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Dimensional changes of compacts after compression

P. YORK* AND E. D. BAILY†‡

Department of Pharmaceutics, and †Department of Physics, University of Khartoum, Khartoum, Sudan

A non-contact optical technique has been used to measure changes in the heights and diameters of compacts prepared from sodium chloride, spray dried lactose, two samples of methylcellulose powder and two spray-dried lactose-maize starch granulations. Both sodium chloride and spray dried lactose exhibited relatively small dimensional changes whilst the methylcellulose powders showed up to 30% axial and 3% radial expansion. The results are discussed in terms of the inherent properties of the materials. When the lactose was granulated with maize starch, the ratio of axial : radial strain recovery was reduced from 5·9 : 1 to approximately 1 : 1, suggesting an improved distribution of forces during compression of the granulations.

Dimensional changes which take place in tablets after compression and also on extended storage (Shlanta & Milosovich, 1964; Baba & Nagafugi, 1965; Aulton, Travers & White, 1973) have been explained in terms of creep strain recovery and stress relaxation, both of which are time-dependent processes. Such modifications in tablet dimensions are thought to be associated with deterioration of the mechanical properties of tablets (Aulton & others, 1973).

The tablets and compacts so far examined have usually been compressed from multicomponent pharmaceutical formulations in granular form, and the data yielded little information about the relaxation behaviour of the individual constituents. A study of the dimensional changes of compacts produced from individual pharmaceutical powders and simple granulations of two components could therefore prove of significance in that the relaxation behaviour of individual powders might be distinguished, and also the effect of a second component could be evaluated. Previous techniques for measuring changes in compact dimensions have used contact methods which might lead to modification or damage of compact surfaces, and thereby inaccuracy of measurements. We have used a novel technique for measuring compact dimensional changes, in which an optical non-contact method was used.

MATERIALS AND METHODS

Equipment

The measuring apparatus (Fig. 1) consisted of a micrometer screw gauge (Moore & Wright Ltd., Sheffield) mounted vertically on a flat base plate and positioned so that the centre line of the spindle and anvil was in the plane of the jaws of horizontally mounted callipers (Mitotoya Callipers, Japan). The compact rested on a microscope cover slip glued to the anvil of the micrometer and was positioned so that one edge rested against the fixed jaws of the callipers. A locating mark, along a diameter on the upper face of the compact, was aligned to be in the plane of the jaws. The moveable jaw of the callipers was set to the unconstrained edge of the compact to produce a vertical slit. Similarly, a knife edge attached to the micrometer spindle was aligned close to the upper face of the compact to produce a horizontal slit.

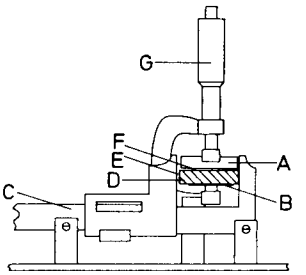

FIG. 1. Compact measuring apparatus. A: Knife edge; B: cover slip; C: callipers; D: compact; E: vertical slit; F: horizontal slit; G: micrometer screw gauge.

The measuring unit was placed in an airtight Perspex box, mounted on a carriage set at one end of an optical bench. At the opposite end of the bench, mounted on carriages, was a helium neon laser (Griffin & George, London) directed so that the light beam could be incident on either of the slits. By observing the Fraunhofer single slit diffraction produced, and by use of a suitable calibration curve, the changes in compact dimension

* Correspondence and present address: Division of Pharmacy, Faculty of Medicine, University of Dar es Salaam, P.O. Box 20693, Dar es Salaam, Tanzania.
‡ Present address: Department of Physics, University of Zambia, P.O. Box 2379, Lusaka, Zambia.

were determined. Full details of the apparatus, theory and calibration technique have been presented elsewhere (Baily & York, 1976).

By displacement of the slits in the horizontal and vertical directions relative to the light beam, it was possible to determine the dimensional changes at various points on the compact surface. The apparatus can be used to detect changes in dimension of the order of 5 nm and thus compares favourably with existing measuring techniques (Aulton & others, 1973).

The Perspex box contained several dishes of silica gel, and the temperature and relative humidity were maintained at 25 ± 1° and 30 ± 5% R.H. throughout the experiments.

Materials

The materials investigated were sodium chloride (Evans Medical Ltd., Liverpool), spray dried lactose (McKesson Robbins, Ramsgate), methylcellulose sample 1 (Tylose MH 1000, Hoechst, Frankfurt, W. Germany) and methylcellulose sample 2 (Tylose MH 4000). The sodium chloride and two methylcellulose powders were sieved to obtain a 355–710 nm size fraction, and the spray dried lactose was used as supplied. All four powders were dried in a hot air oven at 110° for 48 h then stored in dessiccators over silica gel.

The two granulations were made to contain 1·75 and 3·50% w/w maize starch (Hopkins & Williams, Chadwell Heath, Essex). They were prepared by mixing spray dried lactose with a sufficient quantity of an aqueous paste containing 10 and 20% w/w maize starch respectively. The damp mass was passed through a 44 mesh B.S. sieve and the resulting granules were dried at 60° for 48 h in a hot air oven. The granules were then passed through a 120 mesh B.S. sieve to achieve a particle size distribution similar to that of the spray dried lactose (see Fig. 2). The granules were dried further at 110° for 24 h, then stored in desiccators over silica gel.

Relevant physical properties of the powders and granulations are listed in Table 1. Moisture contents were determined by drying samples to constant weight in a hot air oven, particle size measurements by optical microscopy and effective particle densities by the specific gravity bottle technique.

Methods

Powder and granulation weights were determined by preliminary investigations to give a compact nominal height of 6 mm. Compacts were prepared

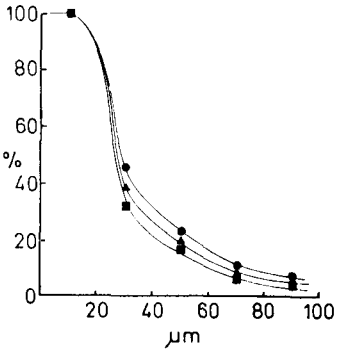

FIG. 2. Particle size distributions of spray dried lactose and the lactose/maize starch granulations. ● Spray dried lactose; ■ 98·25% w/w lactose/1·75% w/w/ maize starch; ▲ 96·5% w/w lactose/3·5% maize starch. y axis–% number of particles less than stated size.

by compressing accurately weighed samples of the materials, using a hydraulic press (Avery Press, Type A806, Avery Balances Ltd., Birmingham), in a 19·0 mm diameter stainless steel die fitted with a close fitting flat-faced stainless steel punch. The die rested on a flat stainless steel plate. The compressing pressure used was 100 MN m^{-2} and the strain rate during compression, constant for all samples, was 3·2 mm s^{-1}. The initial height of the powder bed was determined using a calliper gauge to ± 0·1 mm, and the distance of punch travel during compression was recorded to ± 0·025 mm using a dial gauge. In this way, the volume of the compact under pressure was determined. Before each compression, the die and punch were brushed with a 1% w/v suspension of magnesium stearate in carbon tetrachloride to act as lubricant.

Compacts were ejected from the die in the same direction of compression and at the same machine speed. Immediately after ejection, compact dimensions were measured with a calliper gauge, the compact was marked with a locating mark along a

Table 1. *Physical properties of the powders and granulations.*

Substance	Moisture content (% w/w)	Mean particle size (nm)	Effective particle density (g cm^{-3})
Sodium chloride	0·05	—	2·17
Spray dried lactose	0·27	27·9	1·52
Methylcellulose sample 1	0·21	—	1·37
Methylcellulose sample 2	0·18	—	1·28
Granulation 1 (98·75% lactose, 1·25% maize starch)	0·24	21·7	—
Granulation 2 (96·5% lactose, 3·5% maize starch)	0·29	25·1	—

diameter and then positioned in the measuring apparatus. The dimensions of the compact were then determined in five positions across a selected diameter, in three positions along the edge and the results were averaged. This procedure was repeated at suitable times until no further changes were recorded. In general, five replicate compacts for each powder and granulation were studied, and the results for individual systems averaged. From these measurements, the percentage changes in compact height and diameter, and also changes in porosity, compared with values determined under pressure, were calculated. Values of porosity were obtained using the expression $\epsilon = (1 - \rho_b/\rho)$, where ϵ = porosity, ρ_b = bulk density and ρ = effective particle density.

RESULTS AND DISCUSSION

When a powder is compressed in a die, a complex distribution of residual stresses is established in the compact (Train, 1956). If the pressure is removed and the compact released, an instantaneous elastic recovery results in both axial and radial directions. This is followed by a slower anelastic strain recovery until, finally, irrecoverable plastic strain alone remains (Goldhoff, 1971).

During the period of anelastic strain recovery, the residual stress in the compact changes in an attempt to unify the stress pattern within the compact. Alterations in compact size and shape result, and the criteria for stress relaxation and creep strain recovery, which are constant deformation and constant stress respectively, are not individually satisfied. Consequently, the changes in compact dimensions after initial elastic recovery may be considered in terms of a combination of both processes (Aulton & others, 1973).

The magnitude of compact dimensional changes occurring during the initial elastic recovery stage and slower anelastic period will clearly depend upon the processing history and the inherent physicochemical properties of the material or materials, in addition to factors such as powder particle size and distribution, the lubrication of the die and punch, and the storage conditions of the compact. The individual powders studied, sodium chloride, spray dried lactose, methylcellulose samples 1, and 2, exhibit different degrees of initial elastic recovery. Mean recorded increases in porosity immediately after ejection were 2·05% for sodium chloride, 2·35% for spray dried lactose, 15·00% for methylcellulose sample 1 and 14·90% for sample 2.

Studies with instrumented tablet machines have shown that sodium chloride exhibits only a small degree of non-linear elastic behaviour under compression (Travers, White & Lewis, 1972). Therefore, only a very small proportion of the energy applied under compression is dissipated as internal friction, that is mechanical hysteresis, the remainder being recovered. The change in porosity on ejection would thus be expected to be small. In addition, Ridgway, Shotton & Glasby (1969) have indicated the dependence of elastic properties of crystals on the number of dislocations, or lattice imperfections, in the crystal structure with the compression process creating such dislocations. A stable ionic crystal structure, such as the cubic structure of sodium chloride, would be expected to be more resistant to dislocation than less regular crystalline forms and this may also explain the relatively small change observed.

Crystalline lactose powder has been shown to consolidate primarily by fragmentation and by particle rearrangement within the die during compression (Hersey & Rees, 1970; Cole, Rees & Hersey, 1975). These processes have been demonstrated to occur during the compression of spray dried lactose (Fell & Newton, 1971). The fact that fragmentation and rearrangement dominate during compression over consolidation by elastic and plastic deformation might account for the small increases in porosity observed for compacts prepared from spray dried lactose. In contrast, the two methylcellulose powders exhibit large degrees of initial elastic recovery, indicating a significant storage of the energy imparted during compression in large numbers of dislocations in the non-regular crystal structure of the polymer molecules.

The mean percentage increases in axial and radial compact dimensions, and increase in compact porosity, compared with calculated values under a pressure of 100 MN m^{-2} are shown in Figs 3, 4 and 5 respectively, for compacts prepared from each of the four single powders. The coefficient of variance for replicate compacts was found to be less than 5%.

The relaxation curves all exhibit a reduction in strain recovery with time and this observation is in direct agreement with results for other pharmaceutical materials (Baba & Nagafuji, 1965; Aulton, & others, 1973). Different times at which the rate of change falls to zero, that is when strain recovery ceases, are observed for the compacts prepared from the different powders. The estimated times are 1 h for sodium chloride and spray dried lactose

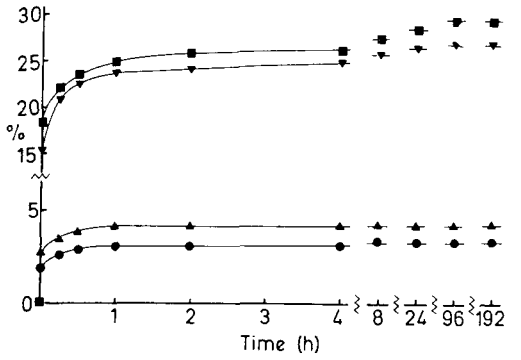

FIG. 3. Changes in compact height. ● Sodium chloride compacts; ▲ spray dried lactose compacts; ▲ methylcellulose, sample 1 compacts; ■ methylcellulose, sample 2 compacts. y axis–% axial strain recovery.

compacts, and approximately 96 h for compacts prepared from the two methylcellulose powders. For the latter two powders, this is associated with larger axial and radial dimensional changes compared with sodium chloride or spray dried lactose.

A short time to attain full strain recovery and stress relaxation with minimal dimensional modification is to be preferred when selecting tablet excipients to minimize changes in physical properties on storage, such as tablet strength (Rees & Shotton, 1970) and tablet cracking (Aulton & others, 1973). For spray dried lactose compacts, the observed 1 h for full relaxation and the small axial and radial changes, 4·2 and 0·75% respectively, point to its suitability as a tablet excipient. For both methylcellulose powders, longer periods of anelastic strain recovery with large dimensional changes are observed. Figures for the overall increase in axial and radial strain recovery are 27·5 and 2·4% respectively for sample 1. Corresponding figures for sample 2 are 29·6 and 2·9%. The larger values for sample 2 are attributed to the longer polymer chain, and thereby more resilient nature of this

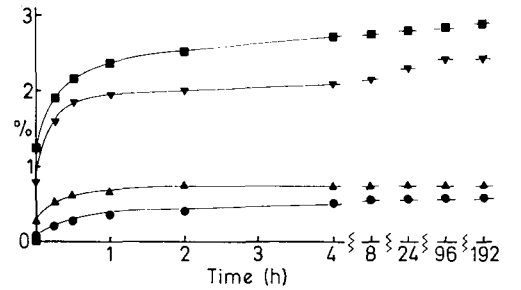

FIG. 4. Changes in compact diameter. Symbols as in Fig. 3. y axis–% radial strain recovery.

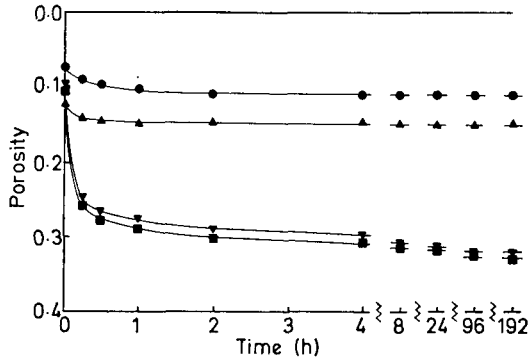

FIG. 5. Changes in compact porosity. Symbols as in Fig. 3.

material, compared with sample 1. It is possible that under pressure the polymer chains would 'coil' with the degree of spiralling related to the molecular weight of the polymer. When the pressure is removed, varying degrees of strain recovery and stress relaxation would result for different molecular weight polymers as the chain 'uncoils'.

Previous workers have used differing time scales when investigating strain recovery of compacts after compression. Baba & Nagafuji (1965) recorded exponential relaxation curves during the first 5 min after compression whilst Aulton & others (1973) obtained similar curves for approximately forty days for certain compacts stored under conditions of high humidity. The latter investigation, however, represents relaxation data for granulated composite materials and in addition incorporates a moisture sorption factor, possibly causing swelling of granulating agents present in the granulations. The time values for complete strain recovery in the present investigation represent a fundamental consideration of the stress relaxation properties of the individual powders and indicate that the time after compression appears to be a factor to be considered when assessing physical properties of compacts.

The ratio of axial : radial strain recovery for the sodium chloride compacts over the period of testing remained approximately constant at 5·5 : 1. The corresponding ratios for spray dried lactose, methylcellulose sample 1 and sample 2 are 5·9 : 1, 11·5 : 1 and 10·2 : 1 respectively. The axial : radial strain recovery ratio has been stated to depend upon the efficiency of the transmission of forces during compression of a powder (Aulton & others, 1973). The lower ratios observed for sodium chloride and spray dried lactose compacts compared with

compacts prepared from the methylcellulose powders suggest less energy loss due to such factors as internal interparticular friction and die wall friction.

The effect of granulating spray dried lactose with maize starch on the axial and radial relaxation curves is illustrated in Figs 6 and 7. Although similar overall percentage radial dimensional changes are observed for both granulations studied, compared with the spray dried lactose alone, significant reductions in the percentage axial recovery are observed for the granulations, with the axial : radial strain recovery ratio approaching 1 : 1. This change in ratio indicates an improvement in the efficiency of force distribution during compression in the presence of maize starch. It is interesting to note from Fig. 6 that the degree of axial strain recovery appears to be dependent on the maize starch concentration. By further experimentations, it might be possible to select suitable tablet excipients and their optimum concentrations in particular formulations with respect to achieving minimum strain recovery.

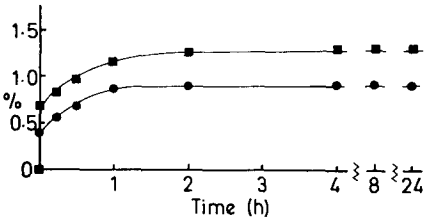

FIG. 6. Changes in height of compacts prepared from the two lactose/maize starch granulations. ● Granulation 1; ■ granulation 2. y axis–% axial strain recovery.

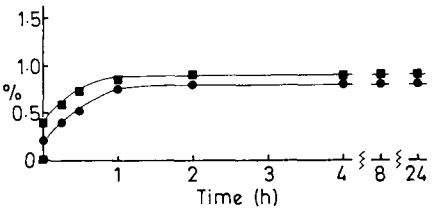

FIG. 7. Changes in diameter of compacts prepared from the two lactose/maize starch granulations. ● Granulation 1; ■ granulation 2. y axis–% radial strain recovery.

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