

Degree of pellet deformation during compaction and its relationship to the tensile strength of tablets formed of microcrystalline cellulose pellets

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Abstract

The degree of deformation and densification of pellets during compression have been quantified. The relationship between the degree of deformation of the pellets and their compactability were also studied. Two sets of pellets of microcrystalline cellulose, showing a marked difference in intragranular porosity, were prepared by extrusion-spheronization. The pellets were mixed with a lubricant and compacted at a series of applied pressures. The individual pellets were retrieved after compression by tablet deaggregation and the porosity (densification behaviour) and dimensions (deformation behaviour) of the retrieved pellets were determined. Tensile strength of compacts prepared of unlubricated pellets was also determined. The incidence of pellet fragmentation was almost non-existent during the compression for both sets of pellets. The low porosity pellets showed only limited local permanent deformation during compression and the pellet porosity was unaffected by the compression. The high porosity pellets showed both a high compression-induced change in shape and a marked decrease in pellet porosity. Tensile strength values of tablets of unlubricated pellets indicated that a marked bulk structure deformation of the pellets was necessary for the formation of intergranular contacts of a high bonding force in the compact.

Keywords: Microcrystalline cellulose pellets; Deformation of pellets; Densification of pellets; Compactability of pellets; Tensile strength of tablets

1. Introduction

In an earlier study (Johansson et al., 1995), the compression behaviour of pellets of microcrystalline cellulose was investigated. It was concluded that during compaction, the pellets compressed by deformation and the incidence of pellet fragmen-

tation during the compression process was low or non-existent. The terms pellet deformation and fragmentation used here refer to structural changes of the granules as such, and not to the primary particles of which the pellets are formed (Nyström and Alderborn, 1993), i.e. the shape of the pellets changes (deformation) or the pellets break down to smaller units (fragmentation). Examination of fracture surfaces of tablets formed of the pellets indicated that the pellets deformed

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to different degrees, depending upon their original porosity. This difference in porosity-controlled degree of pellet deformation, could explain the effect of pellet porosity on both the pore structure and the tensile strength of the compact, i.e. it seems that the degree of deformation undergone by the pellets during compression controlled the process of forming intergranular bonds. It was assumed here that the tensile strength of the compact simplified can be described as the product of the number of interparticulate bonds (contacts) per cross sectional area of compact and the force needed to separate a pair of particles in the tablet from each other (i.e. the interparticulate bonding force) (Eriksson and Alderborn, 1995).

In the earlier study on the microcrystalline cellulose pellets, it was found that these type of pellets were characterized by a high sensitivity, in terms of their compactability, to the addition of a lubricant, i.e. the tensile strength of tablets of lubricated pellets was very low. Thus, a film of magnesium stearate placed on the surface of the pellets resulted in intergranular bonds in the tablet of a very low bonding force. Tablets formed of lubricated pellets could easily be mechanically deaggregated and individual pellets could be retrieved from the tablets. This procedure has been used in this study in order to quantitatively analyze the compression behaviour of individual pellets of microcrystalline cellulose, i.e. to quantify the degree of deformation and densification which the pellets undergo during compression. By comparing the degree of deformation which the lubricated pellets underwent during compression with the tensile strength of tablets formed of unlubricated pellets, a relationship between degree of deformation of the pellets and their compactability could be established.

There is a lack of reports in the literature in which measures of the degree of deformation of individual particles during compression is presented and how this degree of deformation relates to the tensile strength of the formed compacts. The pellets of microcrystalline cellulose is thus used in this study as a model system for such a theoretical study in compaction technology. In

addition, since such pellets also represent a special type of drug delivery system, it is of interest per se to assess to what extent pelletized particles can deform while compressed.

2. Materials and methods

2.1. Materials

2.1.1. Microcrystalline cellulose

The microcrystalline cellulose employed was Avicel PH101 (FMC, USA); apparent particle density of 1.55 g/cm³.

2.1.2. Magnesium stearate

Magnesium stearate (Ph. Eur.) was purchased from (Apoteksbolaget AB, Sweden); permeametry surface area 1.66 m²/g.

2.1.3. Ethanol

The ethanol used in the study was Finsprit 95% w/w, supplied by (Kemetyl, Sweden).

2.2. Preparation of pellets

Two sets of pellets of microcrystalline cellulose were prepared in an identical manner as described earlier (Johansson et al., 1995). From each batch, the size fraction 710–1000 μm was separated by dry sieving and these pellets were stored in a desiccator at 40% relative humidity and room temperature for at least 7 days before any characterization or tableting.

2.3. Determination of pellet porosity

The porosity of the pellets ($n = 3$) was determined as described earlier (Johansson et al., 1995).

2.4. Determination of pellet dimensions

The pellets were photographed in an optical light microscope (Vanox Universal Research Microscope, Japan) at twice magnification. The pellets were placed on a microscope slide and vibrated by hand to ensure that they were ori-

ented in their most stable position. The breadth (B) and the length (L) of the pellets were determined from the photographs according to Heywood (1954) for at least 200 pellets from each set of pellets and the median pellet size based on a number distribution were calculated. The thickness (T) of the pellets was determined by a ring gap sizer (F.O.A., Sweden). Three samples of approximately 2 g were analyzed and from these data, the median pellet size based on a number distribution was calculated.

The flakiness ratio (B/T) and the elongation ratio (L/B) were calculated from the median values of the length, breadth and thickness of the pellets. The Heywood surface to volume shape coefficient (Heywood, 1954) was calculated as described by Nyström (1978) using the values of the flakiness ratio and elongation ratio described above and assuming rounded particles with $\alpha_c = 0.54$ and $C = 2.1$.

2.5. Preparation and deaggregation of tablets from lubricated pellets

The pellets were mixed for 100 min with 0.5% by weight magnesium stearate in a Turbula mixer (W.A. Bachofen, Switzerland) at 90 rpm and tablets of lubricated pellets were compacted in an instrumented single punch press (Korsch EK 0, Germany) at applied pressures of 2, 5, 10, 20, 40 and 80 MPa. The press was equipped with flat-faced punches with a diameter of 1.13 cm. The punches were adjusted to a punch tips separation distance of 3 mm at the respective applied pressures and the amounts of pellets filled into the die were varied to obtain the required pressure. Before each compaction, the die was lubricated with a suspension of 1% by weight of magnesium stearate in ethanol. A number of tablets corresponding to 5 g of material were compacted at each pressure.

In addition to the registration of the upper punch force, the upper punch displacement was registered during compaction at 80 MPa of two tablets of each set of pellets. After correction for the upper punch deformation, the height of the compact in-die at an applied pressure (H_p) was

estimated at each pressure unit. The degree of compression (C) of the pellets in-die was thereafter calculated as: $C\% = ((H_0 - H_p)/H_0) \times 100$, where H_0 is the estimated height of the powder bed in-die before compression (i.e. calculated from the poured bulk density, the powder weight and the die diameter).

After compaction, the tablets were placed in a Petri dish and the Petri dish was then shaken carefully by hand until the tablets fell apart completely. The dimensions and the porosity of these retrieved pellets were then determined as described above. Tablets formed at applied pressures up to 80 MPa could be easily deaggregated. At higher applied pressures, retrieval of individual pellets was not possible and this fact limited the maximum compaction pressure used during the preparation of tablets to 80 MPa.

2.6. Preparation and characterization of tablets from unlubricated pellets

Due to their poor compactability, tablets were prepared of the low porosity pellets only at an applied pressure of 80 MPa but tablets of the high porosity pellets were prepared at applied pressures of 2, 5, 10, 20, 40 and 80 MPa. Five tablets were prepared at each applied pressure as described above and the degree of compression was also calculated. After compaction, the tablets were stored in a desiccator at 40% relative humidity and room temperature for at least 7 days before any characterization.

Tablets were compressed diametrically ($n = 5$) by a materials testing machine (model M30K, J.J. Lloyd Instruments Ltd., UK) at a compression rate of 5 mm/min. From the force needed to fracture the tablets, the tensile strength was derived as given by Fell and Newton (1970).

The total porosity of the compacts was calculated from the weight and height of the compact and the apparent particle density of the pellets ($n = 5$). The intergranular porosity of the compacts was calculated as: $\epsilon\% = ((\epsilon_c - \epsilon_p)/(1 - \epsilon_p)) / 100$, where ϵ_c is the total porosity of the compact and ϵ_p is the porosity of the retrieved pellets after compression.

Table 1
Intragranular porosity, size and shape characteristics of low porosity pellets, before and after compression

Compaction pressure (MPa)	Breadth ^a (μm)	Length ^a (μm)	Thickness ^b (μm)	Elongation (-)	Flakiness (-)	Surface to volume shape coefficient ^c (-)	Pellet porosity (%)
0	892 (234)	1018 (308)	794 (236)	1.14	1.12	7.02	10
2	890 (237)	1034 (361)	797 (263)	1.16	1.12	7.09	9.4
5	891 (195)	1017 (326)	803 (240)	1.14	1.11	7.00	10
10	884 (215)	1014 (322)	810 (249)	1.15	1.09	7.00	9.6
20	912 (200)	1054 (310)	817 (278)	1.16	1.12	7.09	9.2
40	891 (262)	1052 (358)	797 (284)	1.18	1.12	7.16	9.5
80	931 (231)	1056 (323)	777(283)	1.13	1.20	7.16	9.8

^aMedian values from size distributions by number, the range between the values at 90 and 10% is given in parentheses.

^bMedian values from size distribution by number, measured by a ring gap sizer. The range between the values at 90 and 10% is given in parentheses.

^cCalculated according to Heywood (1954) using the elongation and flakiness values and assuming rounded particles with $\alpha_c = 0.54$ and $C = 2.1$.

Table 2
Intragranular porosity, size and shape characteristics of high porosity pellets, before and after compression

Compaction pressure (MPa)	Breadth ^a (μm)	Length ^a (μm)	Thickness ^b (μm)	Elongation (-)	Flakiness (-)	Surface to volume shape coefficient ^c (-)	Pellet porosity (%)
0	854 (227)	970 (410)	764 (229)	1.14	1.12	7.02	44
2	819 (214)	944 (359)	767 (234)	1.15	1.07	6.96	44
5	877 (266)	1005 (388)	754 (253)	1.15	1.16	7.14	44
10	843 (275)	992 (352)	722 (281)	1.18	1.17	7.27	42
20	889 (265)	1033 (353)	685 (286)	1.16	1.30	7.48	37
40	893 (298)	1064 (420)	639 (299)	1.19	1.40	7.83	30
80	912 (305)	1078 (425)	577 (287)	1.18	1.58	8.22	18

^aMedian values from size distributions by number, the range between the values at 90 and 10% is given in parentheses.

^bMedian values from size distribution by number, measured by a ring gap sizer. The range between the values at 90 and 10% is given in parentheses.

^cCalculated according to Heywood (1954) using the elongation and flakiness values and assuming rounded particles with $\alpha_c = 0.54$ and $C = 2.1$.

3. Results and discussion

3.1. Porosity and dimensions of pellets before compression

The original porosity of the pellets (Table 1 and Table 2) showed a 4-fold difference depending on the proportion of ethanol in the agglomeration liquid used during their preparation (Johansson et al., 1995). Due to this difference, the pellets are hereafter referred to as the low porosity (10%) and the high porosity (44%) pellets.

Examinations of the pellets by a scanning electron microscope (S.E.M.) and by an optical light microscope indicated that the pellets were nearly spherical in shape and that the surface of the pellets was smooth (Fig. 1a, Fig. 1c and Fig. 2a, Fig. 2c). The high porosity pellets showed a slightly less smoother surface than the low porosity pellets.

The measures of the shape of the pellets, i.e. their elongation, flakiness and Heywood shape coefficient, showed (Tables 1 and 2) that the pellets were nearly spherical and, in addition, indicated that the low and high porosity pellets were identical in shape with respect to their relative main dimensions. It may also be noticed that the low porosity pellets were slightly larger (Tables 1 and 2) in all three dimensions, i.e. breadth, length and thickness.

3.2. Degree of compression-applied pressure relationships

The degree of compression was assessed for both lubricated and unlubricated pellets in the pressure range 2–80 MPa. In Fig. 3a and Fig. 3b, the degree of compression – applied pressure relationships for lubricated pellets are presented. With an increased applied pressure, the degree of compression per pressure unit decreased. This was most marked for the high porosity pellets. In addition, the compressibility was generally higher for the high porosity pellets. At 80 MPa, the degree of compression was 64.7% for the high porosity pellets and 40.0% for the low porosity pellets.

Since the evaluation of densification and deformation of individual pellets during compression was performed on retrieved lubricated pellets, while the evaluation of compactability of pellets was performed on unlubricated pellets, it was considered of interest to study also the degree of compression – applied pressure relationships for unlubricated pellets. It was concluded that the compression behaviour of lubricated and unlubricated pellets differed only marginally. The degree of compression of unlubricated pellets at 80 MPa was 64.1% and 38.0% for high porosity and low porosity pellets, respectively. Thus, the compressibility of the pellets was hardly influenced by the lubricant addition while the compactability of the pellets was drastically affected by the lubricant addition, i.e. the addition of a lubricant more or less entirely prevented the formation of intergranular bonds. It seems thus that the compression behaviour of a bed of these types of pellets was controlled by the mechanical properties of the individual pellets, i.e. their resistance against deformation during compression, rather than by the bond formation process between the pellets. As a consequence, the work needed to compress the bed of pellets is a reflection of the compression characteristics of the pellets and not of their bond formation ability.

3.3. Porosity and dimensions of compressed and retrieved pellets

The deaggregation procedure generally gave retrieved pellets of a size similar to that of the original pellets and only minute amounts of fragments were observed in the deaggregated compacts. It seems, thus, that the incidence of pellet fragmentation was more or less non-existent during the compression for both types of pellets.

For low porosity pellets, only limited compression-induced changes in pellet size and shape could be quantified (Table 1 and Fig. 4a). Visual inspection, by optical microscopy and by S.E.M., of retrieved pellets compressed at an applied pressure of 80 MPa, showed that no major changes in pellet shape occurred during compression (Figs. 1 and 2). However, it seems that the retrieved pellets had zones on the surface of pellets that were

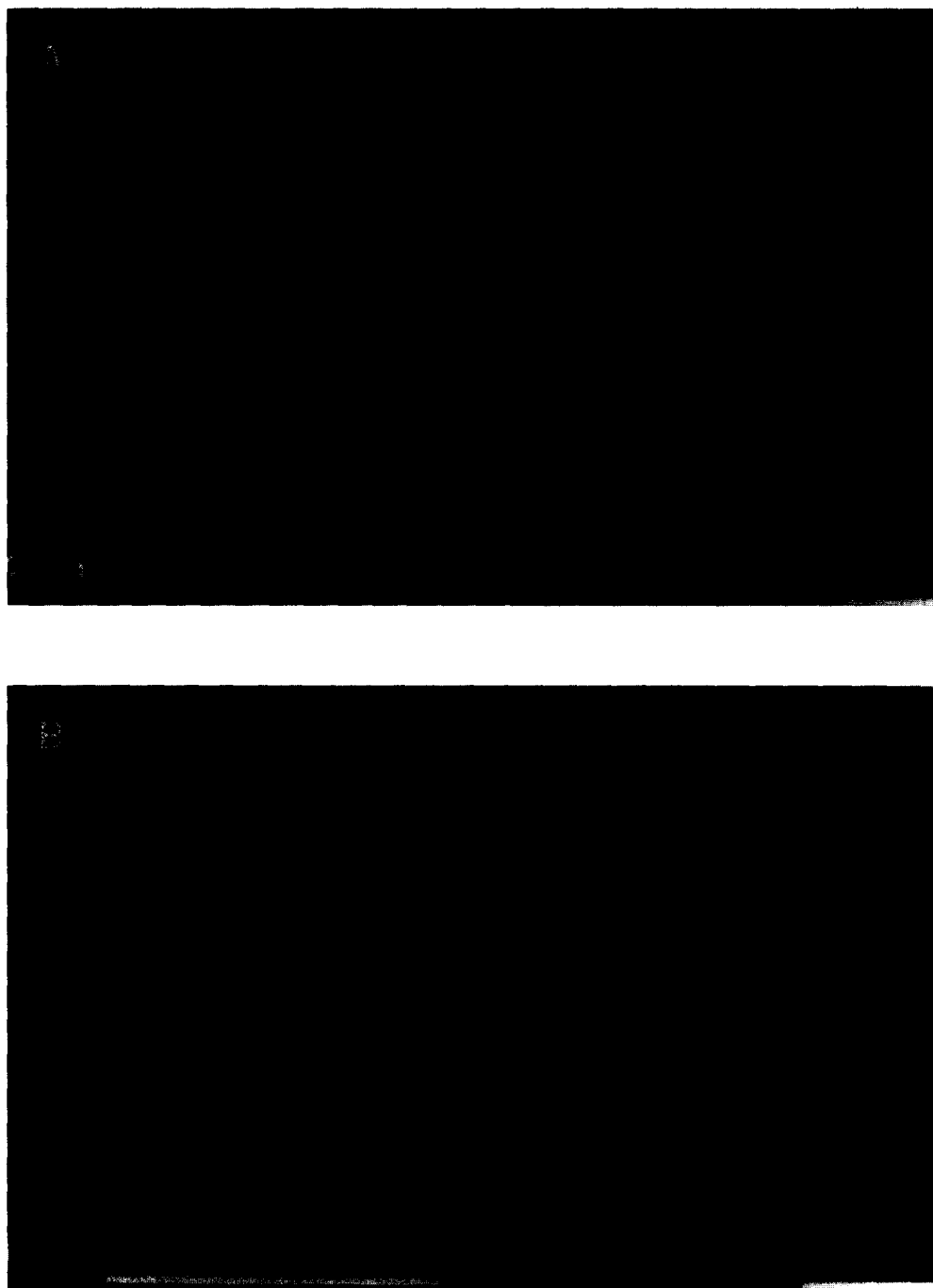


Fig. 1. S.E.M. photomicrographs of pellets; (a) low porosity pellets, before compression; (b) low porosity pellets, retrieved pellets after compression at 80 MPa; (c) high porosity pellets, before compression; (d) high porosity pellets, retrieved pellets after compression at 80 MPa. The white bar denotes 1 mm.

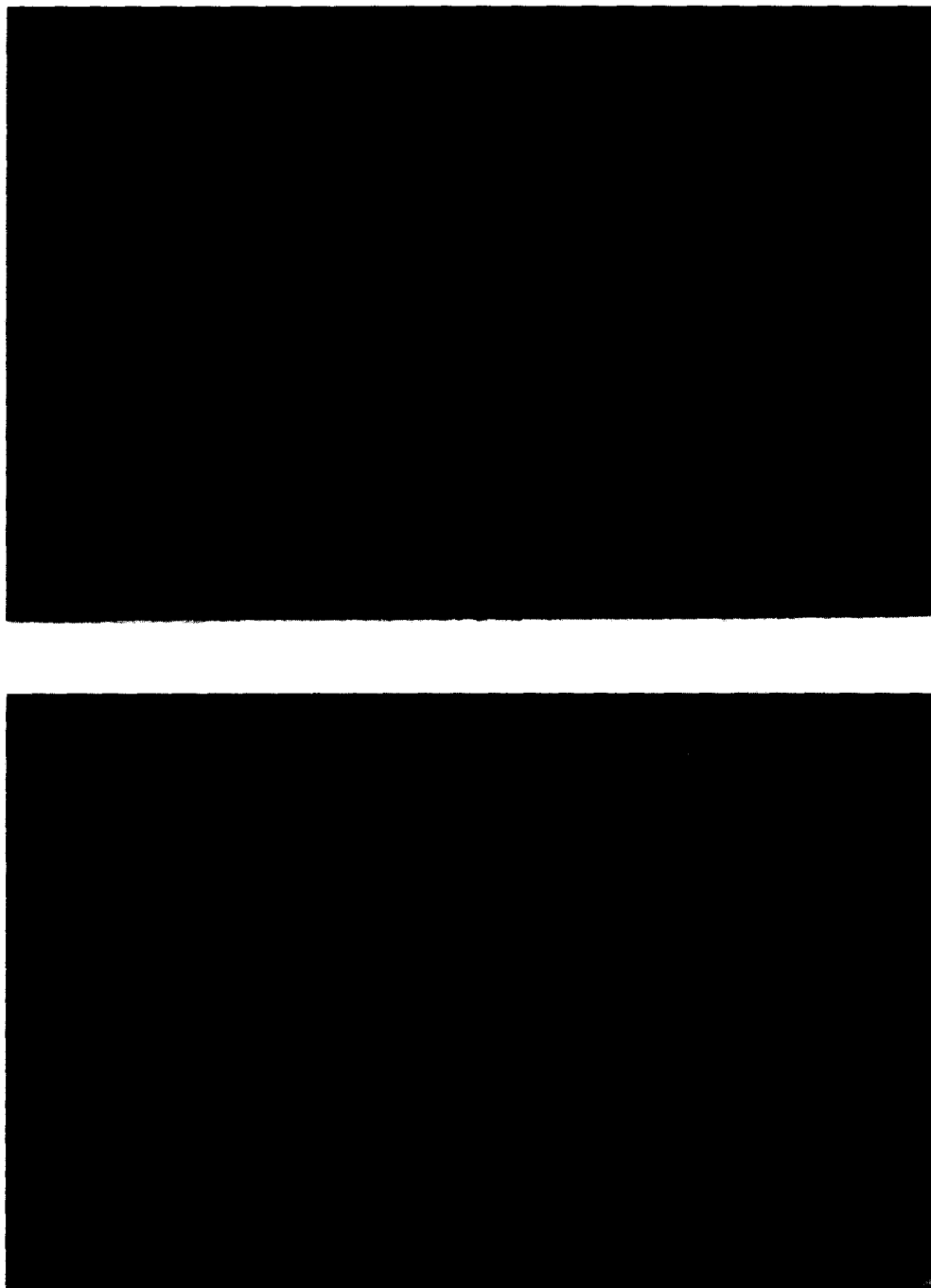


Fig. 1C and D.

nearly flat, i.e. the pellet surface had locally lost its original curvature, which probably represents limited local permanent deformation of pellets

during the compression. These changes in the shape of the pellets could not be quantified in terms of shape factors used in this study since the

main dimensions of the pellets were more or less unaffected.

The porosity of low porosity pellets (Table 1) seemed to be unaffected by the compression process within the range of applied pressures used. At the highest pressure used, the whole bed of pellets in-die decreased in volume by approximately 40%. Since pellet fragmentation and densification was limited for these pellets, the volume reduction occurred probably as a consequence of two processes, i.e. repositioning of pellets followed by pellet deformation. Due to the size and shape characteristics of the pellets, it is reasonable to assume that the pellets packed spontaneously into

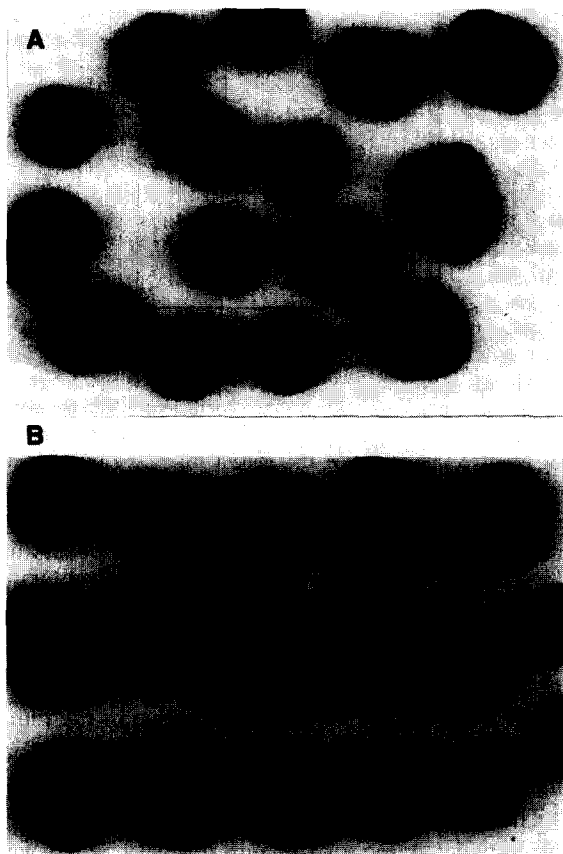


Fig. 2. Optical light microscopy photomicrographs at twice magnification of pellets; (a) low porosity pellets, before compression; (b) low porosity pellets, retrieved pellets after compression at 80 MPa; (c) high porosity pellets, before compression; (d) high porosity pellets, retrieved pellets after compression at 80 MPa.

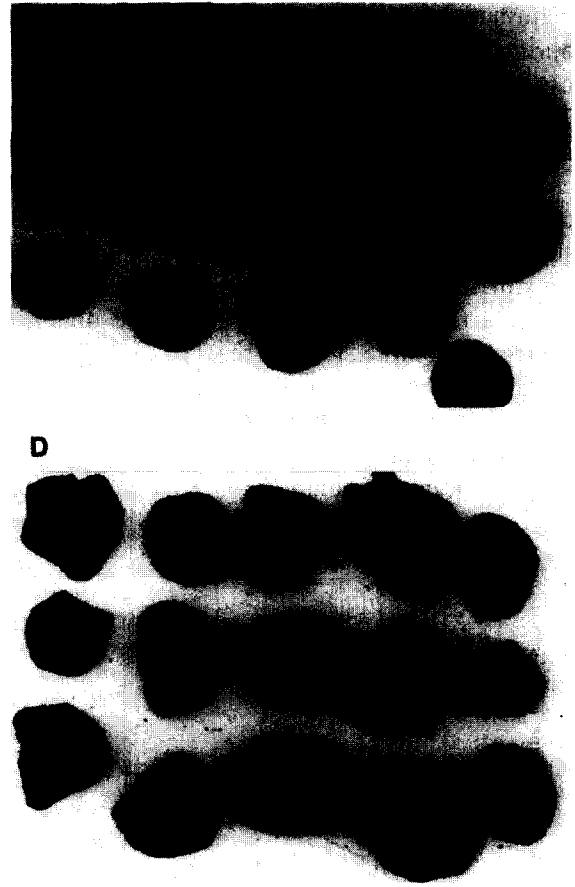


Fig. 2C and D.

a dense structure while being poured into the die. Consequently, the degree of compression caused by pellet repositioning can be assumed to be limited. It seems, thus, that a marked degree of compression of the bed of pellets was obtained as a result of limited and mainly local pellet deformation.

For the high porosity pellets, an increased applied pressure affected significantly the dimensions of the retrieved pellets (Table 2). Both the breadth and the length of the pellets increased slightly (in relative terms up to approximately 5 and 10% in the pressure range used) parallel to a marked decrease in the thickness of the pellets (up to approximately 25%). Thus, compression gave significantly less spherical pellets characterized by a slight increased elongation and a more pronounced increased flakiness. This change in pellet shape towards flatter particles indicates that pellet

deformation occurred mainly in one direction during the compression, i.e. the same direction as used for stress application during compaction. This is consistent with earlier suggestions (Johansson et al., 1995) based on observations of the character of the fracture surface of compacts. The change in pellet shape (quantified as the Heywood surface to volume shape coefficient) followed approximately a linear relationship with applied pressure (Fig. 4a). With respect to the obtained degree of compression of the bed of pellets, a significant change in pellet shape (Fig. 4b) was not obtained until a degree of compression above 30% was reached. It seems, thus, that the pellet shape – degree of compression relationship coin-

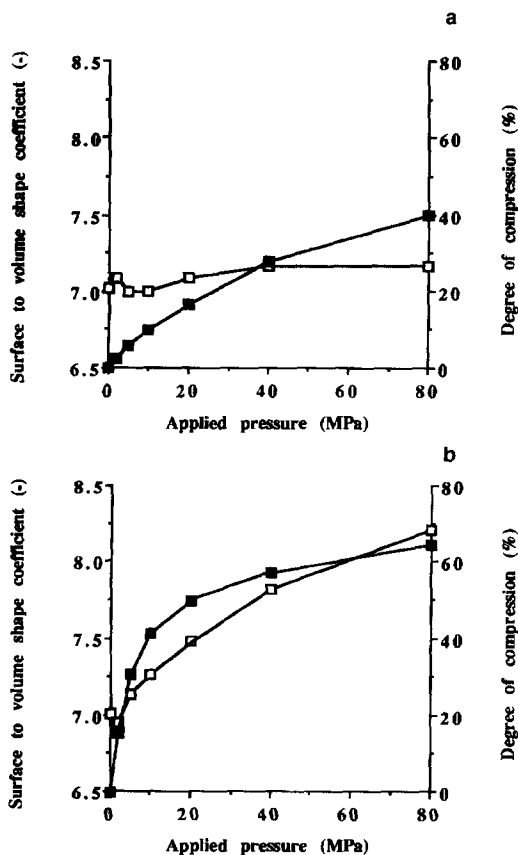


Fig. 3. The surface to volume shape coefficient (\square) and the degree of compression of the pellets (\blacksquare) as a function of the applied pressure. (a) Low porosity pellets; (b) high porosity pellets.

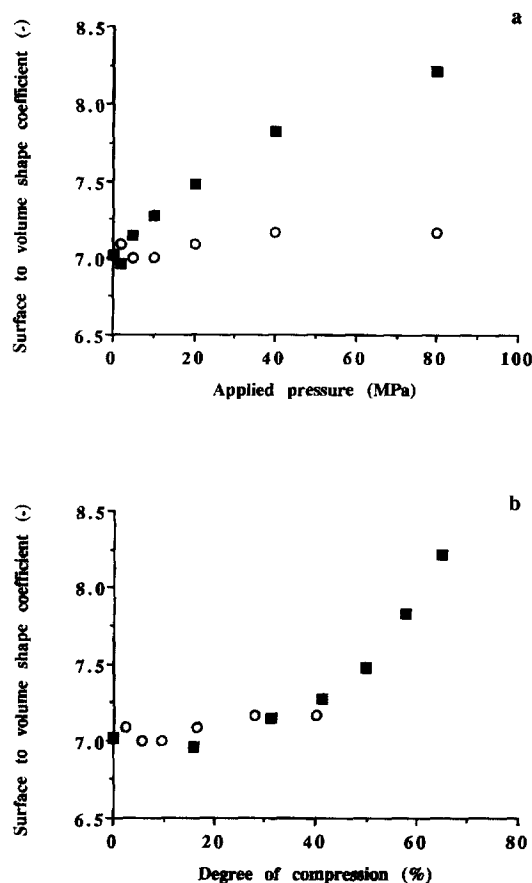


Fig. 4. The surface to volume shape coefficient of the pellets as a function of the applied pressure (a) and as a function of the degree of compression of the pellets (b). \circ , Low porosity pellets; \blacksquare , high porosity pellets.

vided for the low and the high porosity pellets up to a degree of compression of 30–40%. This degree of compression was obtained due to local permanent pellet deformation. Thereafter, the high porosity pellets continued to reduce in volume up to about 65% due to a change in the main dimensions of the pellets, i.e. a permanent deformation of the bulk of the pellet structure.

The more marked change in compression-induced pellet shape for the high porosity pellets was supported by the photomicrographs (Fig. 2b and Fig. 2d). The photomicrographs also indicate that the high porosity pellets showed a more irregular surface than the low porosity granules. Small cracks could also be noticed in the surface of the pellet.

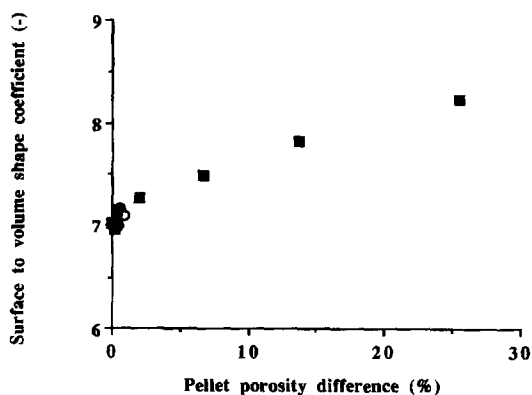


Fig. 5. The surface to volume shape coefficient of the pellets as a function of the difference between the pellet porosity before compression and the pellet porosity of the retrieved pellets after compression. Symbols as in Fig. 4.

For the high porosity pellets, the intragranular porosity also decreased continuously as the applied pressure increased (Table 2). As regards the changes in pellet porosity during compression, the profiles for the low and the high porosity pellets coincided up to a degree of compression of 30–40%.

A nearly linear relationship between the compression-induced changes in pellet shape and pellet porosity was obtained (Fig. 5). It seems, thus, that pellet deformation and densification occurred nearly parallel during compression of the high porosity pellets. Both these processes are probably a result of a repositioning of cellulose particles within the pellets. The decreased deformation and densification with increased applied pressure can

be explained by the suggestion that the porosity of the pellet constitutes a restriction against intragranular particle repositioning and thus against pellet deformation or densification, i.e. at a low pellet porosity, the volume of air that surrounds the primary particles which constitute the pellet is too small to make a repositioning of the primary particles within the pellet possible.

3.4. Porosity and tensile strength of compacts prepared from unlubricated pellets

The low porosity pellets formed cohered compacts only at the highest applied pressure used in this study. However, these compacts fell apart when they were removed from the die and a measure of their tensile strength could thus not be determined. The high porosity pellets formed compacts of measurable porosity and tensile strength at an applied pressure of 5 MPa.

With an increased applied pressure, the total tablet porosity decreased markedly (Table 3) due to a reduction in both intergranular and intragranular porosity. A comparison with the measures of the porosities of the retrieved pellets indicates that the major part of the air within the compact was located within the pellets. The intergranular tablet porosity decreased dramatically with increased applied pressure up to a pressure level of approximately 40 MPa. Thereafter, an increased applied pressure gave a limited decrease in intergranular tablet porosity. If the porosity data are presented as Heckel plots, markedly different profiles will be obtained between total and intergranular tablet porosity (Fig. 6).

Table 3
Characteristics of tablets compacted of unlubricated high porosity pellets

Applied pressure (MPa)	Tablet tensile strength (MN/m ²)	Total porosity (%)	Intergranular porosity (%)
0	0	69.7	46
2	^a	^a	^a
5	0.033 (12)	60.3 (0.20)	30
10	0.135 (11)	53.1 (0.94)	19
20	0.403 (7.6)	45.3 (0.22)	13
40	1.36 (3.3)	34.3 (0.60)	6.0
80	3.29 (2.4)	22.4 (2.1)	5.0

^aIndicates that the tablets were cohered after the compression but fell apart when removing them from the die. The R.S.D. is given in parentheses.

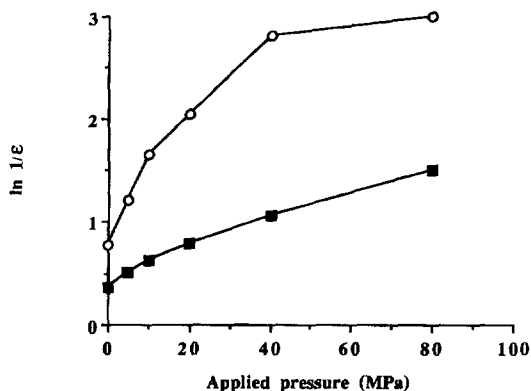


Fig. 6. Tablet porosities, presented in the form of the Heckel function, ($\ln 1/\epsilon$), as a function of the applied pressure. \circ , Intergranular porosity of the compact; \blacksquare , total porosity of the compact.

The tensile strength of the compacts increased (Table 3) in almost a rectilinear manner with the applied pressure. However, the tensile strength of the compacts related exponentially to the shape of the pellets (Fig. 7), as measured by the Heywood surface to volume shape coefficient of the retrieved pellets. A mechanistic explanation of this relationship can be based on the following conception: the tensile strength of the tablet is controlled by the product of the number and the bonding force of the bonds in the fracture plane (Eriksson and Alderborn, 1995). A decreased tablet porosity will probably increase the number of intergranular contact points or zones between

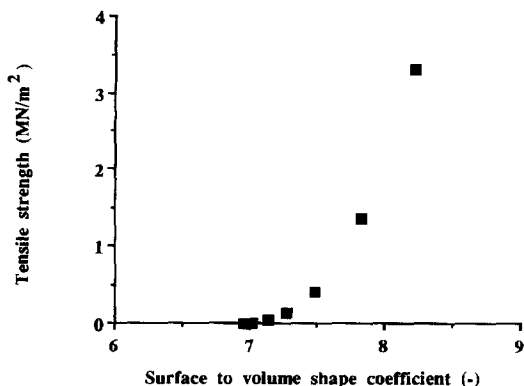


Fig. 7. The tensile strength of tablets prepared from unlubricated high porosity pellets as a function of the surface to volume shape coefficient of the retrieved pellets.

the pellets within the tablet. However, since the pellets compressed by deformation and the incidence of fragmentation was limited, a decreased tablet porosity will probably have a limited effect on the number of contact zones. The degree of pellet deformation during compression will control the area of the individual intergranular contacts which, in turn, will control the bonding force of the intergranular contacts. Since the number of contacts will be limitedly affected by a reduced tablet porosity, the dramatic increase in tablet strength with reduced tablet porosity must be explained in terms of a marked increased mean bonding force of the intergranular contacts due to pellet deformation. However, the results in Fig. 7 indicate that at relatively high tablet porosities, a certain degree of deformation of a pellet will have a limited effect on tablet strength while at low tablet porosities, only a small pellet deformation will markedly affect tablet strength.

To summarise, the results generated in this study on the relationship between degree of pellet deformation and the formation of intergranular bonds indicate that only a small local pellet deformation is not sufficient to give significant bonding forces of the intergranular contacts and make the pellets cohere into a compact. Thus, the formation of relatively large contact areas between the pellets, caused by the deformation of the bulk structure of the pellet, seemed to be necessary for the formation of intergranular contacts of high bonding force in the compact. Contacts of high bonding force are a prerequisite for formation of a compact of significant tensile strength. The results indicate further that the effect of a certain degree of pellet deformation (as assessed by the change in pellet shape) on the bonding force of the intergranular contacts is dependent on the porosity of the compact.

4. Conclusions

The compression behaviour of pellets of microcrystalline cellulose has earlier been investigated (Johansson et al., 1995). In that study it was concluded that:

- (1) the pellets were compressed by deformation and the incidence of pellet fragmentation was low or non-existent;
- (2) the pellet porosity, and not the fracture resistance of the pellets, controlled the degree of their deformation during the compression;
- (3) the degree of pellet deformation during compression controlled the pore structure and the tensile strength of the compact.

In this study, a procedure involving compaction of lubricated pellets followed by deaggregation of the compacts with subsequent analysis of porosity and shape of the retrieved pellets was used in order to study the compression behaviour of microcrystalline cellulose pellets in a quantitative way. By comparing these results with the tensile strength of tablets formed of unlubricated pellets, a relationship between degree of deformation of the pellets and their compactability could be established. In addition to the findings summarized above, the experiments reported in this study have shown that:

- (1) the pellets were compressed initially by a limited deformation, i.e. a local surface deformation involving the flattening of a restricted area of the pellet surface. This local surface deformation did not involve a densification of the individual pellets but gave a marked degree of compression of the bed of pellets in the die, i.e. 30–40%;
- (2) above a degree of compression of 30–40%, a continuing volume reduction of the bed of pellets involved a more marked deformation of the individual pellets characterized by a change in their main dimensions, i.e. bulk structure deformation. Especially the minimum dimension of the pellets changed, i.e. they became flatter. The bulk structure deformation occurred parallel with a densification of the individual pellets;
- (3) the degree of deformation of the pellets controlled the bond formation process between the pellets during compaction. It seems that a local surface deformation gave weak bonds between pellets that were not sufficiently strong to cohere the pellets into a

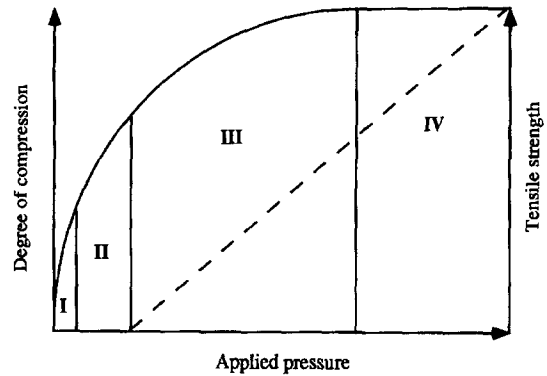


Fig. 8. The degree of compression of the pellets (-) and the tensile strength of tablets prepared from unlubricated pellets (- -) as a function of the applied pressure. The numbers I–IV correspond to the four stages described in the text.

compact. The formation of a coherent compact required a bulk structure deformation of the pellets;

- (4) the effect of a certain degree of pellet deformation on the bonding force between pellets in the compact will increase with a reduced compact porosity.

The mechanistic conception proposed in this paper regarding the compaction process of deformable pellets can be summarized in a 4-stage model (Fig. 8). The different stages represents parts of the compression profiles at which a certain compression process dominates the volume reduction event and how this affects the intergranular bond formation process:

- (I) Volume reduction of the pellet bed by repositioning of pellets. Point contacts between pellets;
- (II) Volume reduction of the pellet bed by surface deformation of pellets. Development of areas of intergranular contacts, intergranular bonds characterized by a low bonding force;
- (III) Volume reduction of the pellet bed by bulk structure deformation and densification of pellets. Development of large areas of intergranular contacts. Intergranular bonds characterized by a high bonding force which is sufficient to form coherent compacts;

(IV) Ceased volume reduction due to low inter- and intragranular porosity. Minute volume reduction and pellet deformation will have a marked effect on the bonding force of the intergranular bonds.

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References

- Eriksson, M. and Alderborn, G., The effect of particle fragmentation and deformation on the interparticulate bond formation process during powder compaction. *Pharm. Res.*, 12 (1995) 1031–1039.
- Fell, J.T. and Newton, J.M. Determination of tablet strength by the diametral-compression test. *J. Pharm. Sci.*, 59 (1970) 688–691.
- Heywood, H., Particle shape coefficients. *J. Imp. Coll. Chem. Eng. Soc.*, 8 (1954) 25–33.
- Johansson, B., Wikberg, M., Ek, R. and Alderborn, G., Compression behaviour and compactability of microcrystalline cellulose pellets in relationship to their pore structure and mechanical properties. *Int. J. Pharm.*, 117 (1995) 57–73.
- Nyström, C. and Alderborn, G., The compactability of pharmaceutical powders. In Sandell, E. (Ed.), *Industrial Aspects of Pharmaceutics*, Swedish Pharmaceutical Press, Stockholm, 1993, pp. 129–152.
- Nyström, C., The use of the ring gap sizer for characterization of particle shape in the sieve range. *Powder Technol.*, 20 (1978) 83–87.