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The Effects of Lag-time and Dwell-time on the Compaction Properties of 1 : 1 Paracetamol/microcrystalline Cellulose Tablets Prepared by Pre-compression and Main Compression

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Abstract

The effects of lag-time and dwell-time on the compaction properties of tablets compressed from a 1 : 1 blend of paracetamol and microcrystalline cellulose have been examined using a compaction simulator.

Increases in lag-times (from 0·06 to 0·53 s) resulted in small increases in the tensile strengths of the tablets when combinations of 80 and 160 MPa were used as the compression pressures. Further increases in lag-time did not alter the tablet strengths. When combinations of 240 and 320 MPa were used for pre-compression and main compression, the effects on the tensile strengths were more complex, partly because the high elastic recoveries of the tablets resulted in greater variability in the data. Increases in lag-times from 0·06 to 0·97 s resulted in an increase of between 12 and 28% in tensile strength. Longer lag-times (1·24 or 1·52 s) did not result in further increases in tensile strength. The application of a dwell-time of 0·26 s during pre-compression or main compression pressures of 80 and 160 MPa generally led to a decrease (14–22%) in tensile strength compared with tablets where no dwell-time was used. This was because of increases in both the elastic recoveries and elastic energies. Subsequent increases in dwell-time from 0·26 to 0·9 s resulted in increases in tablet strength compared with that obtained when no dwell-time was applied. The tensile strengths of tablets made with a pre-compression of 160 MPa then a main compression of 80 MPa were 11–33% higher than those of tablets made with a pre-compression of 80 MPa then a main compression of 160 MPa. This was because higher plastic energies and more plastic deformation occurred at the higher pre-compression.

Generally, the application of dwell-time resulted in greater increases in tensile strengths than lag-time, which had less effect on the compaction properties.

Pre-compression is the preliminary compression force applied by some rotary presses immediately before the main compression. Its force is usually smaller than that used for the main compression. Pre-compression can reduce the incidence of capping and lamination (Hiestand et al 1977; Carstensen et al 1985).

Lag-time is the time interval separating pre-compression and main compression. Vezin et al (1983a) found that pre-compression increased the tensile strengths of tablets compressed from blends of paracetamol with microcrystalline cellulose or a 1 : 1 microcrystalline cellulose–dicalcium phosphate dihydrate mixture. Separating pre-compression and main compression by a relatively long time interval (approximately 0·2 s) was more important than dwell-time in increasing compact strength, suggesting the involvement of relatively slow, time-dependent phenomena. Vezin et al (1983b), using microcrystalline cellulose, dicalcium phosphate dihydrate and Starch 1500, confirmed that the separation time between the two compression events was more important than dwell-time in controlling tablet hardness.

Dwell-time refers to the period when the punch faces of a tablet press are stationary relative to each other during compaction (Jones 1981). The dwell-time on eccentric tableting machines might not be

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well defined because compression forces reach a maximum value and then immediately decrease. In rotary presses a definite, though short, dwell-time is encountered (Armstrong 1989).

Hiestand et al (1977) proposed that pre-compression effectively extended the dwell-time of the compression because the compact was held under load during two periods of contact. This increased the extent of stress-relaxation resulting in the formation of stronger tablets. Mann (1984) showed that the effects of pre-compression were, in fact, a combination of a reduction of air entrapment during compaction and an increase in stress-relaxation during compaction. The extent of each mechanism depended on the porosity of the powder bed, on the punch speed and on the magnitude of the applied pressures (Mann et al 1982).

Paracetamol is poorly compressible and deforms elastically (Obiorah 1978). Microcrystalline cellulose forms extremely strong tablets and deforms plastically (David & Augsburger 1977). Their blends might have plasto-elastic behaviour (Bangudu & Pilpel 1985). The optimum mixture of the two powders with regard to tensile strength, friability and absence of capping, was a 50:50 microcrystalline cellulose–paracetamol mixture (Yu et al 1988).

The aim of this investigation was to determine the effects of lag- and dwell-times on the compaction properties of tablets containing 1:1 paracetamol-microcrystalline cellulose compressed with combinations of pre-compression and main compression pressures.

Materials and Methods

Materials

Paracetamol B.P. (Sterling Organics, Dudley, UK) and microcrystalline cellulose (FMC Corporation, PA) were separately sieved on a nest of test sieves (Endecott Ltd, London, UK) to furnish their 45–125 μm size fractions. These fractions were dried to constant weight at 110°C. A 1:1 blend of the powders was mixed by use of a tumbling mixer (Erweka Apparatebau GmbH, Germany). This mixture, moisture content 0·91%, was stored over silica gel until used.

Methods

Compression. The powder mixtures (500 ± 1 mg) were compressed with a Compaction Simulator (ESH Testing, West Midlands, UK), using double saw-tooth control profiles to provide the required pre-compression and main compression pressures as described previously (Akande et al 1997).

Low pre-compression pressures of 80 and 160 MPa produced tablets with greater increases in tensile strength as the main compression pressure increased (Akande et al 1997), and were thus used for the lag- and dwell-time studies. In addition, pressure combinations of 240 and 320 MPa or 320 and 240 MPa, respectively, were used to provide high pressures for the lag-time studies. Lag-times of 0·06, 0·30, 0·53, 0·70, 0·97, 1·24 or 1·52 s separated the pre-compression and main compression with no dwell-times allowed for each compression during lag-time studies. Adjustments were also made such that the material was held under load during pre-compression for dwell-times of 0, 0·26, 0·38, 0·50, 0·65, 0·77 or 0·90 s followed by main compression with no dwell-time, and vice versa, during dwell-time studies. Four tablets were produced for each experimental variable.

Tablet analyses. The radial and axial thicknesses of the tablets were determined to an accuracy of ± 1 μm with a digital micrometer (Mitutoyo, Tokyo, Japan) immediately after compression. Tablet crushing strengths were determined by use of a hardness tester (Model 2E; Dr K. Schleuniger, Zurich, Switzerland). The crushing strengths and the thickness data were used to determine the tensile strengths of the tablets (Fell & Newton 1970).

For a system in which the upper and lower punches are both mobile, punch separation can be plotted against the upper punch force and the area under this curve will be the work done or the energy of the compression (Ragnarsson & Sjögren 1983, 1985). The plastic and elastic energies of tablets were determined by energy analysis of the force-punch separation plot. The total energies for each combination of compression conditions were obtained by addition of the corresponding energies of pre-compression and main compression.

The elastic recoveries (Armstrong & Haines-Nutt 1972) and stress-relaxations (Malamataris et al 1984) at different stages of compression in-die and on ejection were determined from the tablet thicknesses obtained from the compaction data (Figure 1) or from measurement by micrometer. When no dwell-times were used for either pre-compression or main compression, stress-relaxation was defined as the change in thickness of the tablet from when the maximum pressure was applied to when the upper punch no longer applied any pressure on the tablet or to when the material was held under load when dwell-times were applied. The elastic recoveries were determined when the material was no longer in contact with the punch faces.

The tensile strength data were subjected to statistical analysis using a two-way analysis of var-

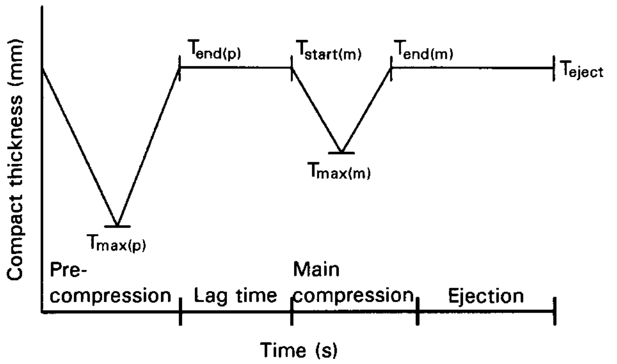

Figure 1. Schematic representation (not drawn to scale) of displacement against time for a typical compression cycle, indicating the points when the thicknesses of compacts were assessed. $T_{max(p)}$ is the thickness of the compact at maximum pre-compression, $T_{end(p)}$ is the thickness at end of the pre-compression, $T_{start(m)}$ is the thickness at start of the main compression after the lag-time, $T_{max(m)}$ is the thickness at the maximum of the main compression, $T_{end(m)}$ is the thickness at end of main compression and T_{eject} is thicknesses of the tablets on ejection.

iance and Tukey's test for the multiple comparison of means. The elastic recoveries, stress-relaxation and energy analyses data were subjected to two-way analysis of variance.

Results and Discussion

Effects of lag-time

Figure 2 shows the effect on tensile strength of varying the lag-time from 0·06 to 1·52 s. Pressure combinations of 320/240 MPa or 240/320 MPa produced tablets with higher tensile strengths than combinations of 160/80 or 80/160 MPa. The total plastic or elastic energies for the pre-compression and main compression combined (Figures 3 and 4) and the ratios of total elastic energy to total plastic energy (Figure 5) were similarly higher for the combinations of higher pressures. The data for stress-relaxation for combinations of 160/80 MPa were lower than when 320/240 MPa were used (Table 1). The elastic recoveries during lag-time were generally lower for 160/80 MPa than for 320/240 MPa and the elastic recoveries of tablets on ejection, ER(e), were not affected by lag-times.

A pre-compression of 160 MPa then a main compression of 80 MPa (Figure 2) generally produced tablets with higher tensile strengths (between 1 and 10%) than when a pre-compression of 80 MPa was followed by a main compression of 160 MPa (Figure 2). Two-way analysis of variance confirmed that these differences were significant. Varying the lag-times from 0·53 to 1·52 s for tablets made using either combination of 160/80 MPa pressures did not affect the tensile strengths (Tukey's test; $P > 0·05$). The tensile strengths only

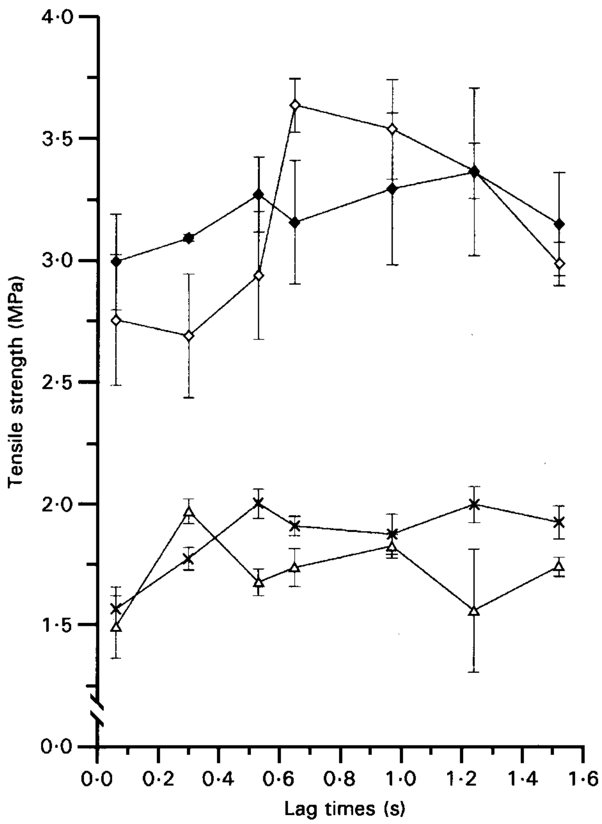

Figure 2. The effect of lag-times on the tensile strengths of tablets produced by: ×, a pre-compression pressure of 160 MPa followed by a main compression pressure of 80 MPa; △, a pre-compression pressure of 80 MPa followed by a main compression pressure of 160 MPa; ◇, a pre-compression pressure of 320 MPa followed by a main compression pressure of 240 MPa and ◆, a pre-compression pressure of 240 MPa followed by a main compression pressure of 320 MPa.

significantly ($P < 0·05$) increased as lag-time was increased from 0·06 to 0·53 s when a pre-compression of 160 MPa was used.

When the pressure combinations of 320/240 or 240/320 MPa were used (Figure 2) the data were more complicated. Lag-time did not appear to influence the tensile strengths of the tablets when the pre-compression pressure was 240 MPa, as the data were statistically indistinguishable ($P > 0·05$; Tukey's test). However, when a pre-compression of 320 MPa was followed by a main compression of 240 MPa, significant ($P < 0·05$) increases in tensile strength (between 10 and 28% over the tensile strengths at 0·06 s lag-time) were observed as the lag-times were increased from 0·30 to 0·65 s. This increase in tensile strength conforms with the observation that the tensile strength of microcrystalline cellulose tablets increased with increasing lag-time (Vezin et al 1983a); this was attributed to provision of a longer interval during which stress-relaxation and escape of air could take

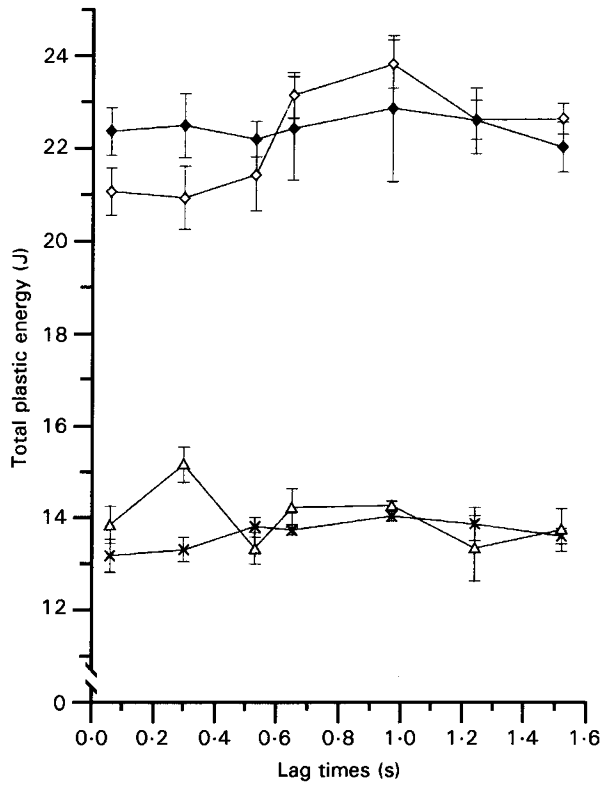

Figure 3. The effect of lag-times on the total plastic energies of both pre-compression and main compression of tablets combined: ×, a pre-compression pressure of 160 MPa followed by a main compression pressure of 80 MPa; △, a pre-compression pressure of 80 MPa followed by a main compression pressure of 160 MPa; ◇, a pre-compression pressure of 320 MPa followed by a main compression pressure of 240 MPa; and ◆, a pre-compression pressure of 240 MPa followed by a main compression pressure of 320 MPa.

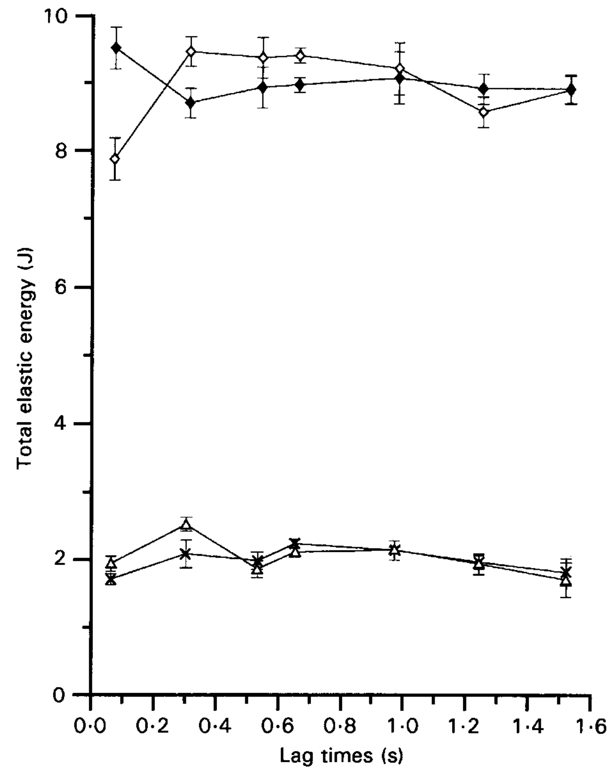

Figure 4. The effect of lag-times on the total elastic energies of both pre-compression and main compression of tablets combined: ×, a pre-compression pressure of 160 MPa followed by a main compression pressure of 80 MPa; △, a pre-compression pressure of 80 MPa followed by a main compression pressure of 160 MPa; ◇, a pre-compression pressure of 320 MPa followed by a main compression pressure of 240 MPa; and ◆, a pre-compression pressure of 240 MPa followed by a main compression pressure of 320 MPa.

place. The tensile strengths (Figure 2) decreased by approximately 16% as the lag-time was further increased from 0·65 to 1·52 s; this might be because of the high values of the ratios of total elastic energy to total plastic energy (Figure 5) as more elastic deformation of the material was taking place with increasing lag-time.

The energy analyses for the combined compressions (Figures 3–5) followed the trends in tensile strengths (Figure 2). The total plastic energies for a pre-compression of 320 MPa increased as the lag-times increased from 0·03 to 0·97 s, whereas those for a pre-compression of 240 MPa were unaffected (Figure 3). The total elastic energies (Figure 4) when a pre-compression of 320 MPa was used increased as the lag-times increased from 0·06 to 0·30 s, but decreased when the pre-compression was 240 MPa. Significant increases in the total plastic and elastic energies were observed only between lag-times of 0·06 and 0·53 s when a pre-compression of 160 MPa were used (Figure 3). With pre-compression of 80 MPa, lag-time did not generally affect the plastic (Figure 3) or elastic energies (Figure 4).

Varying the lag-time had no effect on stress-relaxation during pre-compression as lag-times were applied after pre-compression. Thus, there were no changes in the stress-relaxation during a pre-compression of 160 MPa, a pre-compression of 80 MPa, a pre-compression of 320 MPa or a pre-compression of 240 MPa (Table 1). Stress-relaxation during a main compression was also not significantly affected by increases in lag-times from 0·06 to 1·52 s. That is, main compression of 80 MPa, 160 MPa, 240 MPa or 320 MPa (Table 1) were all similar as the lag-time increased. However, stress-relaxation during a pre-compression of 160 MPa was greater than that during a pre-compression of 80 MPa, indicating that more stress-relaxation occurred at higher pre-compression than at lower pre-compression. Stress-relaxations during a main compression of 80 MPa were also lower than during a main compression of 160 MPa at all lag-times. This indicates that the higher the com-

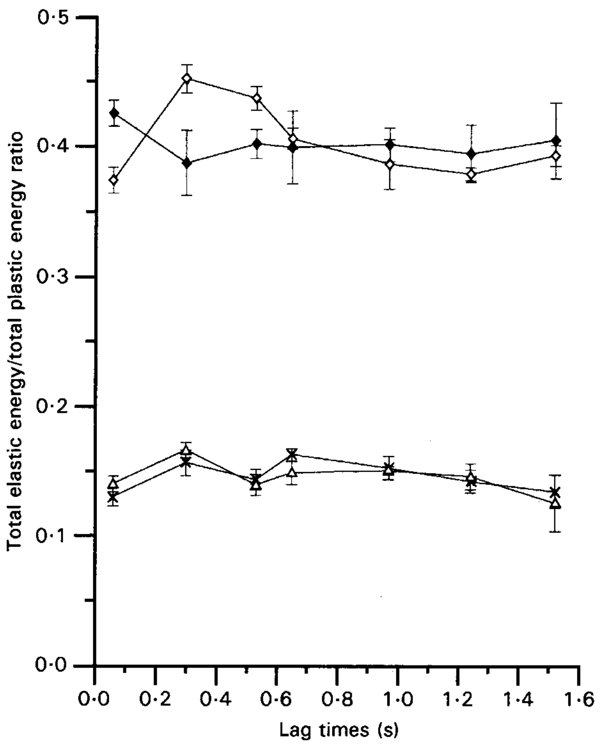

Figure 5. The effect of lag-times on the ratios of total elastic energy to total plastic energy of the pre-compression and main compression pressure of tablets combined: ×, a pre-compression pressure of 160 MPa followed by a main compression pressure of 80 MPa; △ a pre-compression pressure of 80 MPa followed by a main compression pressure of 160 MPa; ◇, a pre-compression pressure of 320 MPa followed by a main compression pressure of 240 MPa; and ◆, a pre-compression pressure of 240 MPa followed by a main compression pressure of 320 MPa.

pression pressure, either as pre-compression or main compression, the greater the extent of stress-relaxation that would take place.

The elastic recoveries during lag-time after pre-compressions of 160 MPa and 80 MPa (Table 1) decreased considerably as the lag-times increased from 0·06 s to 0·65 s. Further increases in lag-time did not significantly effect the elastic recoveries. The elastic recoveries after a pre-compression of 80 MPa were higher than after a pre-compression of 160 MPa at all lag-times. The stress-relaxations increased and the elastic recoveries decreased with increasing pre-compression pressure. From the values of the elastic recoveries when pressure combinations of 80/160 or 160/80 MPa were used (Table 1), a lag-time of 0·53 s seemed to be critical. Subsequent increases in lag-time did not lead to further decreases in the elastic recoveries.

There was a significant increase in recoveries during the lag-time after a pre-compression of 320 MPa or 240 MPa (Table 1) as the lag-time increased from 0·06 to 0·30 s. Recovery during the lag-time after a pre-compression of 320 MPa decreased as the lag-times were increased to 0·97 s, with no further significant change as the lag-time was increased to 1·52 s. Trends in the recoveries during the lag-time after a pre-compression of 240 MPa were similar. The large increases in the elastic recoveries as the lag-times increased from 0·06 to 0·30 s (Table 1) were probably associated with the high total plastic and elastic energies (Figures 3 and 4) and the ratios of total elastic energy to total plastic energy (Figure 5). The elastic recoveries of the tablets on ejection, (Table 1) were unaffected by increases in the lag-times as the values did not change significantly as the lag-times increased from 0·06 to 1·52 s. High values of elastic recoveries were a result of the high ratios of elastic energy to plastic energy resulting from the material becoming more resistant to deformation.

The high values of the elastic recoveries after pressures of 240 and 320 MPa also confirm that such pressures could cause capping and lamination. The observed increase in tensile strengths (Figure 2) despite the high elastic recovery, was because of the high main compression pressure of 240 and 320 MPa that followed the high pre-compression that then helped in the consolidation of the bonds that might have broken as a result of the elastic recovery after pre-compression.

Hiestand et al (1977) suggested that the pre-compression pressure should be near the maximum that would not introduce lamination to maximize stress-relaxation. High pre-compression pressures of 240 and 320 MPa approximate those pressures which could produce lamination, because lamination was observed for some tablets during testing for crushing strength. However, these tablets had not shown signs of capping or lamination before testing.

The results seem to indicate that there was a length of lag-time between pre-compression and main compression that resulted in an increase in tensile strength, especially at the higher pressures used in this study. However, the decrease in tensile strength when the lag-time was 1·52 s at the high pressure combinations, and the erratic changes in tensile strengths at the pre-compression pressure of 320 MPa (Figure 2) suggest that such a high pressure is not ideal for use as pre-compression with the particular blend used in this study. The data for the 240/320 MPa pressures (Figure 2) also showed considerable spread indicative of a weakening of the tablets because of the high elastic recoveries of the compacts and the high amounts of energy stored in the compact, as reflected by the ratios of elastic energy to plastic energy.

Table 1. Effect of varying the lag-times between pre-compression and main compression on stress-relaxation and elastic recovery of 1 : 1 paracetamol-microcrystalline cellulose tablets.

Lag-time (s)	0·06	0·30	0·53	0·65	0·97	1·24	1·52
Pre-compression 160 MPa; main compression 80 MPa							
Stress-relaxation during pre-compression (%)	7·3 ± 0·5	7·2 ± 0·4	6·8 ± 0·2	6·8 ± 0·2	6·6 ± 0·1	6·8 ± 0·4	6·6 ± 0·3
Elastic recovery during lag-time after pre-compression before main compression (%)	17·1 ± 1·7	11·7 ± 1·8	6·4 ± 0·3	6·3 ± 0·3	6·9 ± 0·8	6·6 ± 0·3	6·5 ± 0·2
Stress-relaxation during main compression (%)	3·0 ± 0·3	5·1 ± 0·2	5·2 ± 0·4	6·1 ± 0·2	5·9 ± 0·3	5·3 ± 0·2	4·8 ± 0·3
Elastic recovery on ejection (%)	10·3 ± 0·2	9·7 ± 0·1	9·0 ± 0·3	9·3 ± 0·2	9·5 ± 0·4	9·2 ± 0·3	9·1 ± 0·4
Pre-compression 80 MPa; main compression 160 MPa							
Stress-relaxation during pre-compression (%)	5·2 ± 0·2	5·5 ± 0·2	4·9 ± 0·0	5·1 ± 0·2	5·0 ± 0·3	5·0 ± 0·3	5·0 ± 0·1
Elastic recovery during lag-time after pre-compression before main compression (%)	31·2 ± 0·2	20·2 ± 1·0	9·1 ± 1·9	7·2 ± 0·5	7·1 ± 0·5	8·4 ± 0·8	6·9 ± 0·6
Stress-relaxation during main compression (%)	7·5 ± 0·1	8·3 ± 0·2	7·5 ± 0·7	7·5 ± 0·1	7·6 ± 0·1	7·4 ± 0·3	6·9 ± 0·4
Elastic recovery on ejection (%)	8·4 ± 0·5	8·1 ± 0·3	8·8 ± 1·4	8·1 ± 0·3	7·9 ± 0·3	8·7 ± 0·9	8·1 ± 0·3
Pre-compression 320 MPa; main compression 240 MPa							
Stress-relaxation during pre-compression (%)	13·2 ± 0·4	12·7 ± 0·3	12·3 ± 0·2	11·9 ± 0·2	11·7 ± 0·2	11·5 ± 0·2	11·8 ± 0·5
Elastic recovery during lag-time after pre-compression before main compression (%)	11·4 ± 1·4	25·7 ± 1·2	24·9 ± 0·5	23·6 ± 0·6	21·0 ± 1·8	20·2 ± 0·7	20·9 ± 1·0
Stress-relaxation during main compression (%)	9·3 ± 0·1	10·6 ± 0·3	10·7 ± 0·1	10·5 ± 0·3	10·6 ± 0·5	10·1 ± 0·4	10·3 ± 0·3
Elastic recovery on ejection (%)	7·9 ± 0·5	8·2 ± 0·5	7·6 ± 0·6	7·1 ± 0·3	7·6 ± 0·4	7·4 ± 0·4	7·5 ± 0·4
Pre-compression 240 MPa; main compression 320 MPa							
Stress-relaxation during pre-compression (%)	12·9 ± 0·8	11·3 ± 0·4	11·9 ± 0·2	11·7 ± 0·4	11·7 ± 0·2	11·3 ± 0·5	11·7 ± 0·2
Elastic recovery during lag-time after pre-compression before main compression (%)	18·8 ± 0·4	32·5 ± 1·3	28·8 ± 0·3	27·7 ± 1·1	27·9 ± 0·8	26·3 ± 0·3	27·3 ± 1·1
Stress-relaxation during main compression (%)	14·2 ± 0·2	13·8 ± 0·5	13·8 ± 0·2	13·7 ± 0·4	13·9 ± 0·2	13·8 ± 0·3	14·0 ± 0·1
Elastic recovery on ejection (%)	13·9 ± 0·4	13·8 ± 0·3	13·1 ± 0·4	13·2 ± 0·5	13·2 ± 0·6	13·2 ± 0·2	13·2 ± 0·3

Values are the means of results from four tablets ± s.d.

Effects of dwell-time

The effects of dwell-time on the tensile strengths of tablets are shown in Figure 6. The effects of dwell-times on total plastic energies (Figure 7), the total elastic energies (Figure 8) and the ratios of total elastic energy to total plastic energy (Figure 9) of tablets made with both pre-compression and main compression combined are also shown. For tablets compressed with a pre-compression pressure of 160 MPa then a main compression of 80 MPa (Figure 6), increases in the dwell-times from 0·0 to 0·90 s during the main compression resulted in significant increases ($P < 0{\cdot}05$) of approximately 22% in the tensile strengths of the tablets compared with when there was no dwell-time. Tukey's test showed that the data with dwell-times of 0·65, 0·77 and 0·90 s were indistinguishable from each other ($P > 0{\cdot}05$) but were significantly higher ($P < 0{\cdot}05$) than the data obtained with lower dwell-times.

The total plastic energies for combined pre-compression and main compression also increased significantly ($P < 0{\cdot}05$) with increases in dwell-time during main compression (Figure 7); this is similar to the observed increase in the tensile strength data. The stress-relaxation after the pre-compression and main compression increased, and the elastic recoveries decreased.

For the other three combinations of pre-compression and main compression pressures (Figure 6), an increase in dwell-time from 0·00 to 0·26 s resulted in significant ($P < 0{\cdot}05$) decreases (between 14 and 22%) in the tensile strength of the tablets. Subsequently, as the dwell-times were increased from 0·26 to 0·90 s, tensile strength increased significantly ($P < 0{\cdot}05$), between 22 and 35% for all the pre-compression and main compression pressure-combinations. The total plastic energies for pre-compression and main compression combined also decreased as the dwell-time was increased from 0 to 0·26 s (Figure 7). The elastic recoveries during a pre-compression of 160 MPa or a pre-compression of 80 MPa increased (between 7–18% and 7–21%, respectively) as the dwell-times increased from 0 to 0·26 s (Table 2). Subsequent compressions, either low or high, had similar effect on the elastic recoveries.

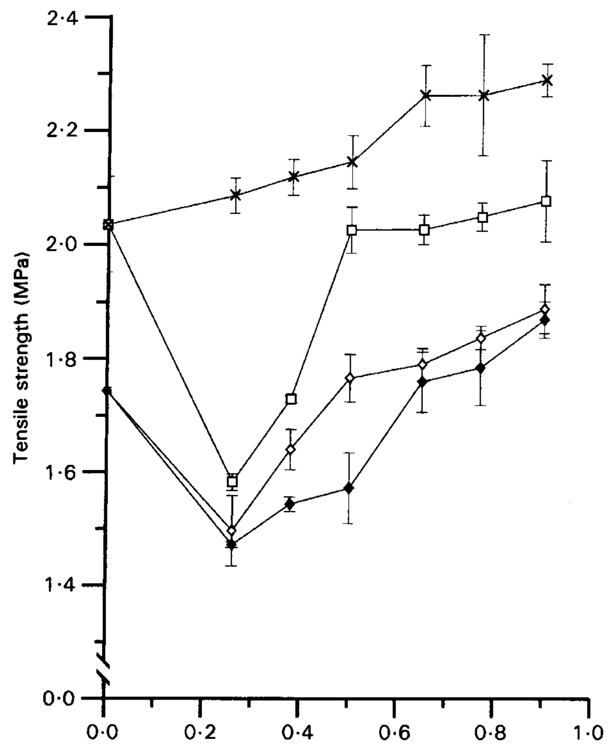

Figure 6. The effect of dwell-times on the tensile strength of tablets produced at different pre-compression and main compression pressures: ×, a pre-compression pressure of 160 MPa followed by a main compression pressure of 80 MPa with varied dwell-times; □, a pre-compression pressure of 160 MPa with varied dwell-times followed by a main compression pressure of 80 MPa; ◇, a pre-compression pressure of 80 MPa followed by a main compression pressure of 160 MPa with varied dwell-times; and ◆, a pre-compression pressure of 80 MPa with varied dwell-times followed by a main compression pressure of 160 MPa.

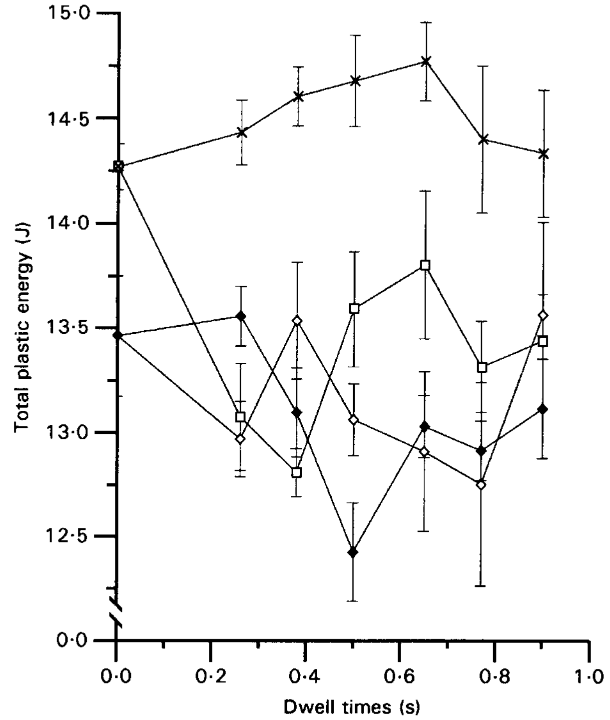

Figure 7. The effect of dwell-times on the total plastic energies of the pre-compression and main compression pressures of the tablets combined: ×, a pre-compression pressure of 160 MPa followed by a main compression pressure of 80 MPa with varied dwell-times; □, a pre-compression pressure of 160 MPa with varied dwell-times followed by a main compression pressure of 80 MPa; ◇, a pre-compression pressure of 80 MPa followed by a main compression pressure of 160 MPa with varied dwell-times; and ◆, a pre-compression pressure of 80 MPa with varied dwell-times followed by a main compression pressure of 160 MPa.

For tablets compressed with a pre-compression or main compression of 160 MPa and dwell-times from 0·50 to 0·90 s (Figure 6), the increase in the tensile strengths of tablets could not be differentiated from each other ($P > 0.05$) but were significantly higher ($P < 0.05$) than when dwell-times of 0·26 or 0·38 s were used. When a pre-compression of 80 MPa was used with a varied dwell-time (Figure 6), the data corresponding to times of 0·65, 0·77 and 0·90 s were indistinguishable ($P > 0.05$) but were statistically higher than the data for dwell-times of 0·26, 0·38 and 0·50 s. The total energies of combined pre-compression and main compression (Figures 7 and 9) and the stress-relaxation and elastic-recovery data (Table 2) also supported the observed tablet tensile strengths as they varied correspondingly with each other.

Taking into consideration all the compression data for the studied combinations of pre-compression and main compression pressures, there were generally significant decreases in the tensile strength of tablets as dwell-times were increased from 0·00 to 0·26 s. There were also very significant increases ($P < 0.05$) in the ratios of elastic energy to plastic energy as the dwell-times increased from 0·00 to 0·26 s. (Figure 9). This meant that more elastic deformation of the material took place when the dwell-time was 0·26 s during the compression compared with when there was no dwell-time. The elastic recovery data similarly showed a maximum increase for dwell-time between 0·00 and 0·26 s after either pre-compression or main compression. Thus the high elastic energies absorbed were relieved as higher elastic energies leading to the significant reduction in tensile strength.

The application of dwell-times from 0·26 to 0·90 s during pre-compression or main compression resulted in increases in the tensile strengths of the tablets approximately to the level attained with no dwell-times. This was because the elastic energies became less and the plastic energies increased leading to more energy utilization in bond formation, resulting in increased tablet tensile strength. The elastic recovery data also decreased as dwell-

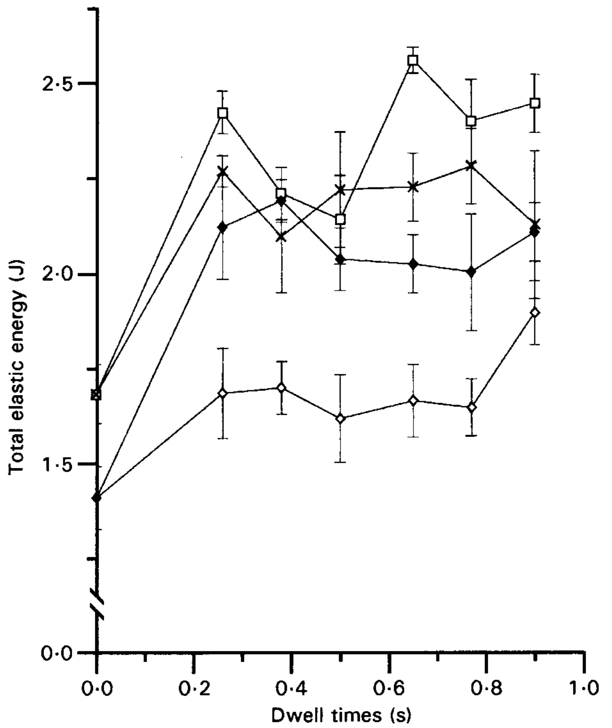

Figure 8. The effect of dwell-times on the total elastic energies of the pre-compression and main compression pressure of the tables combined: ×, a pre-compression pressure of 160 MPa followed by a main compression pressure of 80 MPa with varied dwell-times; □, a pre-compression pressure of 160 MPa with varied dwell-times followed by a main compression pressure of 80 MPa; ◇, a pre-compression pressure of 80 MPa followed by a main compression pressure of 160 MPa with varied dwell-times and ◆, a pre-compression pressure of 80 MPa with varied dwell-times followed by a main compression pressure of 160 MPa.

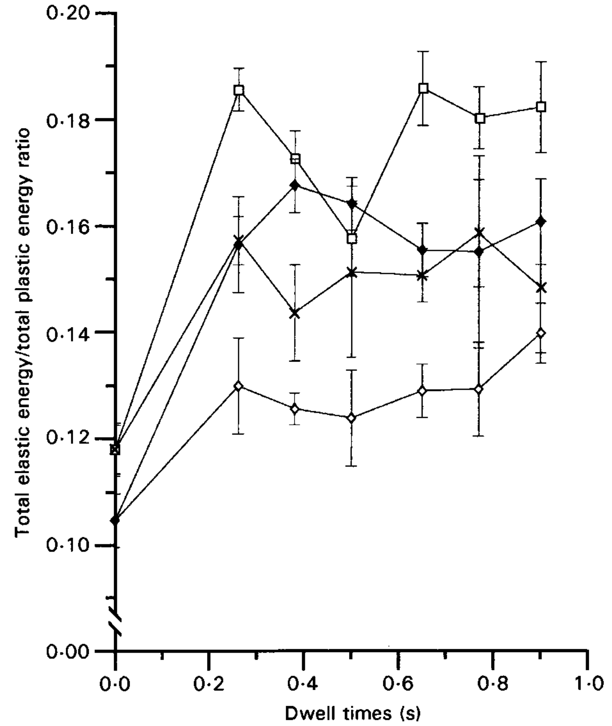

Figure 9. The effect of dwell-times on the ratios of total elastic energy to total plastic energy of the pre-compression and main compression pressure of the tablets combined: ×, a pre-compression pressure of 160 MPa followed by a main compression pressure of 80 MPa with varied dwell-times; □, a pre-compression pressure of 160 MPa with varied dwell-times followed by a main compression pressure of 160 MPa; ◇, a pre-compression pressure of 80 MPa followed by a main compression pressure of 160 MPa with varied dwell-times; and ◆, a pre-compression pressure of 80 MPa with varied dwell-times followed by a main compression pressure of 160 MPa.

times increased. It seemed that the strengths of the tablets were especially sensitive to dwell-times between 0·26 and 0·50 s as further increases in dwell-time only marginally affected the resulting tensile strength of the tablets.

Two-way analysis of variance showed that the tensile strengths of tablets which were subjected to a pre-compression of 160 MPa and a main compression of 80 MPa were higher than those of tablets made by use of a pre-compression of 80 MPa and a main compression of 160 MPa (Figure 6). Further two-way analysis of variance showed that the application of a dwell-time to the main compression resulted in tablets with higher tensile strengths than tablets similarly compressed but with the application of dwell-times to the pre-compression (Figure 6).

The stress-relaxation data were almost doubled when high pre-compression of 160 MPa was applied with or without dwell-times compared with when low pre-compression of 80 MPa was applied with or without dwell-times (Table 2). This implies that better consolidation by plastic deformation was occurring, leading to the formation of tablets with higher tensile strength. The plastic energies were also higher for tablets pre-compressed with a higher pressure of 160 MPa compared with tablets pre-compressed with a lower pressure of 80 MPa. Bateman et al (1990) have found similar increases in tensile strength when pre-compression pressure was higher than main compression pressure. They proposed that an increase in temperature during the application of a high pre-compression pressure results in greater ductility and greater bonding during main compression (Bateman et al 1990).

The data also tend to support previous findings (Hiestand et al 1977) that with increasing dwell-time, sufficient time is allowed for stress-relaxation and consolidation of the material which would lead to an increase in tensile strength.

Conclusions

Increasing lag-times from 0·06 to 0·53 s resulted in a small increase in the tensile strength of the tablets when combinations of 80 and 160 MPa were used

Table 2. Stress-relaxation and elastic recovery of 1 : 1 paracetamol-microcrystalline cellulose compacts compressed with varying pre-compression and main compression dwell-times.

Dwell time (s)	0·00	0·26	0·38	0·50	0·65	0·77	0·90
Pre-compression pressure 160 MPa; main compression pressure 80 MPa with varied dwell-times							
Stress-relaxation during pre-compression (%)	6·1 ± 0·1	7·6 ± 0·2	7·3 ± 0·2	7·5 ± 0·5	7·1 ± 0·2	7·5 ± 0·3	7·2 ± 0·2
Elastic recovery on the pre-compression before main compression (%)	7·1 ± 0·4	6·5 ± 0·2	6·8 ± 0·3	6·6 ± 0·6	6·7 ± 0·2	6·5 ± 0·5	6·6 ± 0·2
Stress-relaxation during main compression (%)	3·8 ± 0·1	5·3 ± 0·3	4·9 ± 0·1	5·2 ± 0·1	5·0 ± 0·2	4·9 ± 0·1	4·5 ± 0·1
Elastic recovery of tablets on ejection (%)	8·8 ± 0·4	13·0 ± 0·6	13·4 ± 0·5	12·8 ± 0·4	12·4 ± 0·4	12·4 ± 0·3	12·8 ± 0·5
Pre-compression pressure 160 MPa with varied dwell-times; main compression pressure 80 MPa							
Stress-relaxation during pre-compression (%)	6·1 ± 0·1	8·4 ± 0·3	8·1 ± 0·3	6·6 ± 0·2	8·1 ± 0·4	8·2 ± 0·3	8·1 ± 0·4
Elastic recovery on the pre-compression before main compression (%)	7·1 ± 0·4	18·9 ± 1·6	19·1 ± 0·3	14·8 ± 0·5	7·3 ± 0·4	7·0 ± 1·6	6·2 ± 0·4
Stress-relaxation during main compression (%)	3·8 ± 0·1	5·3 ± 0·2	5·1 ± 0·1	4·1 ± 0·1	5·0 ± 0·2	4·8 ± 0·3	4·4 ± 0·2
Elastic recovery of tablets on ejection (%)	8·8 ± 0·4	13·7 ± 0·3	13·1 ± 1·2	8·7 ± 0·4	12·7 ± 0·2	13·4 ± 1·6	12·8 ± 0·1
Pre-compression pressure 80 MPa; main compression pressure 160 MPa with varied dwell-times							
Stress-relaxation during pre-compression (%)	3·8 ± 0·1	4·1 ± 0·2	3·9 ± 0·3	3·9 ± 0·1	4·0 ± 0·2	3·9 ± 0·1	3·9 ± 0·2
Elastic recovery on the pre-compression before main compression (%)	7·6 ± 0·8	7·3 ± 0·6	7·6 ± 0·3	7·3 ± 0·2	7·3 ± 0·4	7·1 ± 0·3	6·8 ± 0·4
Stress-relaxation during main compression (%)	5·6 ± 0·2	6·9 ± 0·2	6·7 ± 0·2	6·4 ± 0·2	6·5 ± 0·3	6·8 ± 0·2	7·2 ± 0·3
Elastic recovery of tablets on ejection (%)	10·9 ± 0·4	11·5 ± 1·5	10·9 ± 0·1	10·8 ± 0·2	10·1 ± 0·5	10·0 ± 0·8	9·7 ± 0·5
Pre-compression pressure 80 MPa with varied dwell-times; main compression pressure 160 MPa							
Stress-relaxation during pre-compression (%)	3·8 ± 0·1	5·5 ± 0·2	5·0 ± 0·2	4·4 ± 0·1	4·8 ± 0·3	5·4 ± 0·3	5·1 ± 0·6
Elastic recovery on the pre-compression before main compression (%)	7·6 ± 0·8	21·3 ± 0·8	21·1 ± 0·8	13·8 ± 2·8	19·7 ± 1·1	19·7 ± 0·8	19·9 ± 0·4
Stress-relaxation during main compression (%)	5·6 ± 0·2	8·8 ± 1·5	7·8 ± 0·2	7·4 ± 0·3	7·4 ± 0·3	7·4 ± 0·3	7·4 ± 0·3
Elastic recovery of tablets on ejection (%)	10·9 ± 0·4	13·7 ± 1·8	14·3 ± 0·3	14·4 ± 0·2	14·2 ± 0·3	14·3 ± 0·6	14·3 ± 0·3

Values are the means of results from four tablets ± s.d.

as the compression pressures, but further increases in lag-times did not further change the tablet strengths. The use of pressures of 240 and 320 MPa resulted in tablets for which the effects of lag-time were more difficult to quantify; this was at least in part because of the variability of the data obtained at these pressures and because elastic recovery tended to be significantly higher at high pre-compression pressures. The results of this investigation suggest that lag-time did not seem to have significant effect on the tensile strength of the tablets.

The reduction in the tensile strength of the tablets as the dwell-time was increased from 0·00 to 0·26 s was because of the increased elasticity of the material as the elastic energies and elastic recoveries both increased. Net increase in the tablet tensile strengths however resulted from further increases in dwell-time up to 0·65 s as the elastic recoveries decreased and the plastic energies increased. Generally, dwell-time led to an increase in stress-relaxation, a decrease in the elastic recoveries, a reduction in elastic energy to plastic energy ratio (or more utilization of plastic energies for bond formation) and an increase in the tensile strength of the compacts. The application of pre-compression and main compression pressure in the tableting of visco-elastic materials such as mixtures of paracetamol and microcrystalline cellulose is a complex interaction of many time-dependent factors which include lag-time and dwell-time. The influence of each would depend on the system under consideration as well as on other factors.

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