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# The influence of crystal form on the radial stress transmission characteristics of pharmaceutical materials

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Various crystal forms of sulphathiazole, barbitone and aspirin were compressed in a single-punch tablet machine instrumented to monitor axially applied and radially transmitted forces, and upper punch movement. The changes in radial stress during the compression cycle depended upon the polymorphic form of the compressed material. The results were rationalized in terms of the degree of plastic flow/crushing that occurred with each material, and the degree to which the final compact underwent elastic compression. It is postulated that the reduction in the transition temperature of polymorphic forms of sulphathiazole and barbitone and the polymorphic transition of sulphathiazole Form II was due to the production of dislocations in the crystal and the distortion of the crystals at crystal boundaries formed in the compressed materials.

The production of a compact by compression of powder is dependent, firstly, upon the effective utilization of the forces applied to the powder bed, and secondly, the deformation characteristics of the material.

The force of compression transmitted through the bed will have an axial and radial component. Whereas the axial component has often been investigated (see, for example Rees, 1967), pharmaceutical studies of the radially transmitted force have been relatively few. Using a method similar to that described by Windheuser, Misra & others (1963) and Higuchi, Shimamoto & others (1965), Leigh, Carless & Burt (1967) monitored radial force by bonding two strain gauges to the walls of a modified die of a single-punch tablet machine.

With regard to the deformation characteristics of the powder, Stewart (1950) expressed the view that the greater the plasticity of the powder, the greater was the likelihood of formation of a compact. The deformation would bring the contacting surfaces closer together with a consequent increase in area of contact. Jaffe & Foss (1959) suggested that materials of high melting point formed harder compacts than those of low melting point because of the greater molecular forces of cohesion between particles in the former compacts.

Several workers have speculated on the possible differences in the compression characteristics of polymorphic forms of pharmaceutical materials. Milosovitch (1963) suggested that different polymorphic forms of a material could possess different direct-

compression characteristics. Both he and Shell (1963) indicated that crystal habit could also have a profound effect on the compression of solids, not only because of effects due to particle shape but also because of the anisotropic nature of organic crystals. Thus the influence of polymorphic form on compression characteristics is likely to be a complex function of crystal habit, crystal anisotropy and effects due to the inherent differences in the crystal structure of the polymorphs.

The purpose of the present study has been to investigate the difference in the pressure transmission characteristics of various crystal forms of aspirin, barbitone and sulphathiazole to gain some insight into the above influences.

## MATERIALS AND METHODS

*Instrumentation of tablet machine*

A Manesty E2 single-punch tablet machine fitted with ½in diameter flat faced punches was instrumented in the manner described by Leigh (1969) to enable measurement of applied and transmitted forces. Four strain gauges (Budd Type C6 121A MetaFilm foil gauges) were bonded around the shank of the upper punch in a "Poisson arrangement" (Perry & Lissner, 1962) and connected as a Wheatstone bridge. Similarly, four gauges (Micro Measurements Type EA-06-125AD-120) were mounted on the cut-away die surface to monitor the transmitted radial force. Displacement of the upper punch was measured using a Honeywell Type LD11 linear displacement transducer. The signals from these systems were amplified with Honeywell Type CA2506 carrier amplifiers and recorded on a Honeywell 1706 Visicorder. Each monitoring system was calibrated in the manner described by Leigh (1969).

*Preparation of the crystal forms*

(a) *Aspirin.* Three crystal forms of aspirin (Forms I, II and IV) were prepared as described previously (Summers, Carless & Enever, 1970) and the 250–353 $\mu$m mesh sieve fractions reserved for this study.

(b) *Sulphathiazole.* The Form I and II polymorphs of sulphathiazole (Moustafa & Carless, 1969) were prepared by recrystallization of a commercial sample of sulphathiazole powder from water and n-propanol respectively. Both 190–251 and 104–152 $\mu$m mesh sieve fractions were used.

(c) *Barbitone.* Forms I, II and III of barbitone were prepared (Huang, 1951). Forms II and III were obtained by crystallization of a commerical sample of barbitone powder from water and a dilute, ammoniacal, aqueous solution respectively, while Form I was prepared by heating Form II at 160° until the transformation to Form I was complete (10 to 20 min). The 190–251 and 104–152 $\mu$m mesh sieve fractions of all three forms were obtained, and, in addition granules of barbitone Form II crystals were prepared by wet granulation of 104–152 $\mu$m crystals using a 4% w/v solution of gelatin in water, and subsequently collecting the 190–251 $\mu$m fraction.

*Characterization of crystal forms*

The crystal forms of aspirin, sulphathiazole and barbitone were characterized by differential scanning calorimetry (Perkin-Elmer D.S.C.1). Infrared spectra were also obtained for sulphathiazole and barbitone polymorphs (examined as Nujol mulls with a Unicam SP200 recording spectrophotometer). The apparent densities of the crystal forms were determined at 20° using 20 cm$^3$ specific gravity bottles and approx-

imately 1 g quantities of the materials. The displacement media used for aspirin, sulphathiazole and barbitone were light petroleum (B.P. 100–120°), light liquid paraffin and water respectively.

*Tableting procedure*

From a knowledge of the diameter of the die, the weight of crystals placed in the die, and the depth of penetration of the upper punch, it was possible to calculate the density of the compact and relate it to the crystal density. With all materials examined, it was found that the relative density of the compact reached a value of at least 0·99 at an applied pressure of 237 MN $m^{-2}$. Thus it was shown that the weight of material necessary to give a final compact height of 4·00 mm could be calculated using the crystal density. The required weight of material to give a final compact height of 4·00 mm at 237 MN $m^{-2}$ was placed in the die and compressed in pressure increments of 21·6 MN $m^{-2}$ every 0·5 s to the maximum of 237 MN $m^{-2}$ using the method of Leigh (1969). After ejection, a portion of the material was removed from different regions of the compact with a scalpel and subjected to differential scanning calorimetry to determine whether there was any change in crystal form of the material. Four replicate determinations were performed for each crystal form. Subsequently, two compacts of each crystal form were prepared as described, and, after relubricating the die, each compact was returned to the die and recompressed up to a maximum pressure of 237 MN $m^{-2}$. When the compact laminated it was not ejected from the die before recompression.

The above procedure was carried out for all the sieve fractions of the various crystal forms of aspirin, sulphathiazole and barbitone. Additionally, the three crystal forms of aspirin were compressed to a pressure of 237 MN $m^{-2}$, the compacts produced were comminuted in a mortar and the 251–353 $\mu$m mesh sieve fractions collected. These slugged fractions were then compressed to the maximum pressure.

The forces transmitted through a compact could be converted to stress values from a knowledge of the dimensions of the die and the change in compact height with compression force. In this work the assumption has been made that the radial stresses are averaged over the length and circumference of the compact. This technique has been discussed by Leigh (1969).

## RESULTS

Table 1 shows the densities, melting points and, where applicable, the transition temperatures of the crystal forms used. The thermal behaviour of the polymorphic forms of barbitone was found to correspond with that reported by Huang (1951), while the infrared spectra of these forms were similar to the data published by Cleverley & Williams (1959). The data obtained for sulphathiazole were consistent with those reported by Moustafa & Carless (1969) for Forms I and II, and Mesley (1971).

Table 1 also shows the values for the melting points and transition temperatures of the crystals after compaction to 237 MN $m^{-2}$.

Figs 1, 2 and 3 show the stress transmission characteristics of the barbitone (190–251 $\mu$m) and aspirin (251–353 $\mu$m) crystal forms. Table 2 shows the radial stress/axial stress slope values (stages labelled OA, AB, BC, CD, DE and EF in Fig. 1), for the whole compression cycle for all three materials. The yield stresses, residual radial stresses and maximum radially transmitted stresses (Point A, distance OF and point B respectively in Fig. 1) are shown in Table 3.

Table 1. *Melting points, transition temperatures and densities of crystal forms.*

| Crystal form | Density (g cm$^{-3}$ at 20°) | Before compression: Transition Temp (°C) | | Before compression: Melting point (°C) | After compression to 237MN m$^{-2}$: Transition temp (°C) | | After compression to 237MN m$^{-2}$: Melting point (°C) |
|---|---|---|---|---|---|---|---|
| Sulphathiazole (190–251 μm) | | | | | | | |
| Form I | 1·54 | 163 | | 201 | 150 | | 200 |
| Form II | 1·53 | — | | 201 | 129‡ | | 200 |
| Barbitone (190–251 μm) | | | | | | | |
| Form I | 1·29 | — | — | 191 | — | — | 189 |
| Form II | 1·30 | — | 156* | 190 | — | 147 | 189 |
| Form III | 1·30 | 116† | 156 | 191 | 114 | 150 | 189 |
| Aspirin (251–353 μm) | | | | | | | |
| Form I | 1·40 | — | | 135 | — | | 133 |
| Form II | 1·38 | — | | 129 | — | | 127 |
| Form IV | 1·36 | — | | 125 | — | | 124 |

‡ This transition was only observed in two of five compacts tested.
* Form II——> Form I
† Form III——> Form II ——> Form I.
Before granulation the barbitone had thermal properties corresponding to Form II.

Table 2. *Radial stress/axial stress slope values for the crystal forms.*

| Crystal Form | Radial stress/axial stress slope values: Loading OA | Loading AB | Unloading BC | Unloading CD | Unloading DE | Unloading EF |
|---|---|---|---|---|---|---|
| Sulphathiazole (190–251 μm) | | | | | | |
| Form I | 0·20 ± 0·004 | 0·33 ± 0·02 | 0·15 | 0·24 | 0·52 | — |
| Form II | 0·21 ± 0·003 | 0·38 ± 0·02 | 0·22 | 0·29 | 0·83 | — |
| Barbitone (190–251 μm) | | | | | | |
| Form I | 0·20 ± 0·01 | 0·27 ± 0·006 | 0·10 | 0·15 | 0·50 | 1·4 |
| Form II | 0·21 ± 0·006 | 0·26 ± 0·02 | 0·11 | 0·17 | 0·40 | 1·8 |
| Granules of Form II | 0·24 ± 0·01 | 0·31 ± 0·02 | 0·10 | 0·20 | 0·30 | 1·4 |
| Form III | 0·22 ± 0·007 | 0·33 ± 0·01 | 0·12 | 0·25 | 0·50 | 2·0 |
| Aspirin (251–353 μm) | | | | | | |
| Form I | 0·32 ± 0·01 | 0·37 ± 0·05 | 0·23 | 0·37 | 0·50 | 1·6 |
| Form II | 0·16 ± 0·006 | 0·29 ± 0·02 | 0·17 | 0·29 | 0·33 | — |
| Form IV | 0·20 ± 0·01 | 0·33 ± 0·01 | 0·12 | 0·33 | 0·50 | 1·0 |
| Slugged aspirin (251–353 μm) | | | | | | |
| Form I | 0·30 ± 0·01 | 0·38 ± 0·05 | 0·20 | 0·32 | 0·50 | 0·83 |
| Form II | 0·23 ± 0·006 | 0·34 ± 0·02 | 0·21 | 0·31 | 0·42 | 0·62 |
| Form IV | 0·20 ± 0·01 | 0·33 ± 0·01 | 0·14 | 0·30 | 0·42 | 0·62 |

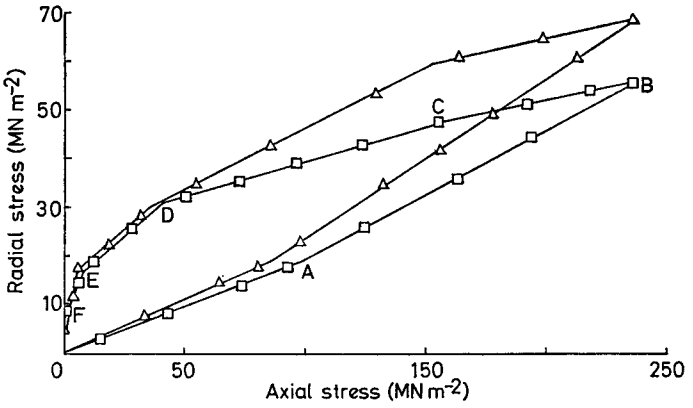


Fig. 1. The relation between axial and radial stress for Form I and Form III barbitone crystals (190–251 $\mu$m) □ Form I. △ Form III. OA—the plastic flow/crushing stage of compact formation. A—the yield stress point. AB—deformation stage of the formed compact. B—maximum radially transmitted stress. BC, CD, DE and EF—stages of relaxation of compact. OF—residual radial stress.

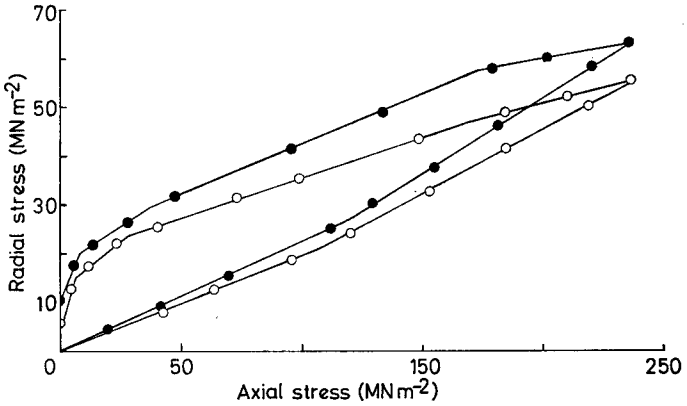


FIG. 2. The relation between axial and radial stress for Form II barbitone crystals and granules (190–251 $\mu$m). ○ Form II crystals. ● Form II granules.

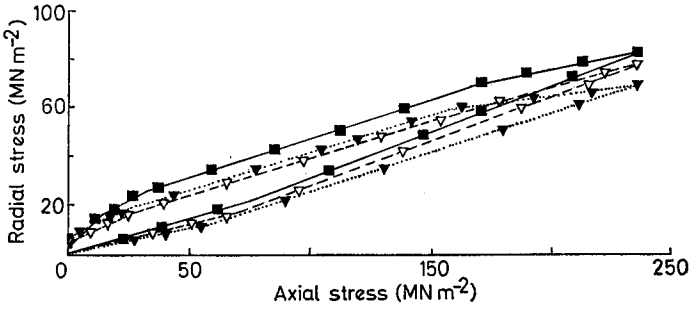


FIG. 3. The relation between axial and radial stress for aspirin crystal forms (251–353 $\mu$m). ■ Form I. ▽ Form IV. ▼ Form II.

Table 3. *The yield stresses, residual radial stresses, and maximum radially transmitted stresses of the crystal forms and Poisson ratios and elastic moduli of compacts of crystal forms.*

| Crystal Form | Yield stress* (MN m$^{-2}$) | Residual radial stress† (MN m$^{-2}$) | Maximum radially transmitted stress (MN m$^{-2}$)‡ | Poisson ratio | Elastic modulus $\times 10^{-3}$MN m$^{-2}$ |
|---|---|---|---|---|---|
| Sulphathiazole (190–251 $\mu$m) | | | | | |
| Form I | 114 ± 5 | 12·3 ± 2·0 | 61·9 ± 4 | 0·160 ± 0·016 | 5·6 ± 0·02 |
| Form II | 102 ± 5 | 7·8 ± 1·1 | 69·7 ± 3 | 0·190 ± 0·014 | 5·1 ± 0·06 |
| Barbitone (190–251 $\mu$m) | | | | | |
| Form I | 100 ± 5 | 5·9 ± 1·2 | 56·0 ± 4 | 0·150 ± 0·015 | 4·9 ± 0·05 |
| Form II | 108 ± 6 | 5·9 ± 0·8 | 55·5 ± 3 | 0·140 ± 0·022 | 4·9 ± 0·04 |
| Granules of Form II | 120 ± 5 | 10·3 ± 0·5 | 63·0 ± 2 | 0·180 ± 0·016 | 5·1 ± 0·09 |
| Form III | 86 ± 7 | 4·9 ± 0·5 | 68·5 ± 2 | 0·185 ± 0·012 | 4·7 ± 0·05 |
| Aspirin (251–353 $\mu$m) | | | | | |
| Form I | 59 ± 2 | 2·0 ± 0·7 | 84·5 ± 3 | 0·240 ± 0·008 | 5·1 ± 0·09 |
| Form II | 53 ± 4 | 4·0 ± 0·6 | 63·0 ± 3 | 0·170 ± 0·009 | 7·5 ± 0·20 |
| Form IV | 41 ± 6 | 5·0 ± 0·8 | 77·0 ± 2 | 0·200 ± 0·011 | 6·3 ± 0·08 |
| Sulphathiazole (104–152 $\mu$m) | | | | | |
| Form I | | | | 0·155 ± 0·016 | 5·7 ± 0·02 |
| Form II | | | | 0·195 ± 0·014 | 5·0 ± 0·06 |
| Barbitone (104–152 $\mu$m) | | | | | |
| Form I | | | | 0·155 ± 0·015 | 5·0 ± 0·05 |
| Form II | | | | 0·145 ± 0·022 | 5·0 ± 0·04 |
| Form III | | | | 0·190 ± 0·012 | 4·8 ± 0·05 |
| Slugged Aspirin (251–353 $\mu$m) | | | | | |
| Form I | 75 ± 2 | 2·9 ± 0·7 | 83·5 ± 2 | 0·230 ± 0·008 | 6·1 ± 0·09 |
| Form II | 70 ± 4 | 4·2 ± 0·6 | 78·5 ± 2 | 0·190 ± 0·009 | 6·5 ± 0·20 |
| Form IV | 57 ± 4 | 5·5 ± 0·6 | 68·7 ± 2 | 0·180 ± 0·011 | 7·5 ± 0·08 |

* Point A, Fig. 1. † OF Fig. 1. ‡ Point B, Fig. 1.

## DISCUSSION

### *The effect of crystal form on the yield stress*

It is evident from Table 3 that there are differences in the yield stresses of crystal forms of a material. These yield stresses (point A, Fig. 1) were found to be in reasonable agreement with the yield strength value of the material obtained by application of the Heckel (1961) equation as described by Hersey & Rees (1970), see also Summers (1972). To explain these differences in yield stress, it is necessary to consider the phenomenon of crushing and plastic flow of a material. Crushing is essentially a process of bond rupture under stress, usually perpendicular to a given crystal plane. Plastic flow occurs in order to relieve the applied stress in a material, and is usually a process of molecular movement caused by movement of dislocations in the crystal. Plastic flow will occur more easily in structures having high potential energy (weak molecular attractive forces), since imposition of even small stresses will impart sufficient additional energy to induce molecular movement (Griffith, 1920; Houwink, 1958). Since the higher-temperature-stable forms of crystals (e.g. sulphathiazole

Form II and barbitone Form I) usually have a more open structure than the low-temperature-stable forms (i.e. sulphathiazole Form I and barbitone Form II) and are regarded as forms of higher potential energy (Bueger, 1951), then this phenomenon would account for their lower yield stress values (Table 3). Since barbitone Form III is unstable and transforms to Form II over a period of time, it probably exists in a higher energy state than Form II. This fact also correlates with the observed lower yield stress value for the Form III polymorph.

The increased yield stress of barbitone Form II granules compared with barbitone Form II crystals of the same sieve fraction may be due to their surface roughness which produces a greater number of point contacts within a bed of granules. Thus the area of contact between granules will be greater than between crystals. It therefore follows that for a given applied axial force, the pressure developed at the points of contact will be lower and hence the recorded yield stress value for the granule bed will be higher.

The yield stresses of the 251–353 $\mu$m mesh aspirin crystal forms are in the order Form I > Form IV, and this corresponds to the order of their melting points (Summers & others, 1970). Houwink (1958) considered the relation between the interatomic energy of an atomic bond, and the melting point of a solid. His conclusions indicate that, for a material having several crystal forms, the form with the lowest melting point will have the least intermolecular attractive forces and probably the least yield stress value at a given temperature. Thus, our data are consistent with this hypothesis, and further reinforce the suggestion that the observed differences in the melting point of these forms may be due to differences in the crystal structure.

*The radial stress/axial stress slope values obtained during loading*

The relation between axial and radial stress during loading may be divided into two stages represented by slope values OA and AB (Table 2). Slope OA gives a measure of transmission during the plastic flow/crushing stage of compact formation, whereas slope AB reflects the transmission of stresses once the compact has been formed (Leigh, 1969). The marginally higher values (OA) obtained with sulphathiazole Form II and barbitone Form III correlate with their lower yield stress values and also point to a greater degree of plastic flow occurring with these forms. For barbitone Form I however, statistical analysis shows that the slope OA is not significantly different from that of the low-temperature-stable Form II. The reason for this anomaly is not understood. The increase in the value of OA for barbitone Form II crystals after granulation is probably the result of the greater number of point contacts in the bed. Once sufficient axial force has been applied to exceed the yield point of the material, there will be a greater number of points at which plastic flow can occur and hence a greater degree of flow will result.

The aspirin form with the highest melting point (Form I) has higher radial stress/axial stress slope values (both OA and AB) than the lowest melting point form, Form IV. This is thought to be due to the exceptional behaviour of Form II and Form IV crystals. Compression of crystals causes movement of dislocations. If this movement is hindered by the presence of other dislocations, then a greater stress must be applied before further dislocational movement occurs. This phenomenon is termed work-hardening, and it may be responsible for the low radial transmission characteristics of Form IV. Ridgway, Glasby & Rosser (1969) showed that aspirin crystals undergo work hardening, and it is possible that many dislocations were

produced in this Form because of its rapid crystallization from highly supersaturated solution (Parker & Washburn, 1955). The very low values of the slopes OA and AB of Form II aspirin are thought to be due to preferred orientation of the crystals in the die. The flat needles of this form tended to align themselves parallel to the punch face forming a layered structure. Windheuser & others (1963) have found that such structures exhibit low lateral stress transmission characteristics. Crystals of Forms I and IV were of a more chunky shape and did not form this layered structure.

*The influence of crystal form on the relaxation behaviour of compressed materials*

With all three materials some degree of elastic hysteresis was observed when the compression force was gradually reduced. Fig. 1 is an example of the hysteresis exhibited by barbitone Forms I and III. The induced elastic potential energy will be released on removal of the compressive forces, but the plastic component will remain as a residual radial pressure because of the permanent strain induced in the compact.

(a) *Elastic component.* It is apparent that the elastic component is released in definite stages (Figs 1, 2 and 3) of increasing magnitude characterized by the slopes BC, CD, DE, and EF. From Tables 2 and 3 it seems that for any one of the three materials, the polymorphic form having the greatest maximum radially transmitted stress on compression has the higher slope values for all stages of relaxation.

(b) *Plastic component.* Barbitone Form III and sulphathiazole Form II have lower residual radial stress and higher maximum radially transmitted stress values than their corresponding low-temperature-stable forms. Aspirin Forms IV and I show a similar inverse relation, whereas aspirin Form II departs from this general behaviour. This is probably due to the formation of the layered structure on compression of the Form II crystals. With the exception of the latter form, the differences in the residual radial stress values must reflect the differences in the elastic/plastic properties of the polymorphic forms of the materials.

*Derivation of the Poisson ratios and elastic moduli of formed compacts*

The Poisson ratio, $\nu$, defines the degree to which a body expands laterally when compressed axially, i.e.

$$\nu = \Delta DL/D\,\Delta L \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad (1)$$

where $\Delta D$ is the increase in diameter D, and $\Delta L$ is the decrease of length L. Bodies that have little tendency to expand radially will therefore have low Poisson ratio values.

From considerations of perfect elastic behaviour, Leigh (1969) suggested that the Poisson ratio of a material could be calculated from the force ratio, $n_F$, of a formed compact after yield:

$$n_F = 2\nu \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad (2)$$

where $n_F$ is the ratio of the radially transmitted to the axially applied force for a compact of material after yield.

From the decrease in height of a formed compact when subjected to recompression, Leigh (1969) defined the elastic modulus, E, as:

$$E = \sigma_A L/\Delta L \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad (3)$$

where $\sigma_A$ is the axial pressure.

Table 3 shows the derived Poisson ratios and elastic moduli of the compacts obtained from 190–251 $\mu$m mesh crystals of barbitone and sulphathiazole and the 251–353 $\mu$m mesh aspirin. The higher Poisson ratios and lower elastic moduli obtained with sulphathiazole Form II and barbitone Form III when compared with their other polymorphic forms indicate that the solid compacts are more compressible. If the behaviour of a solid compact is similar to the crystalline material, then there is a correlation with their lower yield stresses and higher values of OA, and is a consequence of the more open lattice structure of these crystals.

Since sulphathiazole Form II, barbitone Form III and aspirin Form I are the most compressible of their crystal forms, they will possess the greatest amount of elastic strain energy which is released on removal of axial pressure. This accounts for the more rapid relaxation of radial stress with these forms as manifested by their higher stress ratios BC (Table 2). This effect is reinforced in the cases of sulphathiazole Form II and barbitone Form III because their low yield stresses result in the polymorphs undergoing elastic compression over a greater range of axial pressure.

Form II aspirin compacts are relatively inelastic when compared with the other aspirin forms (lowest Poisson ratio and highest elastic modulus) and this again points to the formation of a layered structure on compression of this form.

*Plastic flow, residual strain and change in polymorphic form*

Table 1 shows that the values obtained for the transition temperatures and melting points of the various crystal forms were modified upon compression. The melting points were all reduced by 1 or 2°, whilst sulphathiazole Form I and barbitone Forms II and III showed lower transition temperatures after compression. In addition, sulphathiazole Form II showed transition to Form I in two of five compacts examined.

Phenomena associated with solid phase changes and reductions in melting points are likely to be due to the influence of dislocational strain in crystals (Gregg, 1968; Thomas, 1970). Polymorphic transitions in the solid state occur through a mechanism of nucleation and growth of a second phase within the first (Cahn, 1950). Dislocations act as preferential nucleation sites because they possess higher free energy and this effectively reduces the energy necessary for transition. The abnormal stereochemistry in the vicinity of the dislocation also aids nucleation (Cahn, 1950).

Dislocational strain will be induced in a crystal during plastic flow and this will enable nucleation to proceed more readily. In addition the junctions between crystals in the compact will be highly strained due to mismatch of the crystal lattices and these grain boundaries have also been reported as nucleation centres (Azarof, 1960). These mechanisms could account for the transformation of sulphathiazole Form II to Form I as well as the lowering of transition temperatures in the present work.

It is unlikely that these results are due to impurities or moisture, as the same material was tested before, and after compression. Any impurity would, therefore, be present in both instances, and the moisture content will not be significantly different after compression. Since the same thermal data were obtained using samples from both the interior and the surface of the compact, the die wall lubricant cannot be responsible for this.

*Examination of the influence of crystal habit upon compression chracteristics*

In order to eliminate the influence of crystal habit, the aspirin crystal forms were slugged, and, subsequent to comminution to the same sieve fraction, the compression

characteristics re-examined. It was possible to adopt this approach, since the aspirin forms did not undergo phase transformation upon compression. Tables 2 and 3 contain the relevant information upon the compression characteristics, and Fig. 4 shows the axial-radial stress relationships. The slugged forms of the crystals were very similar in appearance and confirmed that the original crystal shapes had been eliminated. The maximum radially transmitted stress values (Table 3) of Forms I and IV are slightly lower than those of the original forms. This may be ascribed to the work-hardening of the crystals upon original compression and would also account for the higher values of yield stresses of the slugged crystals. The compression characteristics of the Form II crystals changed drastically after slugging, the level of radial stress

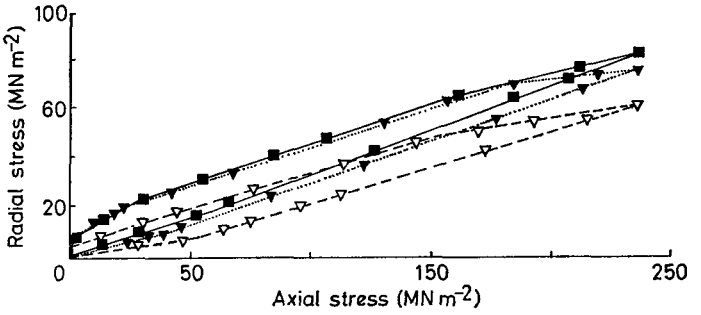


FIG. 4. The relation between axial and radial stress for slugged aspirin crystal forms (251–353 $\mu$m). ■ Form I. ▽ Form IV. ▼ Form II.

transmission increasing above the value observed for Form IV crystals. This increase may be ascribed to the modified material showing less tendency to form a layered structure on compression. In a similar manner, Higuchi & others (1965) demonstrated an increased value of radially transmitted stress with powdered materials originally used by Windheuser & others (1963) in the form of flakes.

Since slugging of sulphathiazole and barbitone crystal forms to modify the crystal habit was not possible because of crystal form transition, smaller sieve fractions (104–152 $\mu$m) of these materials were used in an attempt to eliminate crystal habit effects. However, there was no significant change in the compression characteristics of the different crystal forms, and it would appear that the observed differences in compression characteristics between the crystal forms are due in large measure to the different molecular arrangements which exist in the different polymorphic forms of a crystal.

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