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Consolidation and compaction characteristics of a three-component particulate system

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Summary

The consolidation and compaction characteristics of a three-component particulate system consisting of dibasic calcium phosphate dihydrate (DCP), microcrystalline cellulose (MCC) and polyethylene (PE) has been studied. The effects of compression speed on mean yield pressure, extent of particle rearrangement, crushing strength, elastic recovery and energy analysis were measured. It was found that the incorporation of up to 1% w/w of PE in a mixture composed of 25% DCP and 75% MCC did not significantly compromise tablet properties and it was possible to obtain intact compacts at a relatively low compaction force of 5.0 kN. This suggested that the 25% DCP/75% MCC mixture can suitably accommodate the incorporation of a very viscoelastic material without significantly affecting bond strength. The mean yield pressure of DCP-MCC-PE compacts surprisingly decreased with a progressive increase in concentration of PE. It is suggested that relatively greater fragmentation of DCP and more efficient filling of the pores occurs as the elastic PE absorbs more of the applied force. The crushing strength of the tablets decreased with increasing speed of compression, due probably to the elastic nature and extensive energy-absorption properties of PE reducing the overall net compaction energy available for particle-particle bonding. It was found that as the mass fraction of PE was increased, this produced a corresponding increase in the elastic recovery of the tablets, due again to the high elasticity of PE. The extent of particle rearrangement (Db) decreased with increasing concentration of PE; suggesting that adhesion between the particles correspondingly increased, most likely due to complex interactions of the three components.

Introduction

Studies of direct compression have principally focused on the tableting characteristics of single and binary component systems. Pharmaceutical tablets are, however, usually compacted from multicomponent mixtures of excipients and drug substances. Bossart and Stamm (1977) examined the properties of binary mixtures of lactose with dibasic calcium phosphate dihydrate (DCP) and microcrystalline cellulose (MCC), respectively. They found that the tensile strength of the compacts changed linearly with the proportion of MCC. Newton et al. (1977), however, found that the strength of tablets prepared from mixtures of DCP and phenacetin at a slow compaction rate was not a simple function of the strength of the tablets of the individual components.

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Führer and Schmidt (1979) studied the properties of mixtures of MCC with DCP and potato starch and observed that when the deformation characteristics of the starting materials are different, the total energy input required for compact formation was not the arithmetic sum of the energy contributions of the individual components and noted that up to a certain mixing fraction, the mechanically weaker component predominantly underwent deformation.

Sheikh-Salem and Fell (1981, 1982) examined the compaction properties of mixtures of materials with dissimilar compaction mechanisms and observed no simple relationship between Heckel constants determined from pressure-density relationship and the mass fraction of the individual components. In sharp contrast to this observation, Humbert-Droz et al. (1983) reported that mixtures of hydrochlorothiazide and sodium starch glycolate with MCC and DCP, respectively, showed a linear relationship between the mean yield pressure and the proportions of the ingredients.

In an extensive study, Leuenberger (1982, 1985), Leuenberger and Jetzer (1984) and Leuenberger and Rohera (1986a,b) evaluated the compactability and compressibility of binary mixtures of substances with similar and dissimilar compaction mechanisms. A non-linear relationship was found between the compactability of mixtures of anhydrous lactose-sucrose, anhydrous lactose-MCC and aspirin-DCP with the proportion of the individual components. The observed negative interaction between the components was ascribed to the predominant cohesive attraction between the same substances over the adhesive attraction between different substances. However, mixtures of potassium bromide-potassium chloride manifested positive interactions, attributed to the presence of mixed crystals formed under the compaction pressure. The compressibility of the mixtures, with the exception of potassium bromide-potassium chloride mix, was concluded to be the arithmetic mean of the relative proportions of the individual components.

Vromans and Lerk (1988), in a study on the densification properties and compactability of mixtures of excipients with and without magnesium stearate, observed a positive interaction on the consolidation and compaction of binary mixtures of a microfine cellulose with roller-dried β-lactose. The improved compactability was attributed to increased consolidation of the mixture enhanced by the lubricant properties of microfine cellulose.

In 1984, Jackson observed that the addition of small quantities of polyethylene (PE) to plastically deforming materials resulted in greater modifications in compaction behaviour under conditions of dynamic compression compared to static conditions, irrespective of the applied pressure. Time-dependent interparticle bonding, expressed as a function of diametral breaking strength was shown to be significantly reduced. Lactose was found to be able to accommodate similar amounts of PE to those which produced highly detrimental effects on the alkali halides and it was suggested that this was due to the brittle fracture mechanism of lactose.

Garr and Rubinstein (1990) examined the effects of compression speed over the range of 24–1100 mm/s on the properties of mixtures of MCC and DCP, and concluded that the 25% DCP and 75% MCC mixture possessed significant advantages over the individual materials over a wide range of compression speeds.

From a survey of the literature, it appears that no significant work has been reported on the compaction properties of tertiary component systems. The principal aim of the present study was to examine the consolidation and compaction characteristics of the DCP-MCC-PE system employing compression speed, mean yield pressure, extent of particle rearrangement, crushing strength, elastic recovery and energy analysis as parameters for evaluation. The three materials consolidate principally by different mechanisms, MCC by plastic deformation, DCP by fragmentation whilst PE is highly elastic.

Materials and Methods

Materials

MCC and DCP were obtained from Forum Chemicals Ltd, Surrey, U.K. PE (red 44364) was from Micropol Ltd, Stalybridge, U.K. and magnesium stearate was obtained from BDH Chemicals, Poole, U.K.

Particle size fractions

45–125 μm sieve fractions of unsieved PE, MCC and DCP were obtained by sieving the materials through test sieves on a mechanical vibrator (Endecott Ltd).

Mixing

Blends of the materials were prepared by weighing the appropriate quantities and tumbling in a glass bottle attached to an electric motor rotating at 40 rpm for 15 min to produce homogeneous mixtures of 0, 0.25, 0.50, 0.75 and 1.00% of PE in 25% DCP/75% MCC. All the materials were dried in an oven to constant weight at 110°C and stored for 5 days in an oven at 20°C and 45% relative humidity before compression.

Compression

Compression was carried out using The Liverpool School of Pharmacy Modified High Speed Compaction Simulator (ESH Testing Ltd, West Midlands, U.K.), fitted with 12.5 mm flat-faced punches. A sawtooth time-displacement profile was used to control both upper and lower punches. Four tablets were produced at compression speeds from 24 to 500 mm/s. 500 mg constant weight was maintained for all the materials and mixtures, and each tablet was compressed to a maximum compaction force of 5.0 kN. The die wall was cleaned with acetone and prelubricated with 4% w/v magnesium stearate in carbon tetrachloride before each compression.

During compression, upper punch load and punch separation were monitored to an accuracy of ±0.05 kN and ±12 μm, respectively (Bateman, 1988a,b).

Measurement of plastic and elastic energies

The plastic and elastic energies were measured using energy analysis on a force-punch separation plot. A computer program was employed to calculate plastic and elastic energies.

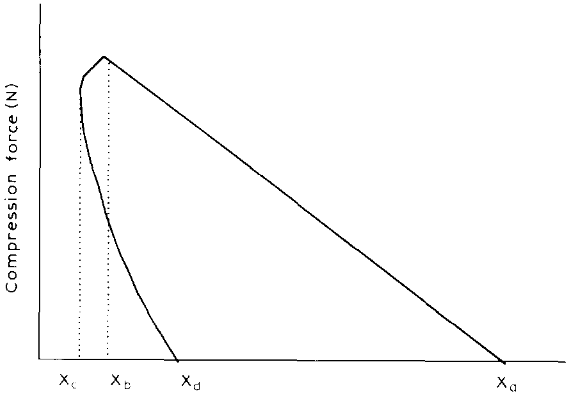

Fig. 1. Schematic diagram of force-punch separation plot used in the energy analysis.

Fig. 1 illustrates schematically the force-punch separation plot, where X_a is the punch separation at the first measurable force, X_b denotes the first occurrence of peak force, X_c is the minimum punch separation and X_d represents the decompression force. The area under the curve X_aX_b (AUC X_aX_b) corresponds to the plastic energy, and that under the curve X_cX_d (AUC X_cX_d) is the elastic energy.

Heckel analysis

An output file of the sorted data was produced from the energy analysis and subsequently used for Heckel analysis employing the Heckel (1961) equation;

$$\ln\left(\frac{1}{1-D}\right)=KP+A$$

where D is the relative density of the tablet at pressure P, and K denotes a material constant which is the slope of the straight line region of the plot, the reciprocal of which is the mean yield pressure. A is the value of the intercept of the straight line and is a function of the initial bulk volume. Regression analyses were carried out on the Heckel plots and the mean yield pressure from four compressions at each speed were determined.

The relative density (D_a) was obtained from the equation:

$$D_a=1-e^{-A}$$

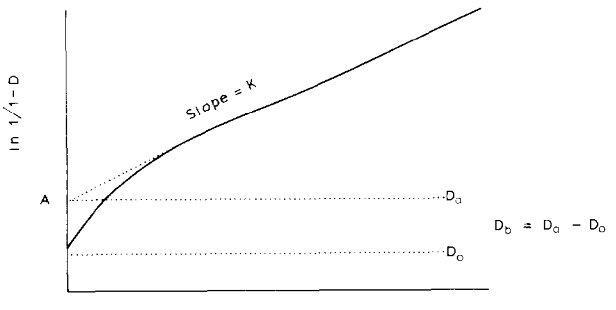

Fig. 2. Schematic representation of the Heckel equation.

The relative density of the powder at the point when a measurable force is applied (D_0) was determined. The extent of particle rearrangement (D_b) was evaluated as the difference between D_a and D_0 (Fig. 2).

Determination of elastic recovery

The elastic recovery of the compact was calculated using the equation described by Armstrong and Haines-Nutt (1972) and Malamataris et al. (1984). The evaluation of elastic recovery is important because the DCP-MCC-PE system contained plastic, elastic and brittle components and may manifest a certain degree of influence on bond disruption and/or rebonding during the decompression phase.

Tablet crushing strength

Tablet crushing strength was determined from the force required to fracture the compacts on a motorised tablet hardness tester (Schleuniger, Model 2E, Switzerland).

Results and Discussion

Earlier work by Jackson (1984), on binary mixtures of sodium chloride and lactose with varying proportions of PE, showed that it was only possible to obtain compacts at a relatively high compaction force of 8.0 kN at low compression speeds of 2, 20 and 50 mm/min (with long dwell times). In the present study, very strong compacts were produced at a lower compaction force of 5.0 kN, at compression speeds ranging from 25 to 500 mm/s (much shorter dwell times), suggesting the capability of the 25% DCP/75% MCC mixture in accommodating incorporation of an elastic material.

The mean yield pressure of DCP-MCC-PE compacts decreased with increasing mass fraction of PE at all speeds of compression (Fig. 3), ascribed to the relatively greater fragmentation of DCP and more efficient filling of the pores as PE absorbs more of the applied compaction force. The nature of the internal matrix of compacts consisting of three components will be a function of the complex interactions occurring during the compression and decompression phases. The application of a compaction force would result in plastic and elastic deformation or brittle fracture, depending on the nature of the materials.

The compaction stages may not normally be ideally separable, however, depending on the magnitude of the compaction force and dwell time, one mechanism of powder consolidation might be expected to predominate. With the application of a compaction force of 5.0 kN to the DCP-MCC-PE system up to a compression speed of 500 mm/s, it appears that the fragmentation of particles is progressively enhanced whilst plastic deformation is correspondingly reduced as compression speed is increased.

The crushing strength of the mixtures decreased with increasing speed of compression, with increasing amounts of PE decreasing the

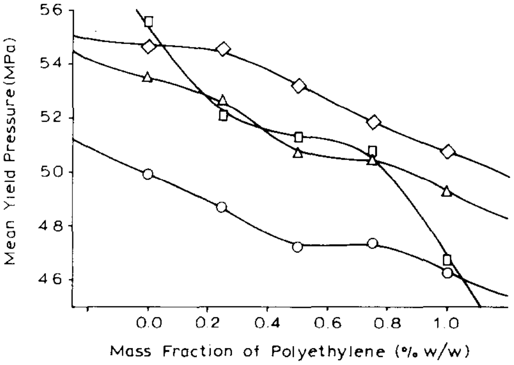

Fig. 3. Mean yield pressure of DCP-MCC-PE compacts at varying speeds of compression. (○——○) 25.0, (△——△) 150.0, (□——□) 330.0, (◇——◇) 500.0 mm/s.

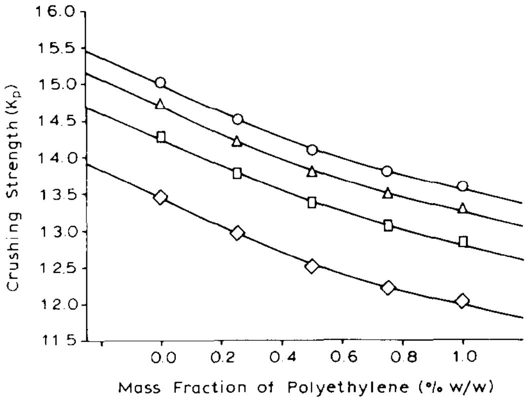

Fig. 4. Crushing strength of DCP-MCC-PE compacts at varying speeds of compression.(○———○) 25.0, (△———△) 150.0, (□———□) 330.0, (◇———◇) 500.0 mm/s.

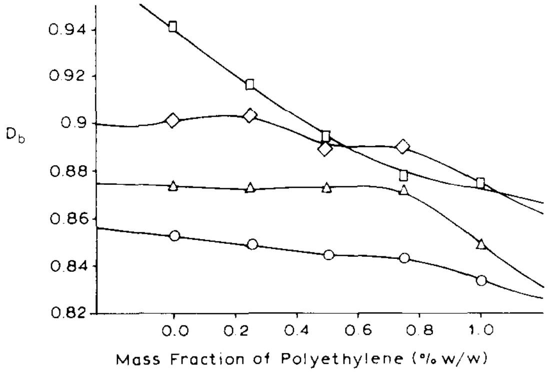

Fig. 6. Extent of particle rearrangement (D_b) for DCP-MCC-PE compacts at varying speeds of compression. (○———○) 25.0, (△———△) 150.0, (□———□) 330.0, (◇———◇) 500.0 mm/s.

tablet strength at all speeds (Fig. 4). This observation can be attributed to PE, being highly elastic in nature and also capable of extensive energy absorption acting as an energy sponge and preferentially absorbing a high proportion of the net energy of compaction. This leads to a possible reduction in the energy available for particle-particle bonding and hence a decrease in crushing strength. PE physically deforms during the compression cycle to increase interstitial contact and subsequently reduces MCC-MCC, DCP-DCP and MCC-DCP particle contact. In addition, high post-compaction elastic recovery of PE may result in bond fracturing of MCC. The use of materials with the same particle size fractions in this study would be expected to promote homogeneous mixing and to prevent the possibility of having areas of high- and low-density PE which may lead to non-uniform stress distributions.

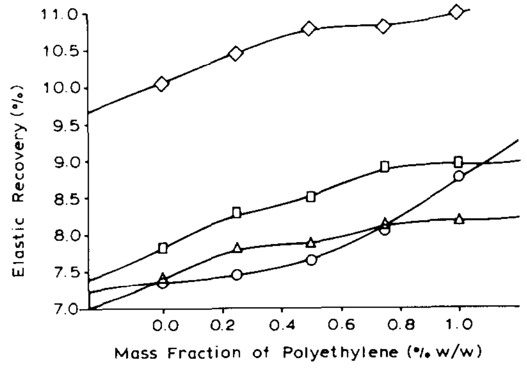

Fig. 5. Elastic recovery of DCP-MCC-PE compacts at varying speeds of compression.(○———○) 25.0, (△———△) 150.0, (□———□) 330.0, (◇———◇) 500.0 mm/s.

The elastic recovery of the DCP-MCC-PE system was found to increase with speed of compression (Fig. 5). Powder mixtures containing viscoelastic materials tend to form compacts less able to resist the recovery of the elastic components. The elastic recovery of the compacts increased with the concentration of PE, attributed to the enhanced elastic deformation of PE. The incorporation of PE (Fig. 6) generally decreased the extent of particle rearrangement (D_b). This can be due to the possibility that complex interactions between the three components resulted in adhesive attraction of powder particles which oppose the rearrangement process.

TABLE 1

Differences in the values of plastic and elastic energies between 0 and 1.0% w/w mass fraction of PE at varying speeds

Compression speed (mm/s)	% increase in plastic energy	% increase in elastic energy
25.00	9.720	60.313
150.00	8.603	61.980
330.00	14.556	52.192
500.00	17.079	27.020

Table 1 summarises the differences in elastic energies between 0 and 1.0% w/w mass fraction of PE. This gives some indication of the relative changes in energy utilisation. At all speeds, the percentage differences in elastic energies were significantly higher than those in plastic energies, as a result of the viscoelastic nature of PE. PE favours energy absorption, stored as elastic energy and thus constrains the plastic energy available for particle bonding. A significant increase in the elastic energy only became apparent at 0.50% w/w of PE, indicating that 0.50% w/w or more of PE will be required for a significant shift in energy ultilization from plastic to elastic dominance.

Conclusion

The consolidation and compaction characteristics of DCP, MCC and PE which exhibit predominantly different compression behaviours have been studied at varying speeds of compression using mean yield pressure, extent of particle rearrangement (D_b) obtained from Heckel analysis, crushing strength, elastic recovery and energy analysis as the basis of the investigation.

The incorporation of up to 1.0% w/w of PE into a 25% DCP/75% MCC mixture did not significantly compromise tablet properties. Intact compacts were obtainable at low compaction forces, hence demonstrating the resistance of a 25% DCP/75% MCC mixture to possible negative effects of incorporating a very viscoelastic material on tablet properties. The mean yield pressure of DCP-MCC-PE compacts decreases with increasing concentration of PE attributed to early fragmentation of DCP which enhanced filling of void spaces and the possible effect of PE in diminishing the impact of MCC on the critical force for fracture of DCP particles.

The crushing strength of the compacts decreased with increasing speed of compression due to the highly elastic nature and extensive energy absorption properties of PE, hence reducing the net energy input available for particle bonding. The elastic recovery of the compacts increased with the mass fraction of PE and compression speed. This can be ascribed to the predominantly elastic nature of PE. The extent of particle rearrangement (D_b) decreased with increasing amounts of PE, due to possible particle adhesions resulting from complex interactions of the components. The elastic energy of the DCP-MCC-PE system significantly increased with the incorporation of PE, the viscoelastic nature of PE tending to promote energy absorption, stored as elastic energy and thus constrained the plastic energy available for particle bonding.

The study indicates the potential of the 25% DCP/75% MCC mixture in favourably accommodating the incorporation of a highly viscoelastic material, although most pharmaceutical powders do not manifest high viscoelasticity. The addition of a perfectly viscoelastic material like PE is an important test in the design of desirable excipient combinations.

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