ambiguous. Ryshkewitch [1] found a linear relationship between the porosity and the logarithm of the strength of tablets. Further, the total pore surface area was suggested to be directly proportional to the breaking force of lactose tablets [2,3]. However, this finding was not confirmed by others [4,5]. A correlation between median pore size (defined as the pore diameter at which 50% of the total volume of intruded mercury is intruded; a parameter that is mainly affected by the number of large pores in a tablet) and tablet strength has been reported for granulated materials [5]. An increase in tablet strength was related to a decrease in the volume of large pores and to a shift in the pore size distribution towards smaller pores [5].

In the literature, pores have been classified as macropores (>0.05 μm in diameter), mesopores (0.002–0.05 μm in diameter) and micropores (<0.002 μm in diameter) [6]. The pore structure of powders, granules and tablets has been characterised using methods such as mercury porosimetry and gas adsorption. These methods cover specific ranges of pore size. With mercury porosimetry, the lower size limit is about 0.003 μm in diameter, a range which excludes micropores, whereas gas adsorption covers the micropore range.

A binder is normally added to a formulation to enhance the compactibility and hence the strength of the resultant tablets. Earlier studies at the department have evaluated the effect of different binder properties on the tensile strength, porosity and disintegration of tablets [7–10]. These studies indicated that a more deformable binder, such as polyethylene glycol (PEG), will markedly decrease the tablet porosity because of its ability to fill the interparticulate voids when added to a compound and will thus increase the tablet strength. When using compounds that formed tablets with a low porosity, e.g. sodium chloride, small particles of highly deformable binders more effectively filled the voids

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0939-6411/01/$ - see front matter
PII: S0939-6411(01)00163-1

Nomenclature

σ_T	radial tensile strength (MPa)
σ_A	adjusted tensile strength (N in Eq. (2) and Pa in Eq. (3))
d_l, r_l	average pore diameter (radius) by length, obtained with porosimetry (μm)
d_v, r_v	average pore diameter (radius) by volume, obtained with porosimetry (μm)
r	pore radius, obtained by permeametry (μm)
S_v	external volume-specific tablet surface area, obtained with permeametry (m^2/m^3)
S_{vpore}	total volume-specific pore surface area, obtained with porosimetry (m^2/m^3)
S_{tot}	total weight-specific pore surface area, obtained with porosimetry (m^2/g)
V_{tot}	total volume of intruded mercury, obtained with porosimetry (ml/g)

between the compound particles and decreased tablet porosity further. It was concluded that a deformable binder could be used as an alternative to the more commonly used microcrystalline cellulose if the objective was to increase the tablet strength [8,9].

In this study, the effect of a binder on the pore structure (porosity, pore surface area, average pore diameter and pore size distribution) of a tablet is emphasised in order to gain further understanding regarding the effect of a binder on tablet strength. The suitability of data obtained from mercury porosimetry for estimating the dominating bond types in tablets was also investigated.

2. Materials and methods

2.1. Materials

The model compounds used were sodium chloride (355–500 μm; lot# F80G, Kebo Lab, Stockholm, Sweden) and sodium bicarbonate (125–180 μm; lot# 97304, Kebo Lab, Stockholm, Sweden). The size fractions were obtained by dry sieving (Retsch, Haan, Germany). The binder materials studied were PEG 3000 (lot# S95393827, Kebo Lab, Stockholm, Sweden), PEG 20000 (lot# 920206, Kebo Lab, Stockholm, Sweden) and pregelatinised starch (PGS; Sepistab® ST 200, lot# 80511, Seppic, Paris, France). The size fraction of the binder (<20 μm) was obtained with an air classifier (100 MZR, Alpine, Augsburg, Germany). PEG was milled in a pin disc mill (63C or 160Z, Alpine, Augsburg, Germany) before air classification. The apparent particle density of the materials was determined using helium pycnometry (AccuPyc 1330 Pycnometer, Micromeritics, Norcross, GA, USA) (Table 1). The external specific surface area of the compounds and binders was determined using Friedrich permeametry [11] and Blaine permeametry [12], respectively (Table 1). The powders were stored for at least 48 h at 40% relative humidity and room temperature before characterisation and further handling.

2.2. Preparation of mixtures

Five, 10 and 20% w/w of PEG 3000 were added to sodium chloride or sodium bicarbonate. Mixtures containing sodium chloride or sodium bicarbonate and 20% w/w of PEG 20000 or 20% w/w of PGS were also prepared. The powders were mixed in a Turbula mixer (2L, W.A. Bachhofen, Basel, Switzerland) at 120 r.p.m. for 100 min.

2.3. Compaction of tablets

Tablets were compacted at a maximum upper punch pressure of 200 MPa using an instrumented single punch press (Korsch EK0, Berlin, Germany) and 1.13 cm flat faced punches. The upper punch pressure was obtained by keeping the distance between the punches constant and adjusting the amount of powder in the die. The upper punch pressure was

Table 1
Characteristics of the test materials[a]

Material	Particle fraction (μm)[b]	Apparent particle density (g/cm^3)[c]	External specific surface area (cm^2/g)[d]	Contact angle of mercury (°)[e]
Sodium bicarbonate	125–180	2.215 (0.001)	270 (3)	113 (1.7)
Sodium chloride	355–500	2.156 (0.000)	70 (0.4)	126 (3.6)
PEG 3000	< 20	1.220 (0.001)	9800 (200)	133 (2.9)
PEG 20000	< 20	1.214 (0.000)	3400 (27)	127 (2.2)
PGS	< 20	1.489 (0.002)	3900 (78)	114 (8.2)

[a] Standard deviation in parentheses.
[b] Obtained by dry sieving or air classification.
[c] Measured with a helium pycnometer (AccuPyc 1330 Pycnometer, Micromeritics, Norcross, GA, USA).
[d] Determined with Friedrich or Blaine permeametry.
[e] Measured with a contact anglometer (Model 1501, Micromeritics, Norcross, GA, USA).

recorded using a strain gauge connected to the upper punch. The punches and die were lubricated with magnesium stearate powder prior to each compaction.

2.4. Characterisation of tablets

The tablets were stored for at least 48 h at 40% relative humidity and room temperature before characterisation.

2.4.1. Tablet strength

The radial tensile strength was calculated using the diametral compression test (Holland C50, Nottingham, UK) [13]. The axial tensile strength was determined using a material tester (M39K, Lloyd Instruments, Fareham, UK); calculations were as described by Nyström et al. [14].

2.4.2. Pore structure

The tablet porosity was characterised in two ways. Firstly, it was calculated from the apparent particle density of the material or mixture and the dimensions and weight of the tablet. Secondly, tablet porosity was obtained from mercury porosimetry measurements (maximum intrusion pressure 379 MPa) (Table 2).

The tablet pore structure was assessed using mercury porosimetry (AutoPore III, Micromeritics, Norcross, GA, USA) and the relationship between the intruded volume of mercury and the intrusion pressure was analysed ($n = 2$–3). The intrusion pressures were between 0.01 and 379 MPa. The pore sizes corresponding to the intrusion pressures were calculated assuming cylindrical pores and a surface tension for mercury of 485 mN/m. The mercury-powder contact angles were measured using a contact anglometer (Model 1501, Micromeritics, Norcross, GA, USA) ($n = 3$) (Table 1). The mercury contact angles for the mixtures were calculated from the contact angles of the pure powders and the proportion by volume of respective material constituting the mixture.

The pore structure of the powders was also determined in order to compare inter- and intraparticulate pores (AutoPore III, Micromeritics, Norcross, GA, USA). In these experiments, the intrusion pressures were between 0.04 and 241 MPa. Otherwise the conditions were as stated above for the tablets.

The average pore diameter was expressed either by length or by volume. The average pore diameter by length (d_l) was obtained from the following equation:

$$d_l = 4 \times \frac{V_{tot}}{S_{tot}} \quad (1)$$

where V_{tot} and S_{tot} are the total intruded volume of mercury and the total pore surface area, respectively. The expression is based on the assumption that the pores are cylindrical and open at the ends [15]. The average pore diameter by volume (d_v) was defined as the pore diameter at which 50% of the total volume of intruded mercury is intruded [16]. Data

Table 2
Pore structure of tablets compacted at 200 MPa[a]

Material/mixture	Average pore diameter (μm)		Porosity (%)	
	By length[b]	By volume[c]	Based on gas pycnometry[d]	Based on Hg-intrusion[e]
Sodium bicarbonate (SB)	0.138 (0.040)	1.22 (0.57)	18.6 (0.32)	12.5 (3.1)
Sodium chloride (SC)	0.122 (0.020)	3.17 (0.70)	8.99 (0.75)	3.96 (0.16)
PEG 3000	0.015 (0.000)	0.044 (0.001)	6.22 (0.66)	5.40 (0.30)
PEG 20000	0.022 (0.000)	0.678 (0.034)	10.7 (0.32)	10.4 (0.25)
PGS	0.029 (0.004)	0.755 (0.008)	18.1 (0.33)	17.7 (0.48)
SB + PEG 3000				
5%	0.066 (0.013)	0.591 (0.037)	12.9 (0.58)	9.20 (0.16)
10%	0.052 (0.004)	0.390 (0.003)	9.72 (0.49)	6.38 (0.01)
20%	0.023 (0.001)	0.164 (0.017)	7.24 (0.49)	3.51(0.22)
SC + PEG 3000				
5%	0.027 (0.002)	0.457 (0.012)	5.84 (0.41)	2.34 (0.06)
10%	0.020 (0.001)	0.187 (0.034)	5.22 (0.59)	1.94 (0.22)
20%	0.014 (0.001)	0.029 (0.001)	5.66 (0.81)	2.08 (0.34)
SB + PEG 20000 20%	0.035 (0.007)	0.398 (0.036)	7.76 (0.46)	5.02 (0.35)
SC + PEG 20000 20%	0.021 (0.000)	0.388 (0.037)	5.87 (0.63)	3.03 (0.01)
SB + PGS 20%	0.069 (0.025)	1.30 (0.098)	16.0 (0.47)	14.3 (2.4)
SC + PGS 20%	0.061 (0.020)	1.80 (0.058)	11.1 (0.73)	9.11 (0.71)

[a] Standard deviation in parentheses.
[b] Calculated using Eq. (1) [15].
[c] Defined as the pore diameter at which 50% of the total volume of intruded mercury is intruded [16].
[d] Calculated from the apparent particle density of the material or mixture and the dimensions and weight of the tablet.
[e] Obtained with mercury porosimetry (AutoPore III, Micromeritics, Norcross, GA, USA).

obtained with mercury porosimetry were also used to estimate the dominating bond types in tablets.

3. Results and discussion

3.1. Pore characteristics of the pure materials

3.1.1. Powders

The pore size distributions, expressed as the log differential intrusion volumes versus pore diameter (log scale), of the powders are shown in Fig. 1. The derivative of the cumulative logarithmic curve has been used previously for reasons of comparison even though it has no physical meaning [16]. All materials tested had a peak in the pore size distribution corresponding to pore diameters of 5–15 μm, i.e. in the macropore range (Fig. 1). Smaller pores than these do not appear to exist; however, it cannot be excluded that this is because of the limitation of mercury porosimetry to detect small pores. Considering the relatively large pore diameter obtained, it is postulated that the pores were interparticulate (between powder particles) and that the particles themselves were essentially non-porous. The similarity in pore diameters suggests that the packing structure was similar among the materials. It was not possible to measure the pore structure of sodium chloride powder under these experimental conditions. However, sodium chloride is regarded in the literature as a non-porous material [17].

3.1.2. Tablets

The pore size distributions of the compacted materials are shown in Fig. 2. The average pore diameters and tablet porosity values are shown in Table 2. The pore size distribution of the compounds was similar but the pore volume was greater for sodium bicarbonate tablets. The pores in tablets of PEG

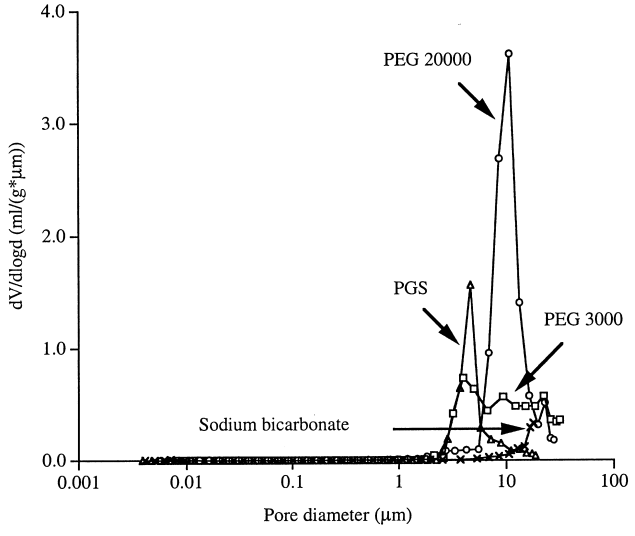

Fig. 1. Pore size distribution of powders of the pure materials (except sodium chloride). Sodium bicarbonate (125–180 μm) (×), PEG 3000 (<20 μm) (□), PEG 20000 (<20 μm) (○) and PGS (<20 μm) (△).

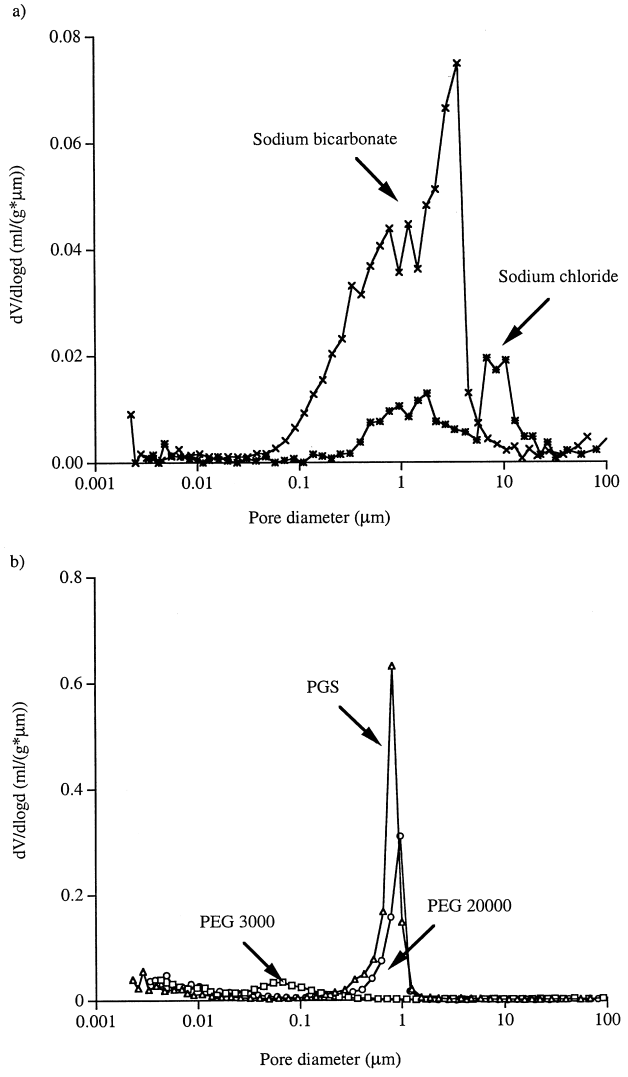

Fig. 2. Pore size distribution of tablets of the pure materials: (a) sodium bicarbonate (125–180 μm) (×) and sodium chloride (355–500 μm) (*); (b) PEG 3000 (<20 μm) (□), PEG 20000 (<20 μm) (○) and PGS (<20 μm) (△).

20000 or PGS were mainly around 1 μm or slightly smaller. The pores in PEG 3000 tablets, on the other hand, were mainly below 0.5 μm in diameter, with a large fraction below 0.1 μm. Since it is proposed that the materials are essentially non-porous, the contribution of intraparticulate pores to total tablet porosity is assumed to be insignificant.

3.2. Pore characteristics of tablets made from the mixtures

3.2.1. Porosity

The decrease in tablet porosity caused by the addition of a binder was most pronounced with PEG 3000 and least pronounced with PGS (Table 2). It has previously been demonstrated that, as the molecular weight of PEG decreases, the material becomes more plastically deformable, with a smaller elastic component (e.g. Refs. [7,8,18,19]). The decrease in porosity on addition of a binder

such as PGS, which has a higher propensity for elastic recovery and a lower degree of plastic deformation, was very small [9]; in fact, the tablet porosity of the combination with sodium chloride was greater than that of the pure compound. In tablets containing PEG 3000, the porosity decreased as the amount of binder was increased (Table 2) [8,9].

The alternative methods of determining tablet porosity (apparent particle density and dimensions and weight of the tablet or mercury porosimetry) resulted in different values (Table 2). The porosity obtained with mercury porosimetry was lower because mercury was probably unable to intrude into the very small pores. Consequently, the greatest difference between the techniques was obtained with the densest tablets, as exemplified by the mixture of sodium chloride and PEG 3000 20% (w/w), where an almost three-fold difference was obtained.

3.2.2. Pore size distribution

The pore size distribution was shifted towards smaller pores and generally became narrower on the addition of a binder (Figs. 3–5). In contrast, a widening of the pore size distribution was reported when cellulose was added to lactose [20]. This was explained by the assumption that new types of pores were formed [20]. When similar amounts (20% w/w) of the different binders were added, the shift towards smaller pores was greatest with the most deformable binder, PEG 3000 (Fig. 3). The results also showed that there was a further gradual shift towards smaller pores when the amount of PEG 3000 was increased (Fig. 4).

Some of the systems (pure sodium bicarbonate, pure PEG 3000 and a mixture containing sodium bicarbonate and 20% PEG 3000) are elucidated in more detail in Fig. 5. The theoretical pore size distribution for the mixture (obtained from the sum of the effects of the pure materials based on the composition of the mixture) is included in the figure as a comparison with the experimentally obtained results. In the mixture, most of the large pores originating from sodium bicarbonate have disappeared, which indicates that the binder has filled the pores between the sodium bicarbonate particles. The interparticulate pores in the tablet composed of the mixture were mainly between 0.1 and 1 μm in diameter, whereas the pores in the tablet of pure binder were mainly below 0.5 μm, with a large fraction below 0.1 μm.

The pore size distributions indicated that the contribution of pores slightly below 0.1 μm, i.e. probably originating from the binder, was smaller than expected from the theoretical distribution (Fig. 5). Therefore, the macrostructure found in tablets of pure binder, in which most pores are around 0.1 μm in diameter, will not exist to the same degree in tablets of the mixture and are not likely to substantially contribute to the pore structure of the tablet. It is therefore suggested that, because the binder undergoes extensive deformation and shearing during compaction, it will mainly exist as smaller lumps or aggregates or even as primary particles when located between the compound particles. It is suggested that the pores in a tablet composed of a mixture are mainly located between the compound particles and the binder phase and are found to a smaller extent within the binder phase.

3.2.3. Average pore diameter

The addition of binder resulted in a decrease in diameter when expressed either as average by length or average by volume (Table 2). Although there were relatively wide variations in individual pore diameters, in most cases the relative standard deviation was acceptable and below 10%. The average pore diameter by volume is greatly affected by the number of large pores [5] and for obvious reasons, the average pore diameter by length will be considerably smaller than the average pore diameter by volume (Table 2).

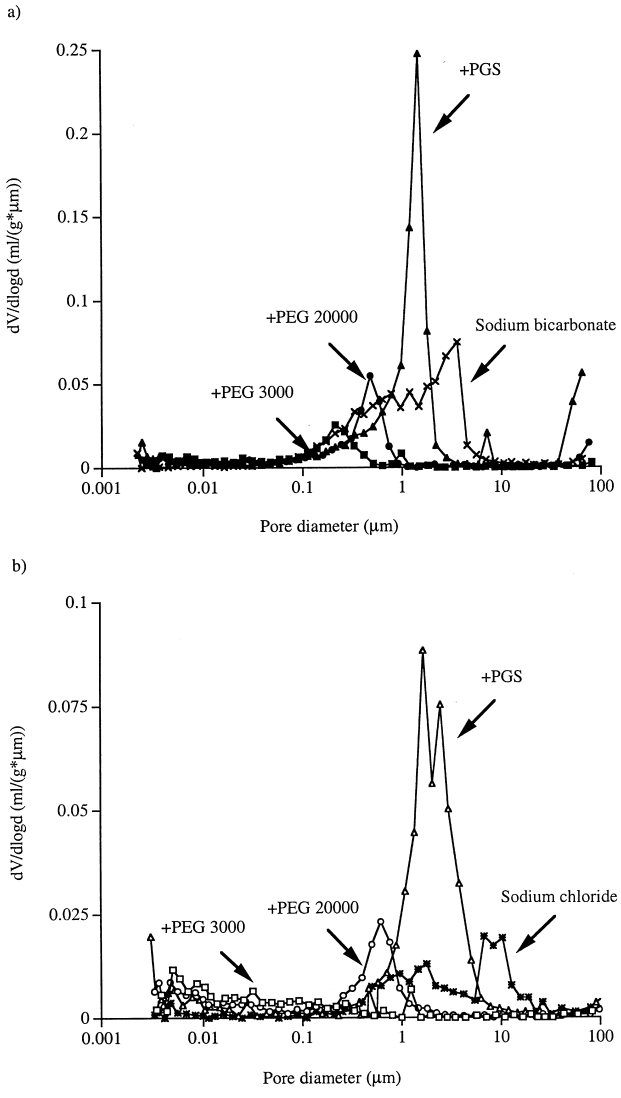

Fig. 3. Pore size distribution of tablets made of pure compounds and mixtures with 20% w/w of binder: (a) sodium bicarbonate (×) and mixtures containing PEG 3000 (■), PEG 20000 (●) and PGS (▲); (b) sodium chloride (*) and mixtures containing PEG 3000 (□), PEG 20000 (○) and PGS (△).

3.2.4. Binder properties and pore structure

The ability of a binder to be effectively distributed into the voids between the compound particles, thereby reducing the tablet porosity, is thought to be an important factor in its strength-enhancing effect [7–9]. This theory was confirmed in the present study by characterising pore size distributions, since there was a shift towards smaller pores compared to the distribution in a pure compound tablet. An increased amount of binder and also an increased ability to be distributed, i.e. a higher deformability, will favour a shift in the distribution towards smaller pores as well as a decrease in tablet porosity. Consequently, the largest effect on pore structure was obtained with the greatest amount of the most deformable binder tested, PEG 3000. The results in this study confirm the applicability of a qualitative tablet model presented earlier in assessing the effect of a binder [7–9]. The binders had similar effects on sodium bicarbonate and sodium chloride, although there were more distinct differences between the binders tested with sodium bicarbonate than with sodium chloride (Figs. 3 and 4).

It appears that the equation used in a previous paper [9] was suitable for the calculation of the degree of binder saturation, which describes the void-filling capacity of a binder. The apparent particle density, obtained from helium pycnometry, is used in this equation to calculate the volume occupied by the binder, assuming that any inherent porosity of the binder phase does not significantly contribute to the porosity of the composed tablet.

3.3. Tablet strength and pore structure

The highest tablet strength was obtained with the more deformable PEG and the lowest tablet strength with the less deformable PGS (Fig. 6), which agrees with the effects of

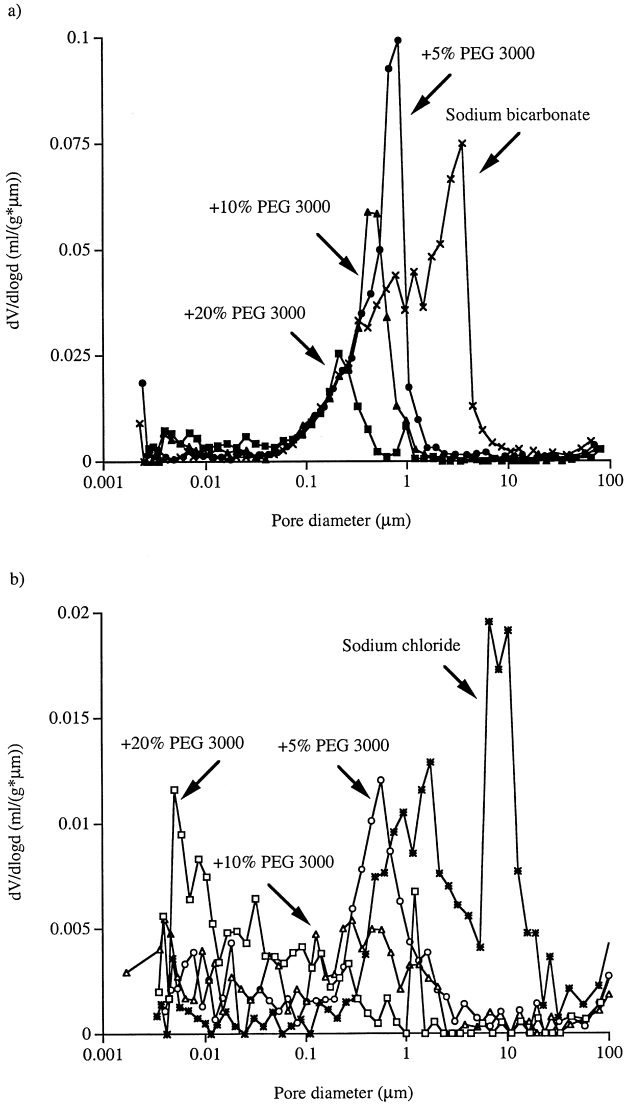

Fig. 4. Pore size distribution of tablets made of pure compounds and mixtures containing different amounts of PEG 3000. (a) Sodium bicarbonate (×) and mixtures containing 5% (●), 10% (▲) and 20% (■). (b) Sodium chloride (*) and mixtures containing 5% (○), 10% (△) and 20% (□).

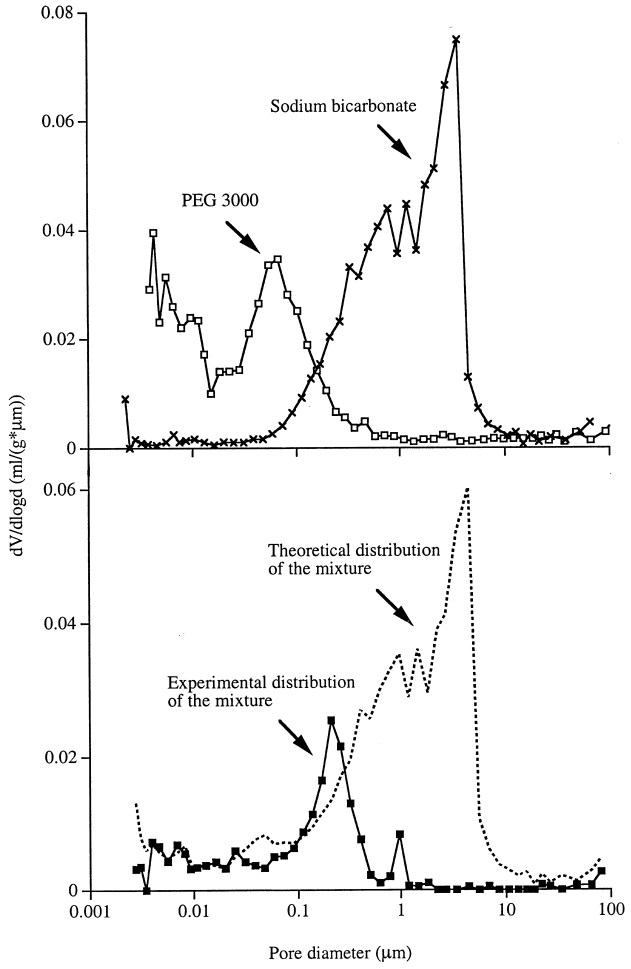

Fig. 5. Upper graph: pore size distribution of tablets made of pure sodium bicarbonate (×), pure PEG 3000 (□). Lower graph: pore size distribution of tablets made of a mixture of sodium bicarbonate and 20% PEG 3000; experimental distribution (■) and theoretical distribution derived from the additive effect of the pure materials based on the composition of the mixture (----).

these binders on pore structure. The strongest sodium chloride tablets, especially when tested in the radial direction, were obtained with a smaller amount of PEG 3000 than was required with sodium bicarbonate (Fig. 6). This is probably because of the lower absolute porosity of pure sodium chloride tablets in combination with a reduced ability to bond with solid bridges when the amount of binder is increased above a certain threshold [7].

The strength of tablets of PGS plus sodium chloride was less than that of pure sodium chloride tablets (Fig. 6). PGS, with its pronounced elastic behaviour, probably caused rupture of interparticulate bonds as well as interfering with the formation of solid bridges [21]. The differences in pore structure between tablets of pure sodium bicarbonate and pure sodium chloride also influenced the effect of a binder. As reported earlier, the deformability of a binder is more important for the increase in tablet strength when the pore size is small, as exemplified by sodium chloride [7].

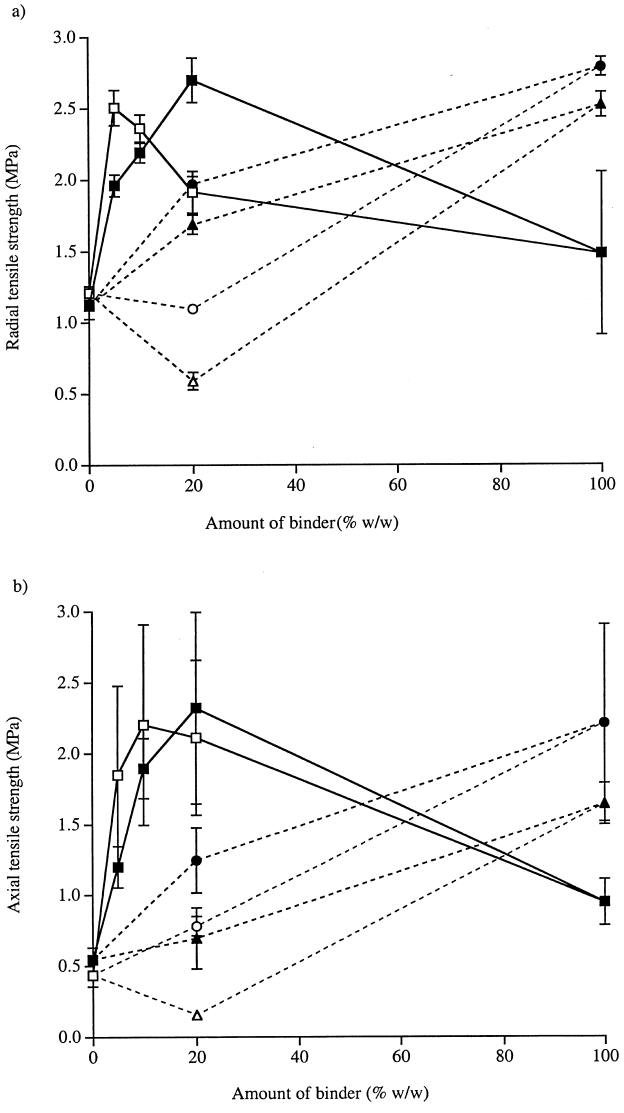

Fig. 6. (a) Radial and (b) axial tensile strengths as a function of amount of binder added. Sodium bicarbonate and mixtures containing PEG 3000 (■), PEG 20000 (●) and PGS (▲), sodium chloride and mixtures containing PEG 3000 (□), PEG 20000 (○) and PGS (△). Dotted lines are used to indicate the uncertainty of obtaining a complete profile based on only three data points.

Although there was no distinct relationship between either average pore diameter by volume or average pore diameter by length and tablet strength (Fig. 7), there was a general tendency that a decrease in pore diameter resulted in an increase in tablet strength [5]. The results were also slightly more scattered when using pore diameter by length, indicating a better agreement between pore diameter by volume and tablet strength. Further, this definition of average pore diameter places more emphasis on the presence of larger pores in a tablet. A decrease in the probability of finding these large pores favours a high tablet strength [5,22]. A clearer relationship with pore diameter was obtained with axial tensile strength than with radial tensile strength. This was expected, considering that the axial strength, as measured by direct tensile testing, will reflect the properties of the weakest plane in the axial direction. The presence of larger pores would then probably serve as starting points for the fracture [23,24].

3.4. Assessment of dominating bond types in tablets

An attempt was made to evaluate the applicability of mercury porosimetry in the characterisation of dominating bond types in tablets. The aim was to confirm the above-mentioned ability of a binder to prevent the formation of solid bridges. Various approaches have been utilised in the estimation of the dominating bonding mechanisms in tablets, e.g. compaction in liquids with differing dielectric constants [25–27] and the degree of change in tablet strength upon addition and removal of magnesium stearate [28]. Two recent approaches have involved adjustment of tablet strength to account for various tablet-related properties.

The first assumption was that adjusting tablet strength for specific tablet surface area could reflect the dominating bond types [28]. This approach was further developed by Adolfsson et al. [29], who proposed that the distance between particles would also influence the tablet strength. Consequently, the tablet strength (σ_T) was adjusted according to both tablet surface area (S_v) and interparticulate distance (r) (both parameters were obtained with air permeametry). In Eqs. (2) and (3), the adjusted tablet strength is symbolised as σ_A:

$$\sigma_A = \frac{\sigma_T}{S_v} r \tag{2}$$

Secondly, tablet strength (σ_T) was adjusted for a structural factor, which consists of the solid fraction of the tablet (1 minus the tablet porosity (ε)) and tablet surface area (S_v) (obtained with air permeametry) (Eq. (3)) [30]:

$$\sigma_A \propto \frac{\sigma_T}{(1-\varepsilon)S_v} \tag{3}$$

Since this equation is expressed as a proportionality, σ_A

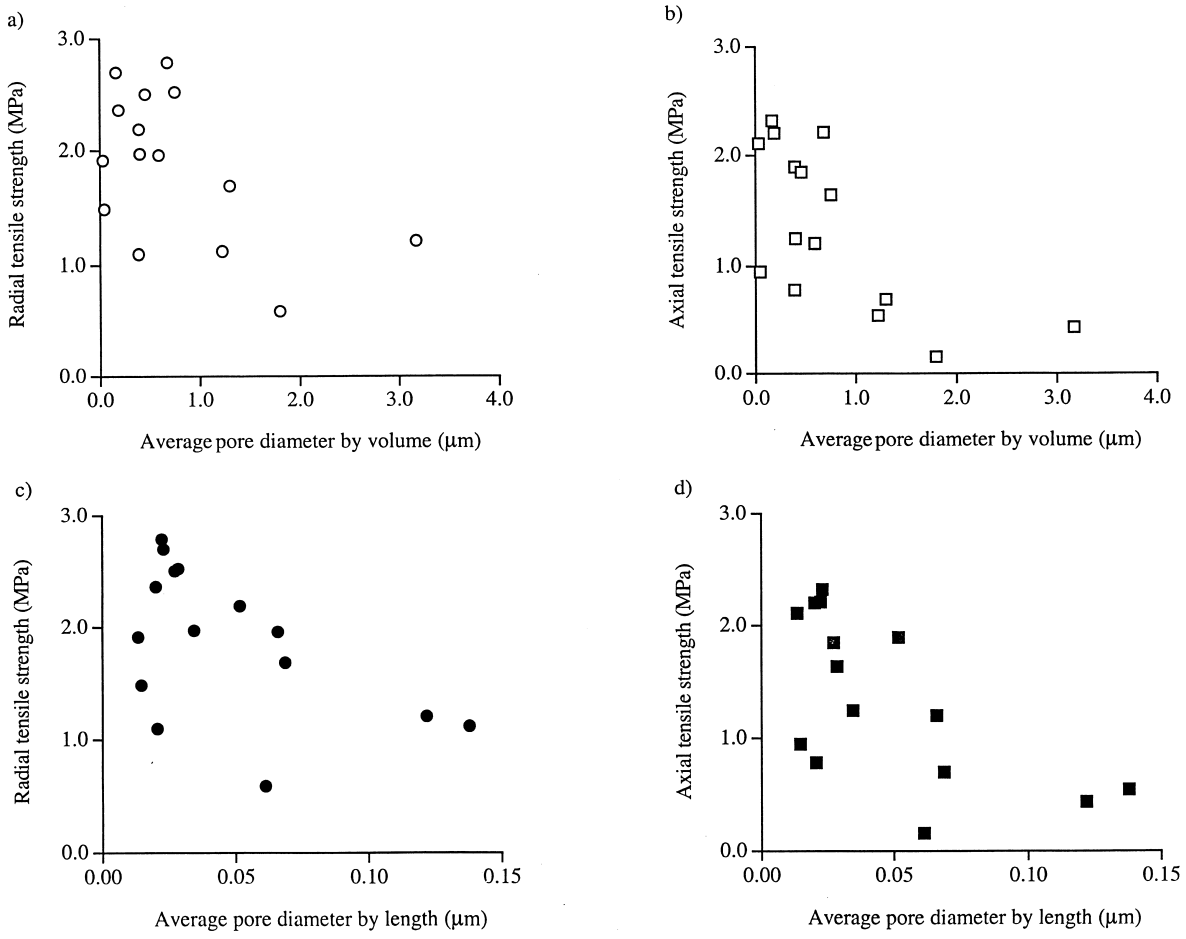

Fig. 7. (a) Radial (○) and (b) axial (□) tensile strengths as a function of average pore diameter by volume of the tablets studied. (c) Radial (●) and (d) axial (■) tensile strengths as a function of average pore diameter by length of the tablets studied.

should be regarded as a qualitative description of the dominating bond types [30]. A complete derivation of the equation and the obtained unit for σ_A is described by Olsson and Nyström [30].

Although both approaches have limitations, both were generally able to differentiate between the dominating bond types (distance forces and solid bridges) in pharmaceutical tablets, in previous studies [29,30]. Neither was able to fully account for the effects of particle size and compaction pressure but their applicability to interactions in tablets composed of mixtures was still considered worth investigating.

The previous use of air permeametry to obtain a surface value could not be applied on the dense compacts obtained here, as exemplified with tablets of the pure PEGs and their mixtures [12]. Thus, in this study, data obtained from mercury porosimetry were used instead of permeametric data. Mercury porosimetry and air permeametry of non-porous materials are, in principle, two alternative techniques for estimating the same type of surface area. The tablet surface area obtained with permeametry (S_v), as used in Eqs. (2) and (3), was thus substituted by the pore surface area obtained with mercury porosimetry (S_{vpore}). The pore radius in Eq. (2) was also obtained with mercury porosimetry and expressed either as average pore radius by length (r_l) or by volume (r_v). The radial tensile strength of the tablets was used in both equations. The consideration of the solid fraction of the tablets, based on either porosity from helium pycnometry or mercury porosimetry in Eq. (3), did not affect the adjusted tablet strength to any significant extent. This is probably because the solid fraction has less effect on adjusted tablet strength than the pore surface area. In this study, the solid fraction in Eq. (3) was obtained using the porosity estimated from helium pycnometry, since this method probably provides the most accurate value, as discussed above.

Addition of a binder affected the total pore surface area, the average pore radius and the solid fraction (Fig. 8a–d). As mentioned previously, the average pore radius estimated by length was considerably smaller than the average pore radius estimated by volume (Fig. 8b,c). The effect of increasing amounts of PEG 3000 on the solid fraction (i.e. porosity) was much smaller with sodium chloride than with sodium bicarbonate (Fig. 8d). This is probably because of the denser sodium chloride tablets, as discussed above.

Overall, both approaches to estimating the dominating bond type by calculating adjusted tablet strength values

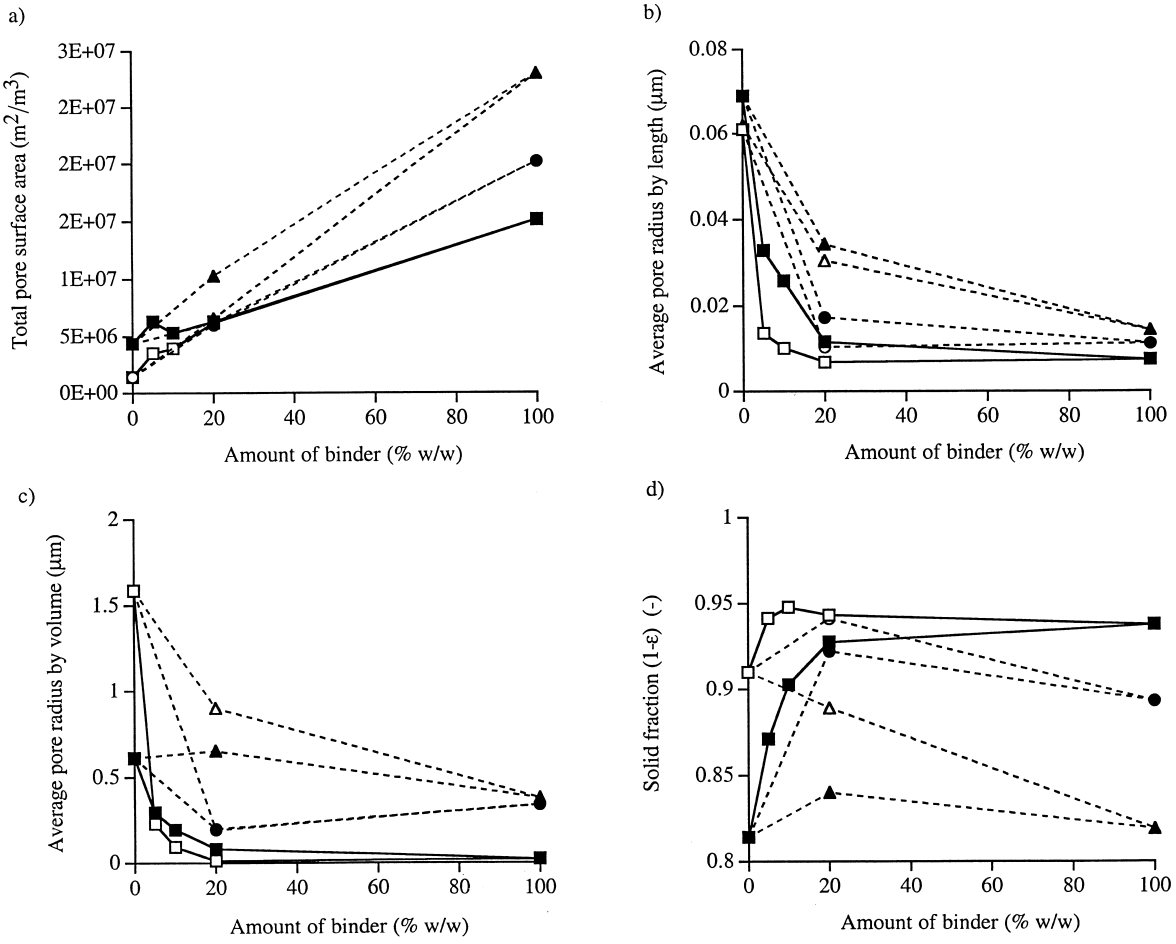

Fig. 8. (a) Total pore surface area, (b) average pore radius by length, (c) average pore radius by volume and (d) solid fraction as a function of amount of binder. Symbols as in Fig. 6.

gave similar results (Fig. 9). The results were also in agreement with those previously obtained for sodium bicarbonate and sodium chloride, in the sense that a material expected to bond with solid bridges (sodium chloride) had a higher value for adjusted tablet strength [28–30]. Accordingly, the bonds in tablets made of the binders were essentially weak distance attraction forces. Sodium bicarbonate had an intermediate value, which suggests mainly distance forces. However, the contribution of solid bridges in tablets of coarse particulate sodium bicarbonate cannot be excluded [29]. The relative importance of different bonding mechanisms was also in agreement with results obtained from other studies investigating dominating bonding mechanisms [26,27].

Addition of a binder to sodium chloride resulted in a decrease in the adjusted tablet strength, indicating a decreased ability to bond with solid bridges, probably because the binder prevented the formation of such bonds (Fig. 9) [7,31]. This effect was also observed when increasing the amount of PEG 3000 in the mixtures containing sodium chloride (Fig. 9). The adjusted tablet strength was not affected as much when a binder was added to sodium bicarbonate, probably because of the smaller probability of the existence of solid bridges (Fig. 9). The decrease in adjusted tablet strength did not directly reflect the measured tablet strength (Figs. 6a and 9). Therefore, it is reasonable to assume that although there is a decreased probability of solid bridges, addition of a binder increases bonding with distance attraction forces, thus resulting in an overall increase in tablet strength.

When comparing the results obtained with Eqs. (2) and (3), both approaches appear to be able to describe the prevention by binder of the formation of solid bridges (Fig. 9). Eq. (3) appeared to better differentiate between different binders, i.e. the decreased ability of forming solid bridges was related to the elastic behaviour of the binder and consequently the lowest adjusted tablet strength was obtained with PGS. However, Eq. (2) described the change in bond type (decrease in adjusted tablet strength) when PEG was added to sodium bicarbonate more accurately. Neither expression appears to be able to completely describe the effect of a binder on the bond types in tablets. Data obtained with mercury porosimetry appear to be valuable in assessing the dominating bond types in tablets, although it is realised that the concept needs further refinement. However, in this study, the objective was primarily to qualitatively assess the effect of a binder on the interactions in a tablet.

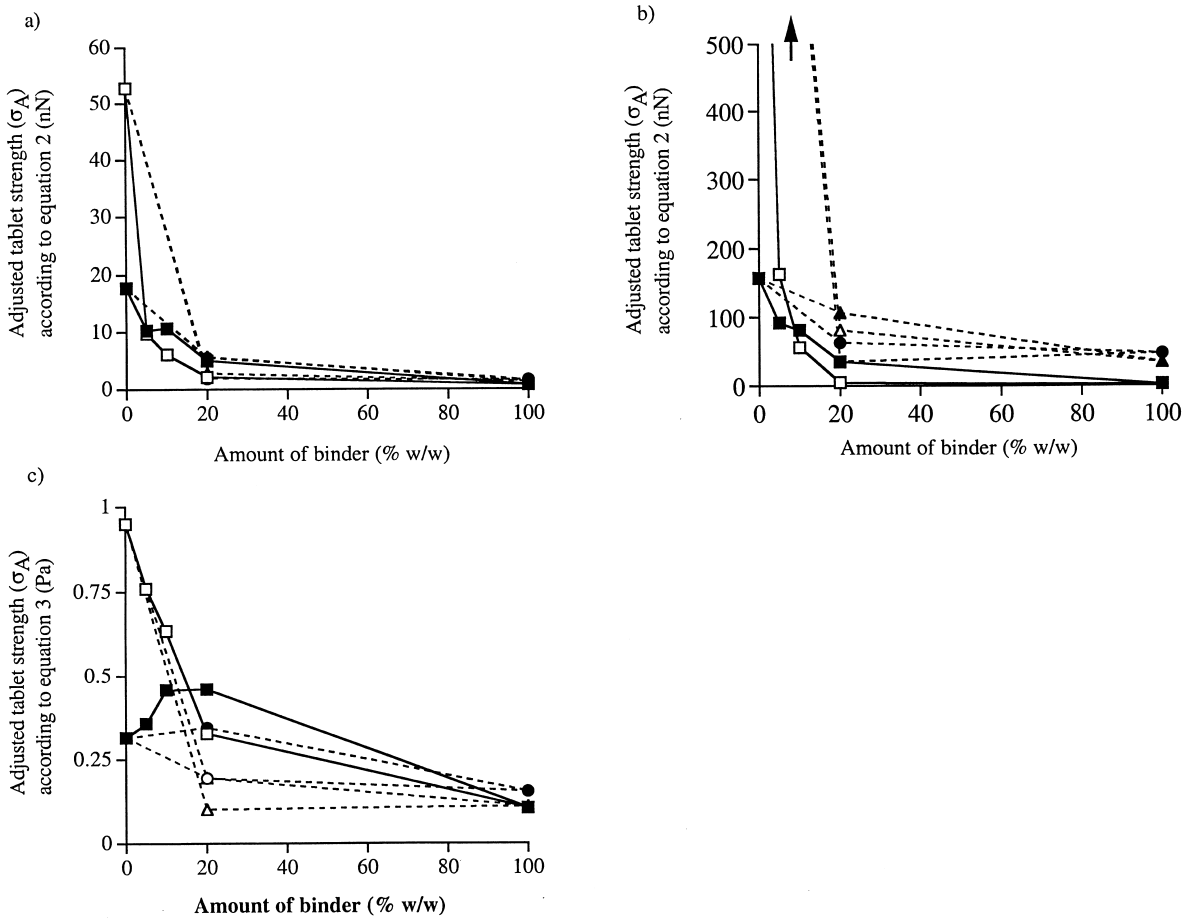

Fig. 9. (a) Adjusted tablet strength according to Eq. (2) (based on average pore radius by length), (b) adjusted tablet strength according to Eq. (2) (based on average pore radius by volume) and (c) adjusted tablet strength according to Eq. (3) as a function of amount of binder. Symbols as in Fig. 6. The arrow in (b) indicates a higher adjusted tablet strength for sodium chloride (= 1370 nN).

An attempt was also made to compare the use of average pore radius by volume and average pore radius by length in Eq. (2) (Fig. 9a,b). However, the results obtained with average values by volume did not agree as well with those expected regarding dominating bonding mechanisms, in the sense that there were quite large differences in adjusted tablet strength between sodium chloride and sodium bicarbonate [29,30] and also between the binders, which were expected to bond with similar bond types. It may therefore be speculated that the average pore radius by length is a better estimate of the distances between particles that are of importance for bonding and consequently more suitable for use when assessing bond types in tablets. The average pore radius by length is relatively dependent on the presence of smaller pores and these pores appear to be more relevant for bonding distances. When using average pore radius by volume, greater consideration is given to large pores in the tablets. These may be of importance for the tablet strength but are not as good a reflection of the interparticulate distances when assessing bond types.

The adjusted values obtained in this study were higher than corresponding values obtained earlier [29,30]. It is likely that this is because the surface area obtained with mercury porosimetry is greater than that obtained with permeametry since, for example, cracks in the particles may be included with the former method. It has previously been suggested that the permeametric technique is preferable since this type of external surface area is expected to provide a closer approximation of the bonding surface area [12]. Also, it is possible that porosimetry measurements include intraparticulate pores, which do not contribute to the tablet strength. However, this latter drawback is of minor importance here, since the materials used in this study are essentially without intraparticulate pores.

4. Conclusions

- The materials used in this study may be considered as mainly non-porous, i.e. intraparticulate pores have a limited contribution to the tablet porosity.
- Addition of a binder caused a decrease in tablet porosity and a shift in the pore size distribution towards smaller pores, thus resulting in a decrease in the average pore diameter. The binder generally caused a narrowing of the pore size distribution compared to that of a pure

compound. The effect on the pore size distribution was dependent on the deformability and amount of the binder.

- The binders were deformed and sheared to such an extent during compaction that the binder phase mainly existed as smaller aggregates or even primary particles when located between the compound particles. Consequently, the pores in tablets of pure binder appear not to exist to the same degree in tablets of the mixtures and are thus assumed not to substantially contribute to the pore structure. The pores in a tablet composed of a mixture are thus believed to be located mainly between the compound particles and the binder phase and to a smaller extent within the binder phase.
- Data obtained with mercury porosimetry reflected interparticulate distances and it was possible to qualitatively assess the dominating bond types in tablets. By using adjusted values of tablet strength, it was possible to investigate the effect of different binders on the bonding properties in tablets. The results indicated that addition of a binder caused a decrease in the probability of forming solid bridges, especially during the compaction of sodium chloride. The results showed good agreement with previous methods for estimating the dominating bonding mechanisms in tablets.

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