International Journal of Pharmaceutics, 94 (1993) 181–187
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IJP 03178

Prediction of the compression behaviour of powder mixtures by the Heckel equation

Jukka Ilkka and Petteri Paronen

Department of Pharmaceutical Technology, University of Kuopio, P.O.B. 1627, SF-70211 Kuopio (Finland)

(Received 9 November 1992)
(Accepted 4 January 1993)

Key words: Powder mixture; Tableting excipient; Compression behavior; Heckel equation; Mean yield pressure

Summary

The compression behaviour of plastically flowing microcrystalline cellulose and pregelatinized corn starch and fragmenting α-lactose monohydrate and dicalcium phosphate dihydrate, and their binary mixtures was evaluated using the Heckel equation. Powders were compressed using an instrumented eccentric tablet press. The Heckel plots for both plastically flowing materials and their binary mixtures were linear in shape. In contrast, on the Heckel plots of the fragmenting materials and their mixtures, an obvious curvature was seen. The mean yield pressures were linearly proportional to the mixture composition of two plastically flowing materials. When mixed with a fragmenting material, a plastically flowing component had a greater effect on the compression behaviour of the mixture than a fragmenting mixture component had. This was explained by the more pronounced effect of plastic flow on volume reduction. When two fragmenting materials were compressed, the densification of their binary mixture was strongly influenced by the less compressible material with higher mean yield pressure. It was concluded that in the mixtures of two fragmenting materials the particles of the less compressible material constituted a firm structure, like a skeleton, which tended to dominate the compression behaviour of the binary mixtures. For binary mixtures of fragmenting materials the mean yield pressures were thus not linearly proportional to the mixture composition. Compression behaviour of powder mixtures seemed to be strongly dependent on the deformation properties of plain materials to be compressed. On the other hand, one mixture component may dominate the compression behaviour of the mixture, and the compressibility may change non-linearly with mixture composition. Therefore, caution is needed when the Heckel equation is applied for predicting compression behaviour of powder mixtures.

Introduction

During the last three decades several authors have distinguished stages during the compression of powders in dies. Numerical values describing the tendency of the material to undergo elastic deformation and plastic flow or fragmentation have been calculated using different compression equations. Practically all the widely used compression equations describe the relationship between relative density or porosity of the compact and the applied pressure (Kawakita and Lüdde, 1970/71). The most frequently utilized is the Heckel equation, which is based on the assumption that the densification of the bulk powder

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Correspondence to: J. Ilkka, Department of Pharmaceutical Technology, University of Kuopio, P.O.Box 1627, SF-70211 Kuopio, Finland.

column follows the first order kinetics (Heckel, 1961). Although the Heckel function has its limitations in describing densification at low and very high compression pressures (Hersey and Rees, 1971; Roberts and Rowe, 1985), it transpires that this equation is nevertheless rather useful for obtaining practical data concerning the densification behaviour of materials compressed.

Most of the published studies, in which the Heckel treatment has been utilized, have been performed by compressing single materials, drug substances or excipients. Reports concerning compression behaviour of powder mixtures are scarcer (Sheikh-Salem and Fell, 1981; Humbert-Droz et al., 1983; Duberg and Nyström, 1985; Vromans and Lerk, 1988; Garr and Rubinstein, 1991). In the literature, contradictory results from the relationship between compression behaviour of powder mixtures and mixture compositions have been reported. For example, the mean yield pressure and/or compact strength have been related both linearly and non-linearly to mixture composition (Duberg and Nyström, 1985; Riepma et al., 1990; Garr and Rubinstein, 1991). Humbert-Droz et al. (1983) reported a linear relationship between the mean yield pressure and the mixture composition, whereas conflicting data were published by Sheikh-Salem and Fell (1981). In published studies, a variety of methods and materials have been utilized, however, no profound explanations have been given for linear and non-linear relationships. It can be concluded that a complex relationship obviously exists which is affected by material properties and compression process variables.

The purpose of the present paper was to study the possibility of predicting compression behaviour of powder mixtures from the properties of plain mixture components. Compression behaviour of both the plain materials and their powder mixtures was evaluated using the Heckel equation.

Materials and Methods

The materials used were microcrystalline cellulose (Avicel PH 101, FMC Corp., New York, U.S.A.) (MCC), pregelatinized corn starch (Starch 1500, Colorcon Ltd, U.K.), α-lactose monohydrate (DMV Veghel, The Netherlands, sieve fraction 150–297 μm) and dicalcium phosphate dihydrate (Emcompress, E. Mendell, New York, U.S.A.) (DCP). Binary powder mixtures studied were MCC/pregelatinized starch, DCP/MCC, lactose/DCP and pregelatinized starch/lactose.

The binary mixtures were prepared in weight proportions of 100:0, 80:20, 65:35, 50:50, 35:65, 20:80 and 0:100. Both the plain materials and the binary mixtures contained 0.5% w/w magnesium stearate as a lubricant. Binary powder blends were mixed with a Turbula 2P-mixer (W.A. Bachofen, Basel, Switzerland) for 15 min at 90 rpm to obtain a homogeneous mixture; after adding magnesium stearate, mixing was continued for 1 min. The degree of filling of a 2 l glass vessel was about 50%.

The apparent particle density of the plain materials was measured with an air comparison pycnometer (Beckman, Model 930, Fullerton, U.S.A.) as a mean of five measurements using helium as an inert gas (MCC, 1.53 g cm^{-3}; pregelatinized starch, 1.50 g cm^{-3}; α-lactose, 1.55 g cm^{-3}; DCP, 2.36 g cm^{-3}). The apparent particle densities of the binary mixtures were calculated from the values of the mixture components according to their weight proportions in the mixture.

Plane faced tablets, 13 mm in diameter and 350 mg in weight, were compressed with an instrumented eccentric tablet press (Korsch, EK-0, Berlin, Germany) at a running speed of 35 rpm by introducing preweighed powder samples manually into the die. Tablets were compressed at a pressure of 210 MPa, and force/displacement measurements were stored in a PC computer for further analysis. For accurate calculations of porosity-load relationship, elastic deformation of the parts of the tablet press was evaluated and taken into account. Compression behaviour of the plain materials and of the powder mixtures was studied using the Heckel equation (Heckel, 1961):

$$\ln(1/1-D) = kP + A \qquad (1)$$

where D is the relative density of the compact at pressure P. D was calculated by dividing then apparent density of a compact at pressure P by the apparent particle density of the material. The mean yield pressure (P_Y) was obtained as the reciprocal of the slope (k) of the linear portion of the plot. The linear part of the Heckel plots was selected by using the method of least squares ($r^2 > 0.965$).

Results and Discussion

Shape of the Heckel plots

In several studies it has been pointed out that microcrystalline cellulose and pregelatinized starch are plastically flowing materials and crystalline lactose and dicalcium phosphate undergo extensive fragmentation under compression (Cole et al., 1975; David and Augsburger, 1977; De Boer et al., 1978). Besides the solid state properties and chemical structure of material, the deformation properties of materials are also more or less dependent on particle properties, especially particle size, and process variables such as contact time and speed of compression (Roberts and Rowe, 1986). However, the above-described deformation properties of the materials used in this study are undoubtedly the most important and predominate for these materials under the conditions of the present study.

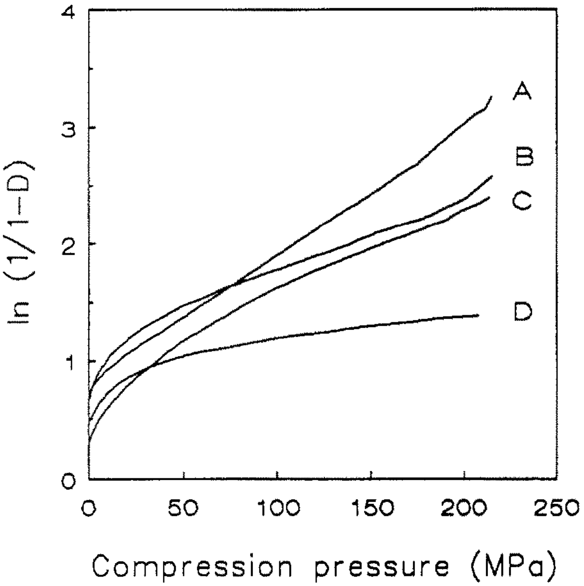

Fig. 1. Heckel plots for plain materials. (A) pregelatinized starch, (B) lactose, (C) microcrystalline cellulose, and (D) dicalcium phosphate dihydrate.

The Heckel plots for the plain materials are presented in Fig. 1. The plots give a general impression of the densification process of the powder column. During the early stages of compression, the densification of lactose and DCP powders was more extensive than that of MCC and pregelatinized starch. This may be partially due to lactose and DCP particles readily undergoing rearrangement at low compression pressure. Obviously, the fragmentation of large aggregates and fracturing of surface asperities of lactose and DCP particles facilitate the further rearrangement and densification at low pressure levels. However, at higher compression pressures, the densification of fragmenting materials was hindered compared to the plastically flowing materials.

In spite of deformation, the plastically flowing primary particles maintain their individuality, and the surface area of particles remains nearly constant (Duberg and Nyström, 1982; Alderborn et al., 1985). It may be assumed that, due to the plastic flow, the contact area between adjacent particles steadily increases as a function of compressional pressure. This means that the porosity, and especially the volume of interparticulate voids decrease steadily with increasing compression pressure. As a consequence, densification of these materials closely follows the Heckel theory over the pressure range, in which particle deformation is the predominant densification process. However, at considerably high pressures the Heckel plots are often curved upwards, which is due to the inadequacy of the function to describe volume changes of a powder column at low porosity and near to the apparent particle density of a material (Roberts and Rowe, 1985). Page and Warpenius (1990) also demonstrated deviations in the Heckel plots for metal powders when compressed close to the apparent particle density. The surface area of lactose and DCP powders is markedly increased due to the fragmentation of particles, especially during the early stages of compression (Alderborn et al., 1985). Thus, at the latter stages, the fracturing of smaller particles becomes increasingly more difficult as more energy is required to initiate particle fracturing (Kendall, 1978). In this respect, an analogy with comminution of solids can be observed (Parrot, 1986). Due to fragmentation, the number of contact points between particles is dramatically increased with increased compressional force, and consequently, stress does not effectively increase (Cole et al., 1975). Curvature of the Heckel plots for the fragmenting lactose and especially DCP is clearly seen, which indicates that the densification of these materials does not follow the Heckel theory as closely as does that of the plastically flowing MCC and pregelatinized starch.

The Heckel plots for the powder mixtures demonstrated that all the mixtures behaved like intermediate materials between the plain mixture components. For example, the Heckel plots for the mixtures of MCC and DCP are observed to be between the plots for plain mixture components (Fig. 2). However, no exact linear relationship in behaviour between the mixtures and plain components was seen. Thus, in most of the cases one mixture component seemed to have more effect on the densification of the powder mixtures than the other.

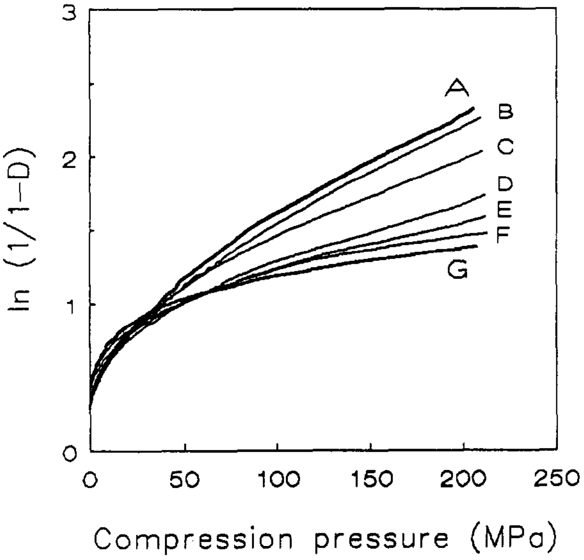

Fig. 2. Heckel plots for the binary mixtures of microcrystalline cellulose (MCC) and dicalcium phosphate dihydrate (DCP). (A) MCC 100%, (B) MCC:DCP 80:20, (C) MCC:DCP 65:35, (D) MCC:DCP 50:50, (E) MCC:DCP 35:65, (F) MCC:DCP 20:80, and (G) DCP 100%.

Deformation properties of powder mixtures

The mean yield pressures (P_Y) for the plain materials and the mixtures are presented in Fig. 3a–d. Deformation described by P_Y may include elastic deformation, plastic flow or fragmentation of particles (Paronen and Juslin, 1983). According to the yield pressures, a clear decreasing tendency of the materials to undergo deformation was seen as pregelatinized starch $>$ MCC $\gg$ lactose $\gg$ DCP. The mean yield pressures with the standard deviations in parentheses were 94 MPa (1 MPa), 106 MPa (2 MPa), 170 MPa (3 MPa), and 471 MPa (7 MPa), respectively. All the mixtures were prepared on a mass fraction basis, and in the case of greatly differing particle densities the volume proportion of the materials deviated from the mass proportion. The relationship between yield pressure and mixture composition is depicted in Fig. 3 by both the mass and volume proportions for DCP/MCC and lactose/DCP mixtures. Due to the very similar apparent particle densities the mass and volume fractions for MCC/starch and starch/lactose mixtures were almost identical, and for the sake of clarity only plots with v/v% fractions have been presented for these mixtures. Powder compaction is a volume reduction process, and the Heckel equation is also based on the volume changes of a powder column during compression. Theoretically, in the analysis of compression behaviour of powder mixtures it is thus more appropriate to consider the volume rather than the mass proportions of components.

For the mixtures of two plastically deforming materials, MCC and pregelatinized starch the relationship between the P_Y and the mixture composition was linear (Fig. 3a). The yield pressures of the plain materials were, however, comparable. A linear relationship can be explained by the nature of deformation process. A plastic flow is dependent on both the applied stress and the duration of the stress at the site of deformation (Cole et al., 1975). Under compression, discrete particles are increasingly deformed after the stress produced by loading has exceeded a yield point of a particle structure. Thus, the total deformation of the powder column proceeds steadily. The mixing of two plastically flowing materials does not change this basic theory.

The constant k ($1/P_Y$) in the Heckel equation may be considered as a rate constant describing the densification as a function of compression pressure. k likely reflects the densification of the whole powder column and not a change in discrete particle. It is then assumed that k, and P_Y, respectively, describe the compression behaviour of a body which consists of discrete particles and voids between them, which is in agreement with literature (Paronen and Juslin, 1983), where yield pressure has been regarded as a constant describing the tendency of compressed material to undergo deformation in general. For plastically flowing materials or mixtures, yield pressure is

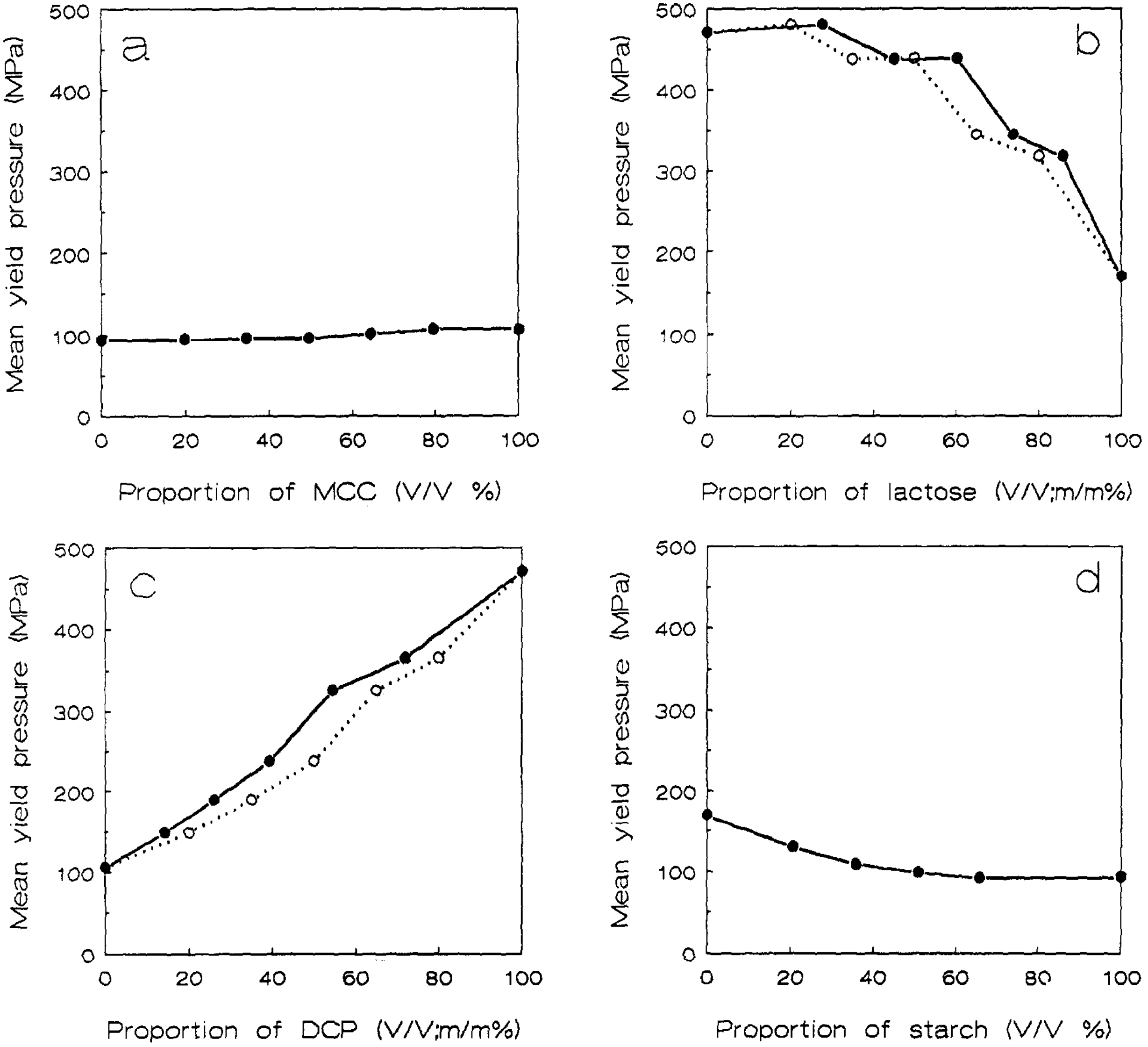

Fig. 3. The mean yield pressures as a function of mixture composition by (●—●) volume (a)–(d) and by (○ · · · ○) mass (b), (c) for the binary mixtures. (a) MCC/pregelatinized starch, (b) lactose/DCP, (c) DCP/MCC, and (d) pregelatinized starch/lactose.

especially relevant, because densification process can be described by linear Heckel plots. According to our results, it seems possible to apply the Heckel equation for a mixture of two plastically flowing materials, and the compression behaviour of a mixture may be regarded as the sum of the behaviour of the components. In this respect, with plastically flowing materials the densification of a particular mixture might be deduced from the densification of the respective mixture components according to their proportions in the mixture. However, due to the very similar behaviour of the plastically flowing test materials used in this study, further experimental data are needed to illustrate this suggestion.

The mean yield pressures for the mixtures of two fragmenting materials, lactose and DCP, showed positive deviations from those predicted from the plain mixture components (Fig. 3b). It seems that the rather poorly compressible DCP, having a markedly higher P_Y, has a greater effect on the compressibility of powder mixtures. The fracturing of brittle particles is basically dependent only on the applied stress (Cole et al., 1975), and fracturing of a brittle particle might be considered as an on/off event. Thus, when the elastic limit of structure is exceeded, fracturing will occur. If the stress is too low, the structure remains intact. It is then suggested that the less deformable particles in powder mixture make up a continuous network or a skeleton which tends to prevent the fracturing of more readily deforming particles. Differences in particle size between the mixture components may have an effect on the event mentioned above. In this study, the greater amounts of DCP (> 50% w/w) mixed with lactose caused rigidity in the powder compact (Fig. 3b). As a result the mean yield pressure of the powder mixture remained close to that of plain DCP.

As discussed earlier, for fragmenting materials non-linear Heckel plots are usually obtained, and generally, the less compressible a material is, the greater is the curvature of the plot obtained. In practice, the mean yield pressure has often been determined for fragmenting materials using a curved Heckel plot, although the application of P_Y is not fully adequate when fragmenting material is considered. The constant *k*, being a linear slope, does not take into account the deviation of the plot from the straight line when obtained from a curved plot. Thus, the constant *k* and P_Y may not describe the densification of a powder column adequately. When two fragmenting materials are involved in a mixture it is theoretically even more inappropriate to evaluate the compressional behaviour of a mixture in respect of the mixture components by using P_Y. This is because P_Y is not an equal measure of densification for all fragmenting materials, i.e., the greater curvature of the plot for harder and less compressible materials is not fully accounted for. This implies that caution is necessary when the Heckel equation is applied for compression studies of powder mixtures, which is in agreement with the study of Duberg and Nyström (1985).

The mean yield pressures for the mixtures of the plastically flowing material with the fragmenting material showed a slight negative deviation from those predicted from the values of plain mixture components (Fig. 3c,d). In the case of DCP/MCC an almost linear relationship was observed (Fig. 3c). In these cases, the mixtures seemed to behave more like the plastically flowing material than the fragmenting material. This may be due to the difference between the nature of the plastic flow and fragmentation. Thus, the more continuous and less stepwise nature of plastic flow tends to dominate the behaviour of a powder mixture at least at higher concentrations of the plastically flowing powder component. Also, due to the nature of plastic flow, more complete volume reduction may occur when a plastically flowing component occupies the pore spaces around the fragmented particles. In the lactose/DCP mixtures DCP, being hard and poorly compressible, seemed to strongly dominate the densification process, however, in DCP/MCC mixtures such an effect was not observed.

Conclusions

Volume reduction mechanisms of powder mixtures seemed to be strongly dependent on the materials. According to our results, it is possible to predict linearly the compression behaviour of the mixtures of two plastically flowing materials. When materials with different deformation properties, i.e., plastically flowing and fragmenting materials, were mixed together the relationship between mixture composition and compression behaviour was non-linear. With DCP/MCC and especially starch/lactose mixtures the mean yield pressures were lower than the values which were interpolated using the mean yield pressures of the plain materials, i.e., the deviation was negative. With the mixtures of two fragmenting materials, lactose and DCP, harder and less compressible DCP seemed to have a strong influence on the compressibility of the mixtures. This was explained by a network of less deformable DCP particles, which prevented deformation of weaker lactose particles. The effect of DCP on compressibility was more pronounced when volume fractions of components were considered. This study has demonstrated that the compression behaviour of powder mixtures is dependent not only on the deformation properties of materials, but also on the combination of different deformation properties. It was concluded that the Heckel equation should be utilized with caution for studies of powder mixtures.

Acknowledgements

The authors wish to thank Ms M. Laakkonen for skilful technical assistance, and the Technology Development Centre of Finland for financial support.

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