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RESEARCH PAPER

Evaluation of Critical Binder Properties Affecting the Compactibility of Binary Mixtures

Sofia Mattsson and Christer Nyström*

Department of Pharmacy, Uppsala University, Box 580, SE-751 23 Uppsala, Sweden

ABSTRACT

The aim of this study was to identify essential physical and mechanical properties of various binders and to investigate their influence on the tensile strength and porosity of tablets made from binary mixtures with sodium bicarbonate. The binders were characterized according to axial and radial tensile strength after compression into tablets, yield pressure and minimum porosity during compression, and elastic recovery after compression. The addition of a binder generally resulted in an increase in the tensile strength and a decrease in the porosity of the sodium bicarbonate tablets. The location of the binder in the voids between the sodium bicarbonate particles thus decreasing the porosity of the tablet seemed to be an important consideration. Consequently, the addition of binders with a low yield pressure value and a relatively small elastic recovery value (e.g., polyethylene glycol 3000 and polyvinylpyrrolidone) resulted in tablets of low porosity and high tensile strength, especially in the axial direction. The tensile strength of the pure binder also seemed to be important, especially for binders with a lower degree of deformability (e.g., microcrystalline cellulose and pregelatinised starch). The results also indicated the value of using both axial and radial tensile strength measurements in assessing the effect of a dry binder and showed that the importance of different binder properties varied according to the direction of the tablet strength measurements. The results demonstrated that the applied characteristics of the binders used in this study may serve as a useful tool in evaluating the effectiveness of binders.

* To whom correspondence should be addressed.

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KEY WORDS: Compaction; Tablet; Binder; Tablet strength; Porosity; Deformability.

INTRODUCTION

Recent studies at our department have focused on the role of dry binders in a binary mixture and the influence of the various properties associated with these binders. The mechanisms responsible for the increase in tablet strength associated with the addition of a binder to a compound have also been investigated (1,2).

A qualitative model of the formation of fractures in a tablet during strength testing has been proposed (1,2). This model is based on the assumption that if a tablet is considered as a large aggregate of particles in which the interparticulate bonds are weaker than the intraparticulate bonds (3), e.g., pure sodium bicarbonate tablets, the fracture occurring during strength testing is more likely to take place around, rather than through, the particles, i.e., the tablet will fracture to a large extent through the air phase (4–6). Results of previous studies offer support for this fracture propagation process (1,2).

When using a compound that forms a relatively porous tablet structure, such as sodium bicarbonate, both the deformability of the binder (i.e., its ability to enter the voids between the sodium bicarbonate particles thereby decreasing the porosity of the tablet) and its intrinsic tensile strength (i.e., the tensile strength of a tablet of a pure binder) appear to be important considerations in determining the properties of tablets composed of a binary mixture (2). The previous study was, however, limited to a small number of binders and then especially to highly deformable binders. This study therefore encompassed a series of binders with a wider range of material properties to investigate the importance of the different binder properties in a more systematic way. Also, in the previous study by Mattsson and Nyström (2) only the axial tensile strength of the tablets was measured. In this study strength measurements in the radial direction are also included to investigate whether different binder properties are of varying importance depending on the direction of the strength measurements.

The aim of this study was thus to further evaluate the material properties of a series of dry binders to establish which properties are important for the compactibility of pharmaceutical powders. The pure binders were characterized according to axial and radial tensile strength after compression into tablets, yield pressure and minimum porosity during compression, and elastic recovery after compression. To evaluate the strength-enhancing effect, binary mixtures of sodium bicarbonate and binder were compacted and characterized regarding axial and radial tensile strength and porosity.

MATERIALS AND METHODS

Sodium bicarbonate (crystalline, puriss, Kebo Lab., Sweden) was used as a model substance. The size fraction, 45 to 63 μm, was obtained by dry sieving (Retsch, Germany). The binder materials used were polyethylene glycol (PEG) 3000 (Kebo Lab., Sweden), microcrystalline cellulose (MCC; Avicel PH 105, FMC, USA), silicified microcrystalline cellulose (SMCC; Prosolv SMCC 90, Mendell, UK), pregelatinised starch (PGS; Sepistab ST 200, Seppic, France), and polyvinylpyrrolidone (PVP; Kollidon 25, BASF, Germany). Finely particulate fractions of the binders were obtained using an air classifier (100 MZR, Alpine, Augsburg, Germany) adjusted to produce a size fraction <20 μm, except for MCC, which was used as supplied. PEG 3000 was milled in a pin disk mill (63C, Alpine, Augsburg, Germany) before air classification.

Apparent Particle Density

The apparent particle densities of the materials and binary mixtures were determined ($n = 3$) using a helium pycnometer (AccuPyc 1330 Pycnometer, Micromeritics, USA) (Table 1).

External Surface Area of the Materials

The external surface area of sodium bicarbonate was determined using Friedrich permeametry ($n = 3$) (7) (Table 1). Blaine permeametry was used to determine the external surface area of the binder materials ($n = 3$) (Table 1) (8).

Addition of Binder to Sodium Bicarbonate

Sodium bicarbonate was mixed with the different binders to produce binary mixtures. Three different amounts of binder were chosen to reflect (1) the amount corresponding to a surface area ratio of unity (9), calculated as described previously by Olsson et al. (1) (Table 2); (2) the amount theoretically required to fill the voids between

Table 1.

Characteristics of the Materials

Material	Particle Size (μm)	Density (g/cm^3)[a]	External Surface Area (cm^2/g)
Sodium bicarbonate	45-63[b]	2.212 (0.001)	631 (4)[e]
MCC	Raw material	1.569 (0.003)	9449 (235)[d]
SMCC	<20[c]	1.572 (0.001)	6974 (87)[d]
PEG 3000	<20[f]	1.240 (0.002)	15975 (1501)[d]
PVP	<20[c]	1.240 (0.003)	7789 (122)[d]
PGS	<20[c]	1.489 (0.002)	4007 (43)[d]

[a]Measured with a helium pycnometer (AccuPyc 1330 Pycnometer, Micromeritics).
[b]Obtained by dry sieving (Retsch, Augsburg, Germany).
[c]Obtained by using an air classifier (100 MZR, Alpine, Augsburg, Germany).
[d]Determined with Blaine permeametry (8).
[e]Determined with Friedrich permeametry (7).
[f]Obtained by using a pin disk mill (63C, Alpine, Augsburg, Germany) and an air classifier (100 MZR, Alpine, Augsburg, Germany).
MCC indicates microcrystalline cellulose; PEG, polyethylene glycol; PVP, polyvinylpyrrolidone; SMCC, silicified MCC; PGS, pregelatinised starch.
The results are the mean value with the corresponding SD in parentheses.

the sodium bicarbonate particles, based on the porosity and dimensions of a pure sodium bicarbonate tablet and the density of the pure binder (2) (Table 2); and (3) a constant amount of binder (21.5% w/w). In all cases, sodium bicarbonate was mixed with the binder material in a Turbula mixer (W.A. Bachhofen, Switzerland) at 120 rpm for 100 min.

Compaction of Tablets

All powders were stored at 40% relative humidity for at least 48 hr before compaction. Tablets were compacted in an instrumented single-punch press (Korsch, EK0, Germany) at 200 MPa (maximum upper punch pressure) using 1.13-cm flat-faced punches. The upper punch pressure was obtained by keeping the distance between the punch faces constant (3 mm at zero pressure) and varying the amount of powder in the die. The powder was weighed on an analytical balance and manually filled into the die. The surfaces of the die and punches were lubricated with magnesium stearate between each compaction. Tablets were compacted of the pure sodium bicarbonate, the pure binders, and the binary mixtures.

Characterization of Tablets

Tensile Strength

All tablets were stored at 40% relative humidity for at least 48 hr before strength testing. The axial tensile strength was determined using a material tester (M39K,

Table 2.

Amounts of Binder Required to Be Added to Sodium Bicarbonate to Achieve a Surface Area Ratio of Unity or to Theoretically Fill the Interparticulate Voids

	Amount of Binder (%)	
Added Binder	Surface Area Ratio = 1	Theoretical Filling of the Voids
MCC	21.5	13.5
SMCC	26.6	13.8
PEG 3000	13.6	11.2
PVP	24.5	11.2
PGS	38.6	13.2

MCC indicates microcrystalline cellulose; PEG, polyethylene glycol; PVP, polyvinylpyrrolidone; SMCC, silicified MCC; PGS, pregelatinized starch.

Lloyd Instruments, UK) and calculated as described by Nyström et al. (10) ($n = 5$ to 10). Strength characterization by diametral compression test (Holland C50, UK or M39K, Lloyd Instruments, UK) was also performed, and the radial tensile strength was calculated according to Fell and Newton (11) ($n = 4$ to 5). The isotropy ratio, i.e., axial/radial tensile strength, was also calculated (10,12).

Porosity

The tablet porosity was calculated from the apparent particle density of the material or binary mixture and the dimensions and weight of the tablets.

Degree of Binder Saturation

The calculation of the amount required to theoretically fill the voids described above is obviously a simplified approach, and it does not take into account the effect the binder has on the compound particles regarding e.g. packing structure and fragmentation propensity. To estimate the actual void fraction in a tablet that is filled with binder, degree of binder saturation (DBS) was calculated:

$$\mathrm{DBS}(\%) = \frac{V_b}{V_b + V_v} 100 \qquad (1)$$
$$V_t = V_c + V_b + V_v$$

V_t is the total volume of a tablet containing sodium bicarbonate and a binder calculated from the dimensions of the tablet, V_c and V_b are the volume of sodium bicarbonate and binder, respectively, and V_v is the volume of void (air) in a tablet. When calculating V_c and V_b, the apparent particle density (obtained from helium pycnometry) of sodium bicarbonate and binder was used. Calculations were also made by using apparent tablet density (calculated from the weight and volume of a pure binder tablet), instead of apparent particle density, of the binder. The drawback with using the apparent particle density (i.e., the maximum density) for the binder fraction is that such a dense state is probably not reached within the assemblies of binder particles incorporated in the sodium bicarbonate tablet. This is supported by data for the pure binder tablets [Fig. 1(a)]. The drawback when using the established apparent tablet density for the binder is that this value reflects the structure and porosity of a pure binder tablet, i.e., a large specimen in comparison with the more limited size of aggregates of binder particles in tablets of binary mixtures. When using the lower density value, there is a risk that DBS is overestimated, especially in the case where the added binder to a significant extent consists of discrete primary particles. Therefore, apparent particle density of the binder is used when calculating DBS.

Characterization of Deformability of the Binders

Apparent Yield Pressure and Minimum Porosity

The deformability of the binders was determined by recording the upper punch pressure and the height of the tablets every millisecond during the compression and decompression cycles (in-die measurements) (Table 3). Tablets were compressed at a maximum load of 150 MPa. Tablet porosity was calculated from the heights of the tablets and was used in the Heckel equation ($n = 3$). The yield pressure of the materials was calculated from the reciprocal of the slope of the linear part of the Heckel plot (13). The yield pressure calculated by this method has been defined as an apparent yield pressure and is considered to reflect the total deformation of the material, i.e., including both plastic and elastic deformation (13–15). The minimum porosity during compaction of the materials was also obtained.

Elastic Recovery

Because a densification of the solid structure was obtained in some cases, resulting in an apparently negative minimum porosity (6), the axial elastic recovery was calculated from changes in tablet height rather than in porosity. The axial elastic recovery was therefore calculated as the relative difference between minimum (during compression) and maximum (after 48-hr storage) tablet heights (16).

RESULTS AND DISCUSSION

Characteristics of the Binders

The deformability of the binders was characterized by their apparent yield pressure and minimum porosity during compression and elastic recovery after compression. The axial and radial tensile strengths of tablets made from pure binder, here denoted the *intrinsic* axial and radial tensile strength, were also used as characteristics of the binder's strength-enhancing ability (see Table 3).

According to the results, the binders may be divided into three groups depending on their characteristics as follows (Table 3):

1. Binders with high intrinsic axial and radial tensile strengths and a moderate degree of deformability (relatively high apparent yield pressure and intermediate elastic recovery): MCC and SMCC.

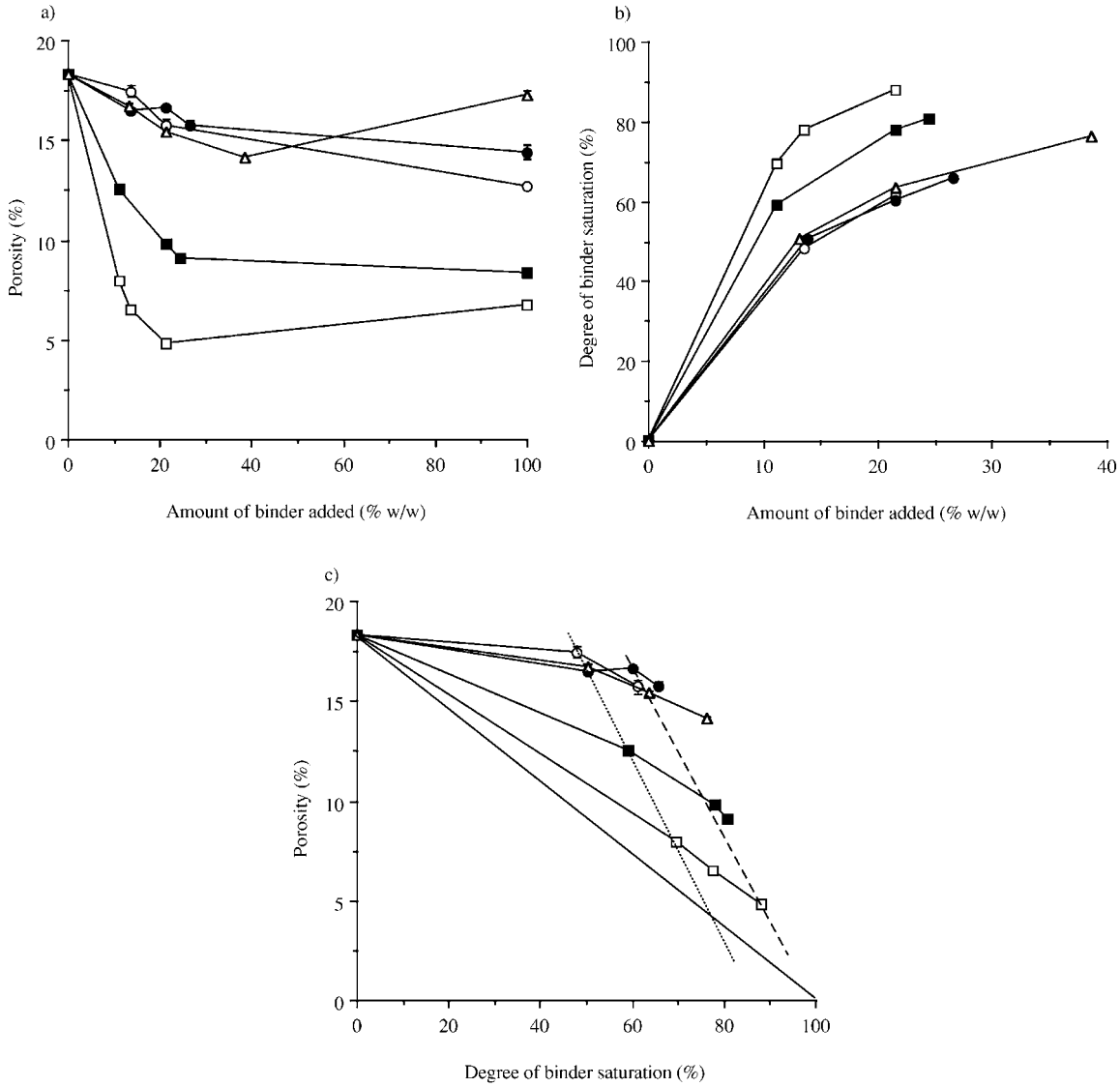

Figure 1. (a) Porosity of tablets, (b) degree of binder saturation as a function of amount of binder added to sodium bicarbonate, and (c) porosity of tablets as a function of degree of binder saturation. PEG 3000 (□), PVP (■), MCC (○), SMCC (●), PGS (△). Confidence intervals for $p = 0.05$ are shown (a,c). In (c) trend lines indicate the amount added of the different binders corresponding to both the assumed amount required to fill the void (dotted line) and 21.5% w/w binder (broken line). The solid line shows the theoretical behavior of addition of a liquid.

2. Binders with low intrinsic axial and radial tensile strengths and a high degree of deformability (relatively low apparent yield pressure and low to intermediate elastic recovery): PEG 3000 and PVP. PEG 3000, with a lower apparent yield pressure, may be considered to be more deformable. Because the elastic behavior of PEG 3000 is limited, the low apparent yield pressure probably reflects a high degree of plastic (permanent) deformation during compaction (1,2).
3. Binders with low intrinsic axial and radial tensile strengths and a moderate degree of deformability (relatively high apparent yield pressure and elastic recovery): PGS.

From Table 3 and Figure 7(b), it can be seen that the intrinsic radial tensile strength of PEG 3000, PVP, and PGS was similar and much lower than the intrinsic radial tensile strength of MCC and SMCC. Regarding the intrinsic axial tensile strength, such a

Table 3.

Characterization of Deformability and Intrinsic Tensile Strength of the Binders

Binder	Apparent Yield Pressure (MPa)[b]	Minimum Porosity During Compression (%)	Elastic Recovery[a] (%)	Axial Tensile Strength (MPa)	Radial Tensile Strength (MPa)
MCC	79.6 (2.2)	6.47 (0.14)	10.6 (0.17)	3.10 (0.37)	14.6 (0.35)
SMCC	80.9 (0.5)	7.33 (0.05)	12.0 (0.10)	3.30 (0.40)	12.9 (0.38)
PEG 3000	29.9 (1.1)	−0.44 (0.06)[c]	5.66 (0.62)	1.39 (0.86)	1.52 (0.10)
PVP	46.9 (0.6)	0.33 (0.06)	10.6 (0.26)	2.33 (0.47)	2.54 (0.51)
PGS	75.7 (0.2)	4.14 (0.10)	19.1 (0.35)	1.41 (0.35)	2.37 (0.06)

[a]Defined as the relative difference between minimum and maximum tablet height (16).
[b]Obtained from the reciprocal of the slope of the linear part of an in-die Heckel plot, thus including both plastic and elastic deformation (13).
[c]Apparent negative minimum porosity, reflecting a densification of the particulate solid structure (6).
MCC indicates microcrystalline cellulose; PEG, polyethylene glycol; PVP, polyvinylpyrrolidone; SMCC, silicified MCC; PGS, pregelatinized starch.
Results are the mean value with the corresponding SD in parentheses.

difference could not be clearly distinguished [Table 3; Fig. 7(a)].

Tablets made from PEG 3000 or PVP were less porous than those made from MCC, SMCC, or PGS [Fig. 1(a) at 100% w/w added binder]. This was expected, considering the greater deformability (ductility) of PEG 3000 and PVP, as indicated by the lower apparent yield pressure values and the lower minimum porosities during compression (Table 3). The high porosity of tablets made from PGS was probably attributable to the high elastic recovery of this binder.

Effect of Addition of a Binder to Sodium Bicarbonate

The addition of any of the binders to sodium bicarbonate resulted in an increase in the tensile strength and a decrease in the porosity of the resultant tablets compared with pure sodium bicarbonate tablets [Figs. 1(a), 2, 3]. However, the effect (the magnitude of the increase in tensile strength and decrease in porosity) of the various binders differed substantially.

Effect on Tablet Porosity

The addition of a binder to sodium bicarbonate resulted in a decrease in tablet porosity [Fig. 1(a)]. This was because the binder partly filled the voids between the sodium bicarbonate particles (1,2). The decrease in porosity was highly pronounced with PEG 3000 and PVP, whereas with MCC, SMCC, and PGS, there was only a slight decrease in porosity.

Effect on Degree of Binder Saturation

Another way of expressing the effect the binder hason tablet porosity, i.e., the ability of the binder to fill the interparticulate voids in a sodium bicarbonate tablet, is to calculate the DBS. DBS is analogous to degree of liquid saturation used in wet agglomeration (17,18), but the difference is that solid materials, not liquids, are used in the former case. When adding a solid material, there is an effect on the pore structure of sodium bicarbonate tablets, i.e., the sodium bicarbonate particles are moved farther apart from each other. In other words, the addition of a binder increases the void that can be filled with binder compared with the void of a pure sodium bicarbonate tablet. As the amount of binder increased, DBS also increased [Fig. 1(b)], and this was reflected in a decrease in tablet porosity [Fig. 1(c)]. The addition of the more deformable binders (PEG and PVP) resulted in a higher DBS, i.e., an increased ability to fill the interparticulate voids in a sodium bicarbonate tablet during compression and lower tablet porosity compared with the corresponding amounts of the other binders [indicated by the trend lines in Fig. 1(c)]. The slope of the porosity-DBS plot would thus be an indication of the deformability of the binder. The assumed behavior of a binder with ideal plastic behavior, i.e., with deformation properties identical to afluid, is also indicated in Figure 1(c). The more deformable binders appear to have a smaller effect on the pore structure of sodium bicarbonate [calculated by using

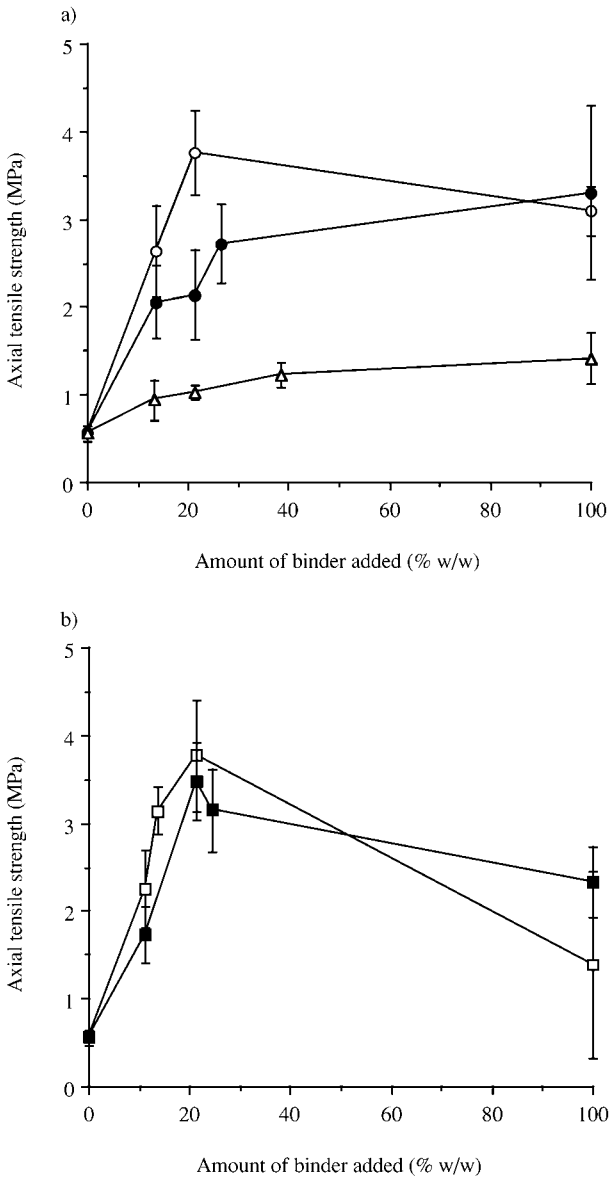

Figure 2. Axial tensile strength of tablets as a function of the amount of binder added to sodium bicarbonate. (a) MCC (○), SMCC (●), PGS (△) and (b) PEG 3000 (□), PVP (■). Confidence intervals for $p = 0.05$ are shown.

V_t and V_c from Eq. (1)]. Because of the fairly close relationship between DBS and porosity, only the latter is discussed and shown in the following figures.

Effect on Tablet Strength

The overall increase in tablet strength on addition of a binder to sodium bicarbonate (Figs. 2, 3) may be explained using the qualitative tablet model proposed by Olsson et al. (1) and evaluated further by Mattsson and Nyström (2). In these studies it was concluded that the fracture during strength testing, both in tablets made of pure materials and those made of mixtures, mainly occurred around the particles. When a binder is present between the sodium bicarbonate particles, the fracture would have to occur through the binder phase, in addition to an air phase, to avoid breaking the sodium bicarbonate particles, and there is thus an increase in tensile strength of the tablet. The tensile strength of a tablet made from a mixture would then be reflected by the properties of the binder present in the voids between the sodium bicarbonate particles. A pronounced void-filling capacity is thus beneficial to a decrease in tablet porosity and an increase in tablet strength. For a more detailed description of the tablet model, refer to Mattsson and Nyström (2).

When PEG or PVP were added to sodium bicarbonate, tablets made from the mixture had a significantly higher tensile strength, especially in the axial direction, than tablets made from the individual materials [Figs. 2(b), 3]. This has been reported earlier for mixtures of dicalcium phosphate and PEG 10000 (19,20) and sodium bicarbonate and PEG of differing molecular weights (1,2) and has been explained in detail elsewhere (1,2).

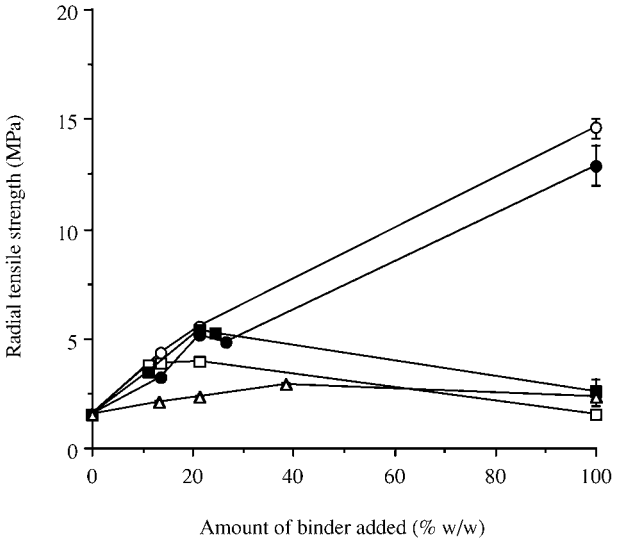

Figure 3. Radial tensile strength of tablets as a function of the amount of binder added to sodium bicarbonate. PEG 3000 (□), PVP (■), MCC (○), SMCC (●), PGS (△). Confidence intervals for $p = 0.05$ are shown.

Differences in Axial and Radial Tensile Strength

Measurements in the radial direction resulted in higher tablet strengths compared with measurements in the axial direction (Figs. 2, 3). This difference may have been the result of different modes of fracture associated with the different test procedures used. When measurements in the axial direction are used, the fracture will occur through the weakest plane in the tablet, whereas radial tensile strength measurements force the fracture through the predetermined diametral cross-section of the tablet and will thus give the mean tablet strength (12,21).

The relative increase in axial tensile strength was greater than the corresponding increase in radial tensile strength when a binder was added to sodium bicarbonate. Similar results have been obtained by Gren and Nyström (21). The influence of defects and flaws on tablet strength is probably more pronounced when the tensile strength is measured in the axial direction. Addition of a binder may reduce the incidence of these defects because the binder is distributed in the voids between the sodium bicarbonate particles. Consequently the effect of a binder would be more pronounced when measuring the axial tensile strength of the tablets.

Isotropy Ratio

Differences between axial and radial tensile strength measurements may also be expressed as the isotropy ratio, i.e., the ratio between axial and radial tensile strength. The isotropy ratio of a tablet is thought to reflect the distribution of bonds (22,23), which in turn is a function of the deformability and bonding properties of the powdered material (22). A high isotropy ratio corresponds to a more homogeneous distribution of bonds, which implies a lower probability of finding a pronounced weak bonding zone. Because of the different modes of fracture associated with axial and radial tensile strength measurements, the axial strength (reflecting the weakest bonding zone) could be assumed to be more susceptible to bond homogeneity than the radial strength (reflecting the average bond strength). Consequently, the isotropy ratio ought to increase more after the addition of binders with a high deformability than of binders with a high intrinsic strength.

The isotropy ratios of the mixtures differed according to the amount and type of binder (Fig. 4). Generally, there was an increase in isotropy ratio when a binder was added to sodium bicarbonate, indicating that the binders conferred some degree of bonding homogeneity to the tablet. Materials with a high degree of deformability (such as PEG 3000 and PVP), which result in tablets with low porosity, may favor the formation of a more homogeneous compact, i.e., a high isotropy ratio. Tablets containing sodium bicarbonate and PEG 3000 had high isotropy ratios probably because of the high degree of deformability of the binder. Mixtures with PGS, on the other hand, had low isotropy ratios, probably because of the high elastic recovery of the binder resulting in rupture of bonds during ejection of the tablet, which would affect particularly the axial tensile strength negatively. Consequently, a more heterogeneous compact was formed. Mixtures containing the other binders had isotropy ratios that were between these two extremes.

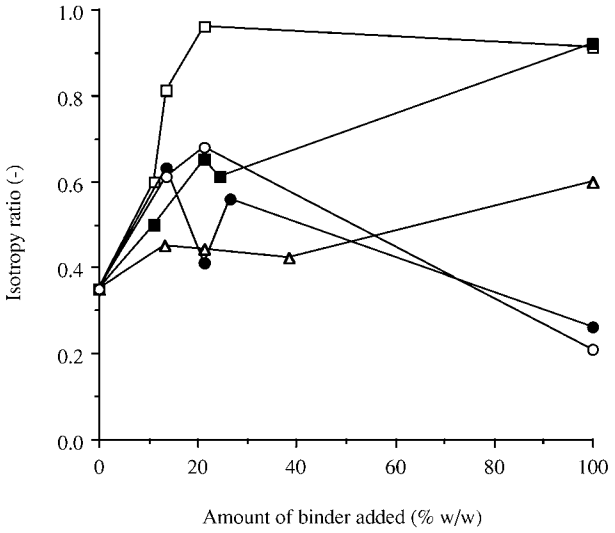

Figure 4. Isotropy ratio (axial/radial tensile strength) as a function of the amount of binder added to sodium bicarbonate. PEG 3000 (□), PVP (■), MCC (○), SMCC (●), PGS (△).

Evaluation of the Amount of Binder Resulting in Maximum Tablet Strength

The effects of the amount of binder added to the mixture were similar to those reported by Mattsson and Nyström (2) in the sense that increasing the amount of binder increased the tensile strength, decreased the porosity and, in addition, increased the degree of binder saturation of the corresponding tablets made from the mixtures [Figs. 1(a), (b), 2, and 3]. Because of the small differences between the two calculated amounts of binder required: 1) an amount corresponding to a surface area ratio of unity, and 2) an amount required to theoretically fill the voids in a tablet, it was difficult to draw any consistent

conclusions (2). However, even though there was a greater difference between the two calculated amounts of binder in this study, no obvious trends regarding the optimal amount of binder were observed. The amount required to theoretically fill the interparticulate voids in the sodium bicarbonate tablets was less than the amount corresponding to a surface area ratio of unity (Table 2). Because the former amount resulted in an underestimation of the amount required to achieve 100% DBS, it is expected that the optimal amount would be higher than this theoretical amount. Also, it is not possible to achieve zero porosity, i.e., 100% DBS, partly because the addition of a binder affects the pore structure of sodium bicarbonate tablets.

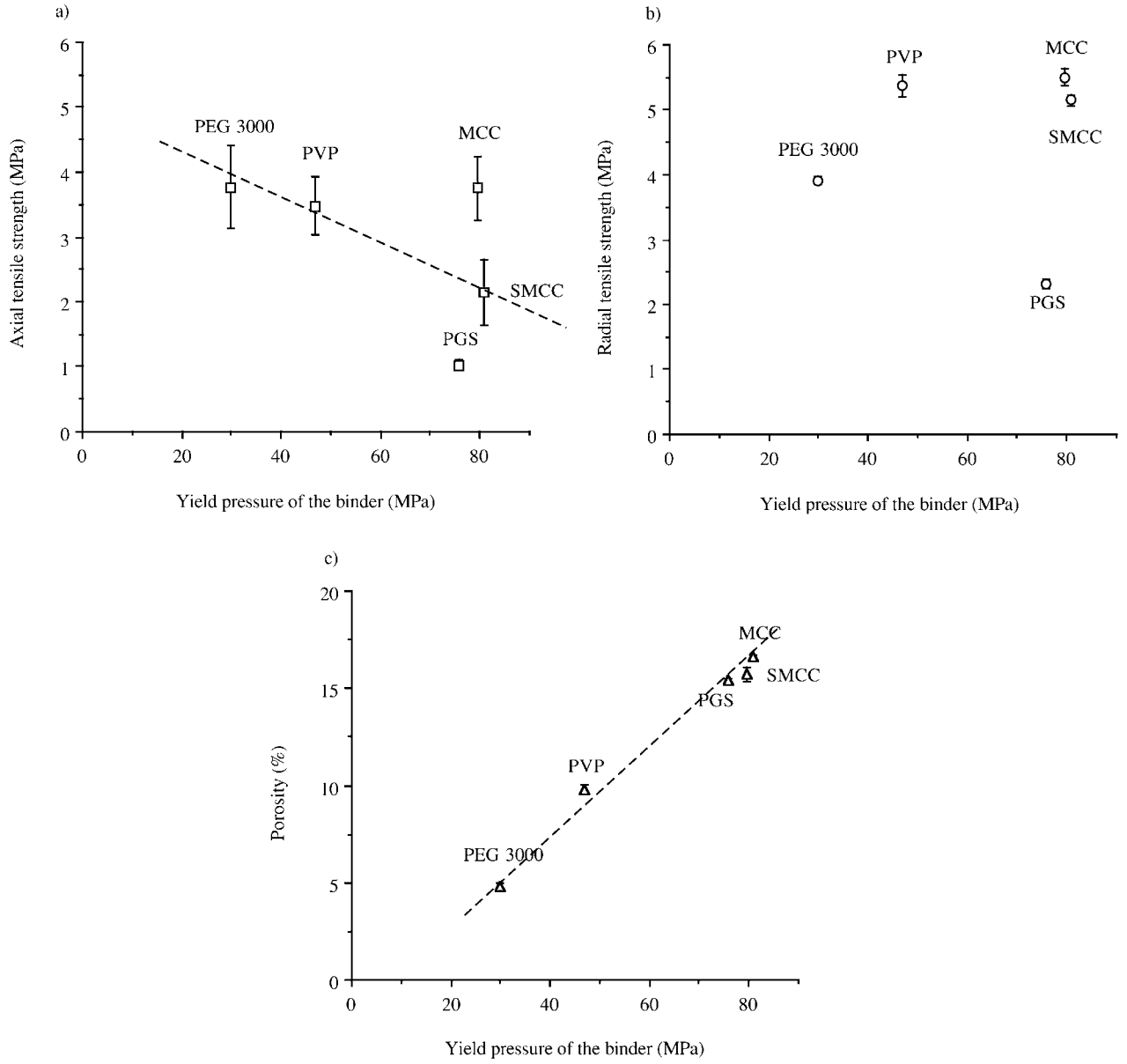

Figure 5. (a) Axial tensile strength, (b) radial tensile strength, and (c) porosity of tablets containing sodium bicarbonate and 21.5% w/w of the binders as a function of yield pressure of the pure binders. The broken line is shown as a guide to indicate deviations from the expected behavior of added binders.

Effects of Different Binder Properties on the Properties of Tablets Made of Binary Mixtures

Figures 5 through 7 show the effects of different binder properties on the axial and radial tensile strengths and porosity of tablets containing sodium bicarbonate and 21.5% w/w of binder. Two factors in particular appear to affect the properties of tablets made from a mixture of sodium bicarbonate and a binder. These are the deformability of the binder (here assessed by measuring the apparent yield pressure, the minimum porosity during compression, and the elastic recovery after compression) and the intrinsic tensile strength of the binder. The

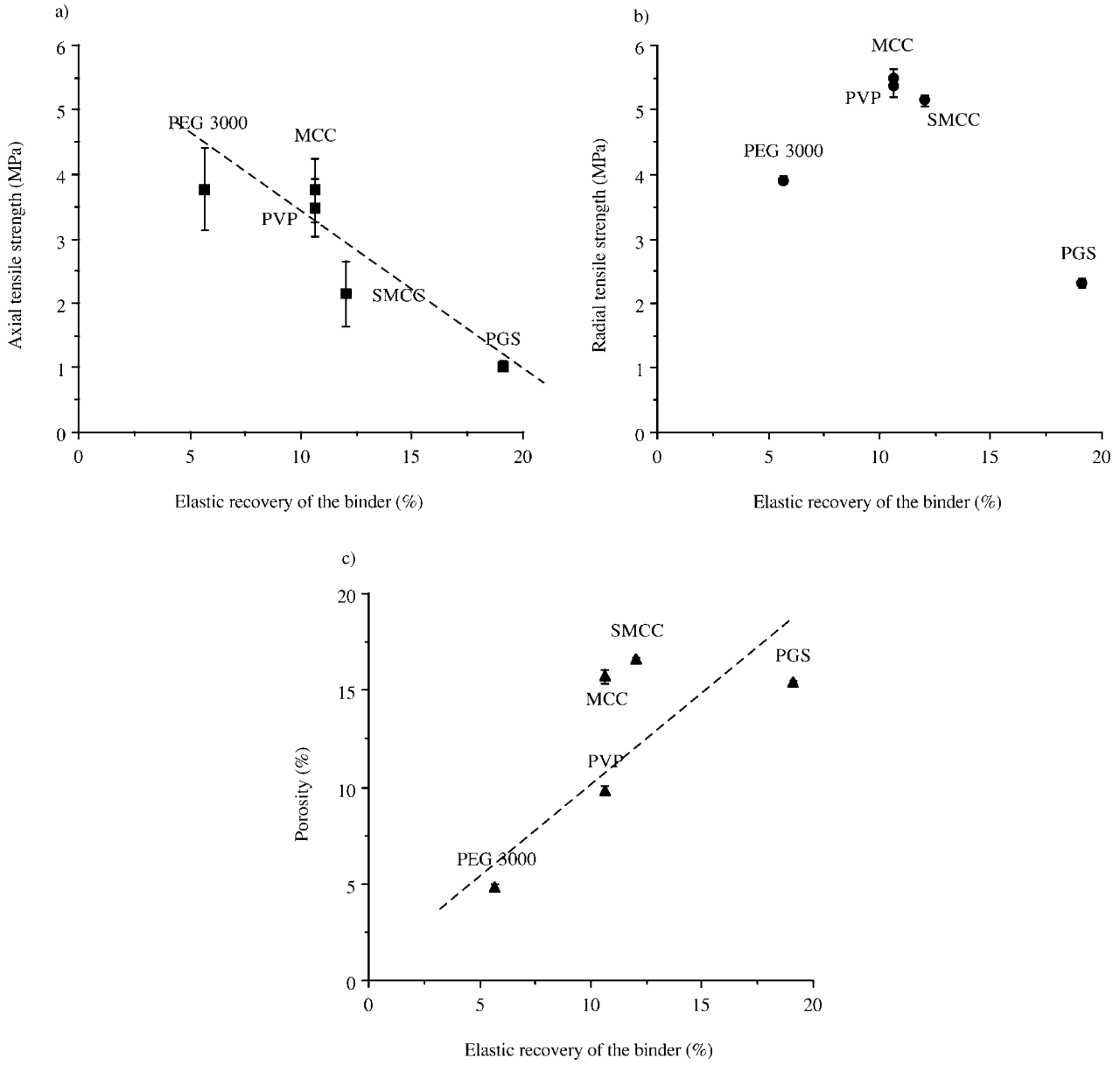

Figure 6. (a) Axial tensile strength, (b) radial tensile strength, and (c) porosity of tablets containing sodium bicarbonate and 21.5% w/w of the binders as a function of elastic recovery of the pure binders. The broken line is shown as a guide to indicate deviations from the expected behavior of added binders.

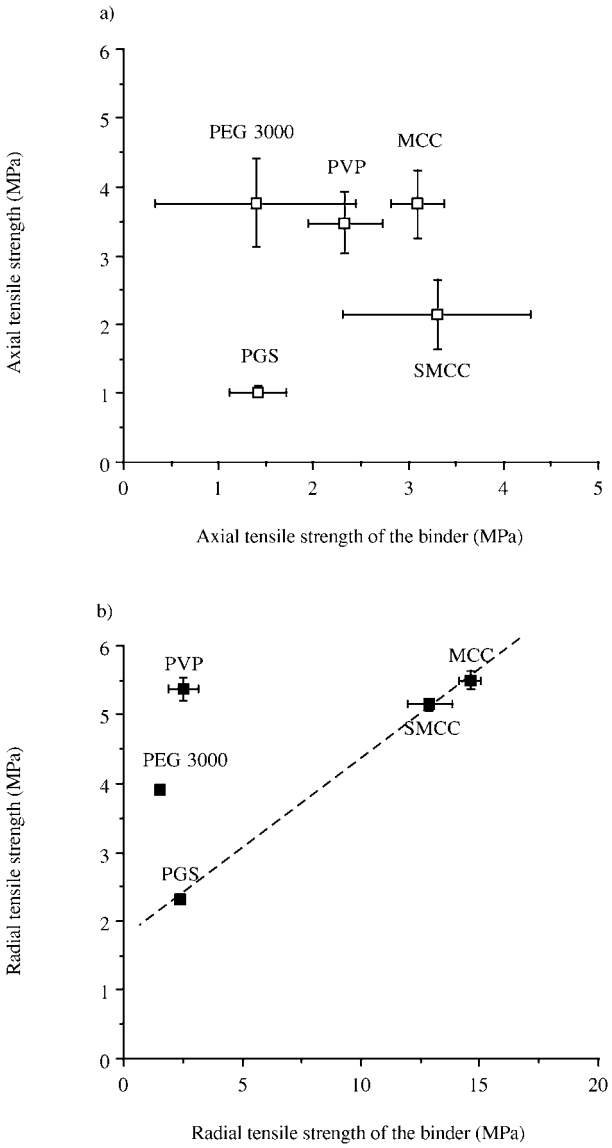

Figure 7. (a) Axial tensile strength of tablets containing sodium bicarbonate and 21.5% w/w of the binders as a function of axial tensile strength of the pure binders. (b) Radial tensile strength of tablets containing sodium bicarbonate and 21.5% w/w of the binders as a function of radial tensile strength of the pure binders. The broken line is shown as a guide to indicate deviations from the expected behavior of added binders.

apparent yield pressure of the binder appears to reflect directly the minimum porosity during compression (13). Thus, when the tablet properties of the mixtures were plotted against the minimum porosity and yield pressure of the binders, the graphs were similar. Therefore, only the latter graphs are shown here.

Effect of the Deformability of the Binder on Tablet Strength

The deformability (apparent yield pressure and elastic recovery) of the binder affected the axial tensile strengths of the sodium bicarbonate/binder tablets [Figs. 5(a), 6(a)]. Even though deformability is evidently not the only factor contributing to the tablet strength, when comparing Figures 5(a) and 6(a) with 7(a), it can be seen that there is some relationship between axial tensile strength and apparent yield pressure [Fig. 5(a)] or elastic recovery [Fig. 5(b)] of the binder in contrast to axial tensile strength and intrinsic axial tensile strength of the binder [Fig. 7(a)]. Generally, the addition of binders with a low apparent yield pressure and elastic recovery (PEG and PVP) resulted in a high axial tensile strength of tablets of sodium bicarbonate/binder mixtures [Figs. 2(b), 5(a), 6(a)]. However, the axial tensile strength of tablets containing sodium bicarbonate and MCC was relatively high despite the relatively low deformability, which would suggest a lower tensile strength. The strength of these tablets was probably affected by the high intrinsic tensile strength of MCC [Figs. 2(a), 5(a), 6(a), 7(b)].

The effects of apparent yield pressure and elastic recovery of the binder on the radial tensile strength were more complex [Figs. 5(b), 6(b)], indicating that the deformability of the binder has a greater effect on the axial than on the radial tensile strength. Instead, it is the intrinsic radial tensile strength of the binder that is important [Fig. 7(b)]. This may explain why tablets made from the mixture with PEG 3000 had a lower and the mixture with MCC or SMCC had a higher radial tensile strength than would be expected from the apparent yield pressure values [Fig. 5(b)]. This lower/higher radial tensile strength is probably a factor of the relatively low/high intrinsic radial tensile strength of these binders. Also, the addition of PEG 3000 resulted in relatively low tablet strength compared with the other binders with respect to elastic recovery [Fig. 6(b)]. The low deformability (high elastic recovery and apparent yield pressure) of PGS may partly explain the low tensile strength of the tablets made from the mixtures with sodium bicarbonate. In addition, PGS had a low intrinsic tensile strength.

Bonds rupture and flaws and defects are introduced into the tablet during elastic recovery after compression; this is reflected as a decrease in tablet strength. Because the axial tensile strength is a measure of the weakest plane in the tablet, the effect of elastic recovery was best demonstrated when testing the tablet strength in this direction [Fig. 6(a)], where an almost linear relationship was obtained. In the radial direction, which represents

a measure of the mean tablet strength, however, more complex results were seen [Fig. 6(b)]. The elastic recovery influences the ability of the binder to remain distributed between the sodium bicarbonate particles, and effective distribution of the binder is probably more crucial for the axial tensile strength of the tablets.

The difference in tensile strength between tablets of MCC mixed with sodium bicarbonate and those of SMCC mixed with sodium bicarbonate may be attributable to a difference in the elastic recovery of the pure binders [Fig. 6(a), (b)]. The more pronounced elastic behavior of SMCC is reflected in the slightly higher tablet porosity and the lower tablet strength of the mixtures with sodium bicarbonate. The effect of elastic recovery of the binder is especially reflected in the axial tensile strength [Fig. 6(a)].

Comparison between MCC and SMCC has shown previously that the silicification process produces a material that is chemically and physically very similar to MCC (24). Also, SMCC has been shown to exhibit improved flow properties and compactibility compared with regular MCC (25). In this study, however, this improved compactibility was not observed and, in the binary mixtures with sodium bicarbonate, SMCC did not show a greater strength-enhancing effect than did MCC when acting as a dry binder.

Effect of the Deformability of the Binder on Tablet Porosity

The deformability, i.e., the elastic recovery and apparent yield pressure, of the binder also had an effect on the tablet porosity of the resulting mixtures [Figs. 5(c) and 6(c)]. However, because the apparent yield pressure (obtained from in die measurements) reflects both plastic and elastic deformation, the best correlation with porosity was obtained with apparent yield pressure [Fig. 5(c)]. The results probably reflected the ability of the binder to fill the voids between the sodium bicarbonate particles. Accordingly, the lowest tablet porosity was obtained with the binders exhibiting the highest degree of deformability, i.e., the lowest apparent yield pressure and elastic recovery. The results indicated that both deformability parameters are important and both should be taken into account to fully understand the effect of the deformability of the binder on the tensile strength and porosity of sodium bicarbonate tablets.

Effect of the Intrinsic Tensile Strength of the Binder on Tablet Strength

As noted above, the intrinsic tensile strength of the binders also seemed to influence the tensile strength of tablets formed from the mixtures. This is illustrated by the binders with a lower degree of deformability such as MCC, which resulted in tablets with a high tensile strength, and PGS, which gave tablets a low tensile strength (Fig. 7). In contrast, despite the lower intrinsic tensile strength of PEG and PVP, tablets made from mixtures containing these binders were relatively strong, probably because of their high degree of deformability (Fig. 7). This again points to the concurrence of several factors in determining the strength of tablets made from a binary mixture.

CONCLUSIONS

The results of this study indicate that several factors are responsible for the strength-enhancing effects of a dry binder. However, it is also apparent that there is no simple relationship between the properties of the binder and those of the corresponding mixture. An attempt was made to systematically classify the binders with respect to their ability to increase the tensile strength of sodium bicarbonate tablets.

There are two main factors affecting the properties of tablets made from a mixture of sodium bicarbonate and a binder. First, the interparticulate voids in the sodium bicarbonate tablet are best filled with a binder with a high degree of plastic deformability and a low degree of elastic recovery, such as PEG 3000 or PVP. The void-filling capacity of a binder was expressed as DBS. If PEG 3000 or PVP is added to sodium bicarbonate, tablets with a relatively low porosity and a high tensile strength, especially in the axial direction, are obtained. Second, the intrinsic tensile strength of the binder is important, especially for binders with a lower degree of deformability such as MCC, SMCC, and PGS. These general conclusions were also made by Mattsson and Nyström (2), and it was shown in this study that these also apply to a larger number of binders. The results also demonstrated that the characteristics of the binders may serve as a useful tool in evaluating the effectiveness of binders.

The results indicated the value of using both axial and radial tensile strength measurements in assessing the effect of a dry binder in a binary mixture and also suggested that different binder properties appear to have differing effects, depending on the direction of the tablet strength measurements. When measuring the axial tensile strength, i.e., a property related to the weakest plane in the tablet, it is desirable to obtain a homogeneous distribution of bonds and a low incidence of defects in the tablets. In this respect, the deformability of the binder is of greater

importance than with radial measurements. On the other hand, measurements in the radial direction, where fracture of the tablet occurs through a predetermined diametral cross-section, a homogeneous bond distribution is not as crucial and, therefore, the radial tensile strength of the tablet depends more on the intrinsic radial tensile strength of the binder.

The results of this study may be useful for the choice of a suitable binder for a new drug formulation, even though the systems used in this study only consisted of two components, the model substance and the binder. If the compactibility of a compound is insufficient, a binder with a high degree of deformability (PEG 3000, PVP) seems to be suitable and in direct compression of tablets may also be an alternative to binders exhibiting a high intrinsic tensile strength (MCC). This may be especially important when adding a binder to a compound that would normally have problems with capping during compaction.

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