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COMPACTION CHARACTERISATION OF PARACETAMOL AND AVICEL MIXTURES

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ABSTRACT

Compression and stress relaxation data from powder mixtures of Avicel and paracetamol have been analysed using the David and Augsburger Maxwell model treatment and the Heckel, Kawakita and Shott equations. Scanning electron microscopy was further used to characterise the compacts. No direct relationship was found between the 1/k value of the Heckel plots, and the 1/B value of the Kawakita equations. However, the compaction mechanism of a material can be elucidated more readily if both methods

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are used together. The slope n of the Shott plot was shown to be a useful parameter for measuring the amount of stress relaxation and the rate of stress decay. The use of David & Augsburger's equation was limited to certain materials, which undergo Maxwell deformation. For binary system and those materials showing deviation from the David & Augsburger equation, a more sophisticated model is required for describing the deformation process.

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INTRODUCTION

Many workers [1,2,3] had studied the effect of stress relaxation on the strength of compacts. Shlanta & Milosovich [1] suggested that the degree of plastic deformation of a material can be measured by monitoring the stress relaxation experienced by the punch after the punch position was held constant at the peak applied force. Cole et al [3] demonstrated different compaction mechanisms for potassium citrate and lactose than for sodium chloride and potasssium chloride. They suggested that materials which undergo plastic deformation exhibit high stress relaxation, whilst brittle materials tend to produce little stress relaxation. David & Augsburger [2] derived a logarithmic relationship, based on the Maxwell model of plastic flow, between the amount of compressional force left in the viscoelastic region and the strain holding time. Linear relationships were found for microcrystalline cellulose, starch, sugar and lactose.

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Another useful technique for the determination of the consolidation behaviour of powders is to analyse the volume changes of the powder bed during consolidation. Numerous equations have been proposed, such as that proposed by Heckel [4,5]

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

where D = relative density of a powder compact at load P;

P = applied pressure;

K = slope of the linear region (= the reciprocal of the mean yield pressure)

A = y-intercept of the extrapolated linear region (= movement of particles during the initial stage of compression)

The other commonly mentioned equation is due to Kawakita [6] :

$$C = \frac{Vo - V}{Vo} = \frac{abP}{1 + bP} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots(2)$$

where P = applied pressure;

C = the degree of volume reduction;

Vo = the initial apparent volume;

V = the powder volume under pressure P;

a & b = constants.

By rearranging equation (2), the Kawakita equation can be expressed as

$$\frac{P}{C} = \frac{1}{ab} + \frac{P}{a} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots(3)$$

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the value of b is identified as a measure of the plasticity of the material.

Recently, Shott [7] evaluated the stress relaxation data by plotting the logarithmic rate of stress decay against the logarithmic stress. He reported that materials exhibiting large amounts of stress relaxation produced slopes of small values.

The aim of this work was to evaluate the compaction data of Avicel/paracetamol compacts using the aforementioned methods, and therefore to study the possible relationship between each equation.

MATERIALS AND METHODS

Using an Alpine air jet sieve, paracetamol powder B.P. (Hilton Davies Chemical Ltd., Newcastle-upon-Tyne, UK.) and Avicel PH101 (FMC Corp., Philadelphia, USA) were classified into less than 105um and 40-105um fractions respectively. The powders were mixed in the proportions shown in Table 1. Powder mixtures were pretreated for 24 hours in an vacuum oven at 100°C and then stored under controlled humidity conditions (RH=40% and 25°C) before compression. True density of each powder mixture was determined using an air comparison pycnometer (Model 930, Beckmann Instruments, UK).

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Table 1. The Heckel analysis of the compaction data over the range 40-140MPa.

Mass fraction of Avicel	1/K (MPa)	Intercept	Da	Db	Dc
0	104.22	1.5228	0.7819	0.3327	0.4492
0.15	101.42	1.3643	0.7444	0.3072	0.4353
0.3	97.28	1.2259	0.7065	0.2757	0.4308
0.5	86.96	1.0681	0.6565	0.2110	0.4455
0.75	80.99	0.9214	0.6020	0.1715	0.4305
1.0	84.35	0.5340	0.4137	0.1920	0.2217

Tablets were prepared using a Universal Testing Machine (Model 1121, Instron Ltd., High Wycombe,UK) fitted with 5/16" flat faced F-tooling. The compression surfaces were pre-lubricated with 4%w/v magnesium stearate in carbon tetrachloride solution. Sufficient powder was used to produce a compact of 1.83mm thick at zero theoretical porosity. The crosshead speed used was 50mm/min and the mininum punch separation was set to give a peak compression force of 7KN. Compacts were then held under load for 60s; the load was removed and the ejected tablets stored in a desiccator for 24 hours before tests for radial tensile strength and friability were performed. Compression data was captured using a computer data

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logging system which enabled force and punch displacement to be recorded simultaneously using an Apple IIe microcomputer. Corrections were made for tooling distortion and machine effects. Five tablets were prepared for each composition of mixture.

METHOD OF ANALYSIS

Heckel and Kawakita equations were used for analysing the compression data. The compacts were held under stress for 60 seconds after attaining the maximum applied load. Stress relaxation and percentage stress decay were computed. The percentage change in porosity during different phases of the compression cycle were also calculated as follows:

$$\%\ \text{change in porosity during compression (Pc)} = \frac{\text{Pstart} - \text{Pmax}}{\text{Pmax} \times \text{wt.}} \times 100 \quad \ldots(4)$$

$$\%\ \text{change in porosity during holding time (Ph)} = \frac{\text{Pmax} - \text{Pend}}{\text{Pend} \times \text{wt.}} \times 100 \quad \ldots(5)$$

$$\%\ \text{change in porosity during decompression (Pd)} = \frac{\text{Pzero} - \text{Pend}}{\text{Pend} \times \text{wt.}} \times 100 \quad \ldots(6)$$

where Pstart = porosity of the compact when the force starts to register;

Pmax = porosity of the compact when the force reaches the maximum value;

Pend = porosity of the compact at the end of the holding period (60s);

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Pzero = porosity of the compact at the end of the decompression phase, ie. when the force returns to zero.

wt. = weight of powder used (g).

The rate of percentage stress decay over the period of 25ms, 50ms, 75ms and 100ms were determined. The Shott equation is

$$\ln(-ds/st) = H + n*\ln(s) \quad \ldots\ldots\ldots\ldots\ldots\ldots (7)$$

where ds/dt = rate of change of stress

s = stress

H = constant

n = slope.

Under the condition of stress relaxation with zero strain change, a plot of ln(-ds/dt) against a function of ln(s) should produce a straight line of slope n and intercept H. Shott reported that materials exhibiting large stress relaxation gave small n values.

Using a mathematical treatment, David and Augsburger[2] derived a relationship between the amount of the compressional force remaining in the viscoelastic region at time t, and the holding time t,

$$\ln(F) = \ln(Fo) - kt \quad \ldots\ldots\ldots\ldots\ldots\ldots (8)$$

where F = the amount of the compressional force left in the viscoelastic region at time t

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Fo = the amount of compressional force at time t=0

t = the holding time

k = the visco-elastic slope.

RESULTS AND DISCUSSION

Table 1, shows a gradual decrease in the mean yield pressure as the amount of Avicel in the compact increased. The resistance to deformation of Avicel is less than that of paracetamol and therefore it forms tablets more readily and so the tablets exhibit a higher tensile strength. The compacts were viewed under the scanning electron microscope. 100% paracetamol tablets (fig.1) exhibit marked fragmentation, with the formation of fines and cracks evident on the coarse drug crystals. Bonding is believed largely due to the formation of new surface, and particle-particle adhesion by Van de Waal's attraction. Pure Avicel tablets (fig. 6), however, show a very dense packing structure and characteristic plastic deformed particles were identified. A gradual change of compaction mechanism was also observed for the intermediate mixtures (fig. 2-5).

The treatment of the compaction data by the Heckel equation is shown graphically in Figure 7. Two groups of curves could be identified; mixtures with 0-30% Avicel and 50-100% Avicel. It is therefore, suggested that 50%w/w of Avicel in paracetamol mixture would be the optimum

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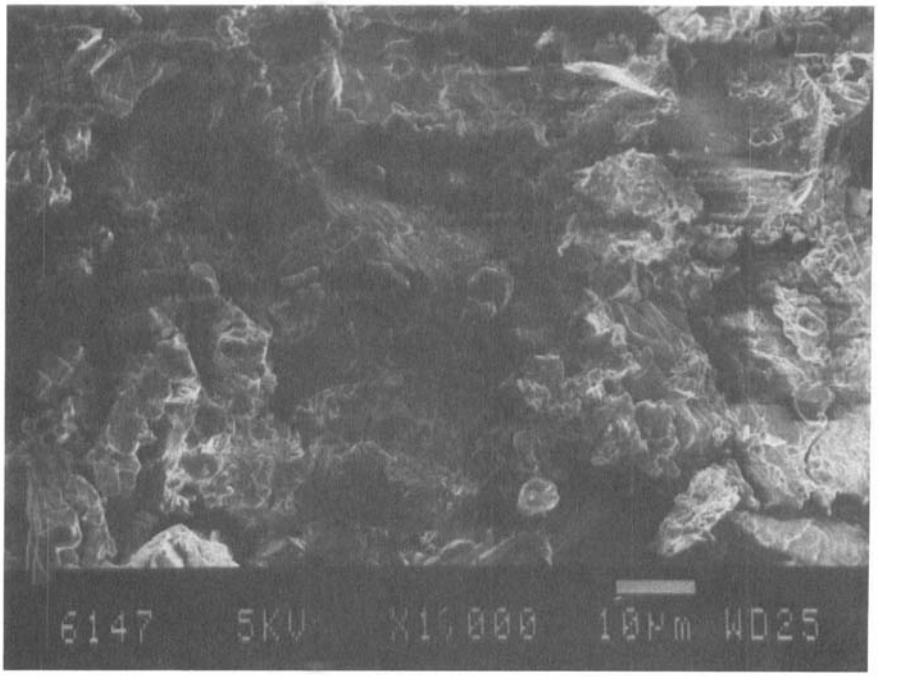

FIG. 1 100% PARACETAMOL COMPACT. MAG. X1000
THE FRACTURE SURFACE.

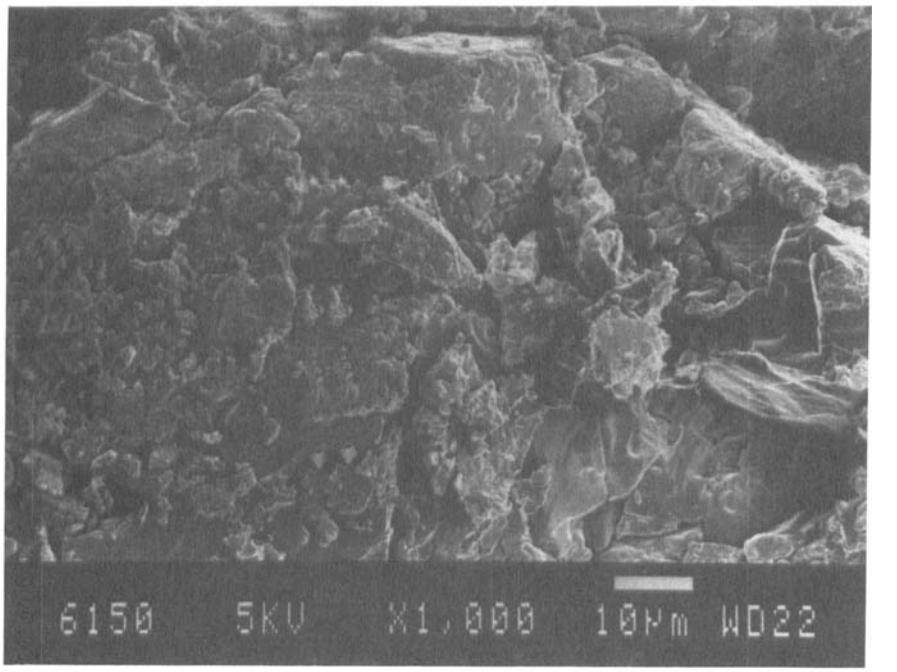

FIG. 2 85/15 PARACETAMOL/AVICEL COMPACT. MAG. X1000
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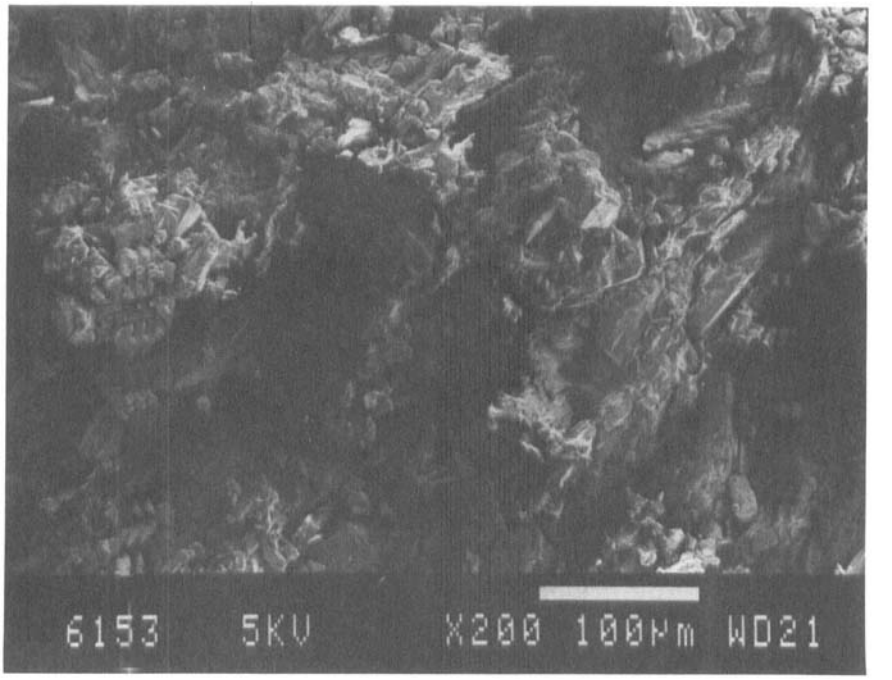

FIG. 3 70/30 PARACETAMOL/AVICEL COMPACT. MAG. x200
THE FRACTURE SURFACE.

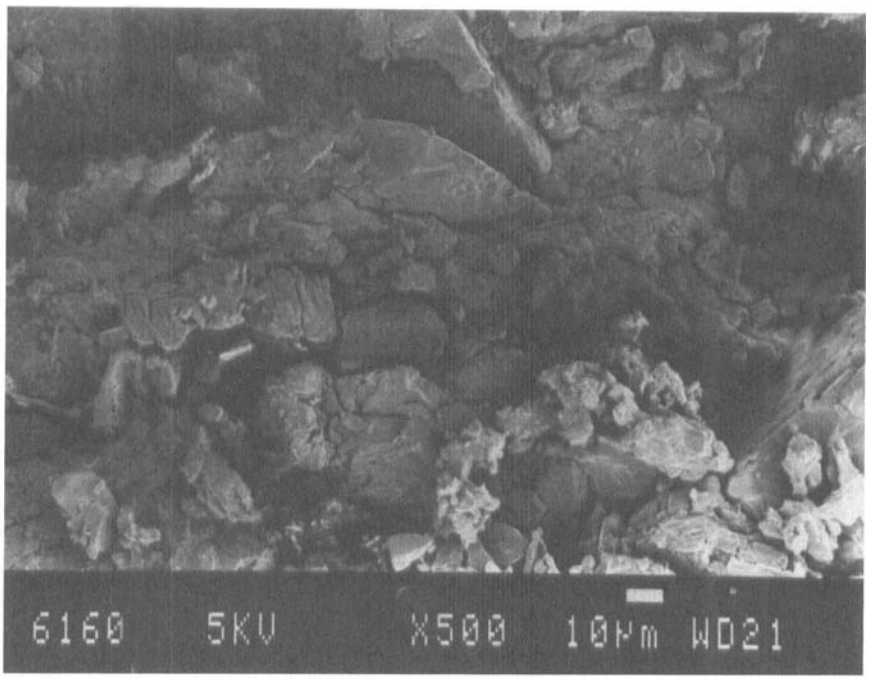

FIG. 4 50/50 PARACETAMOL/AVICEL COMPACT. MAG. x500
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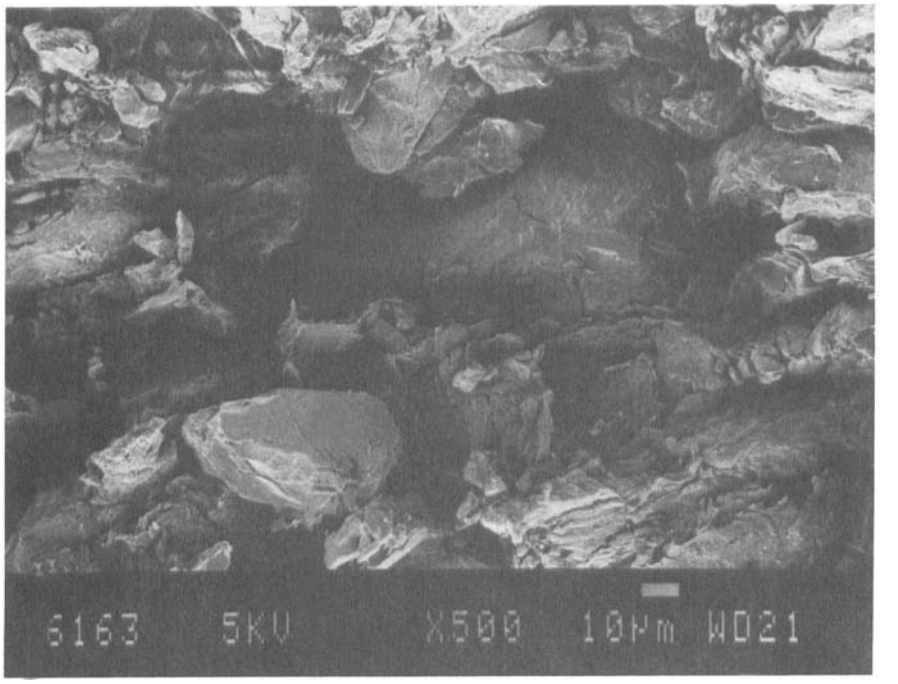

FIG. 5 25/75 PARACETAMOL/AVICEL COMPACT. MAG. X500
THE FRACTURE SURFACE.

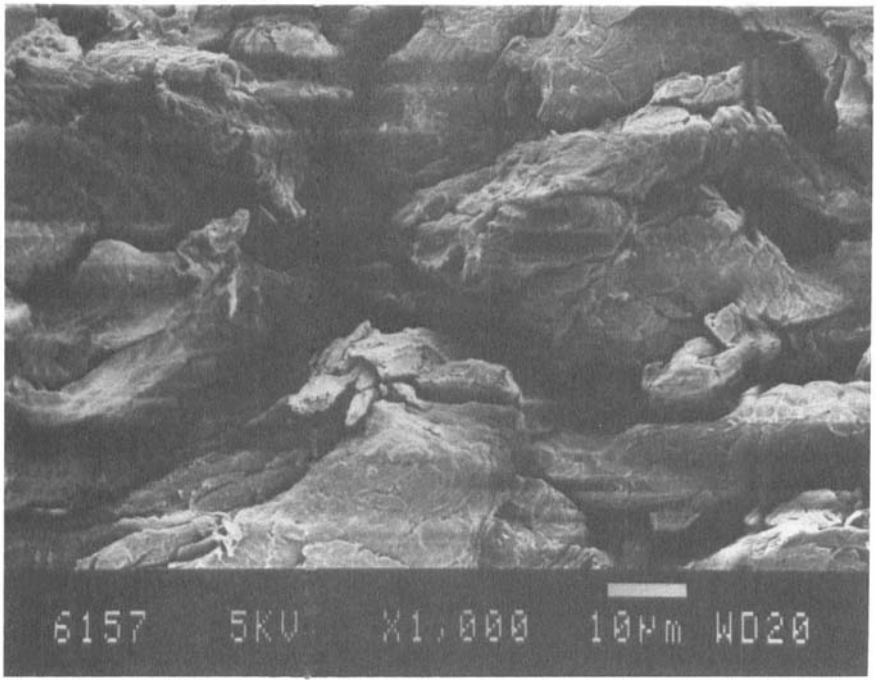

FIG. 6 100% AVICEL COMPACT. MAG. X1000
THE FRACTURE SURFACE.

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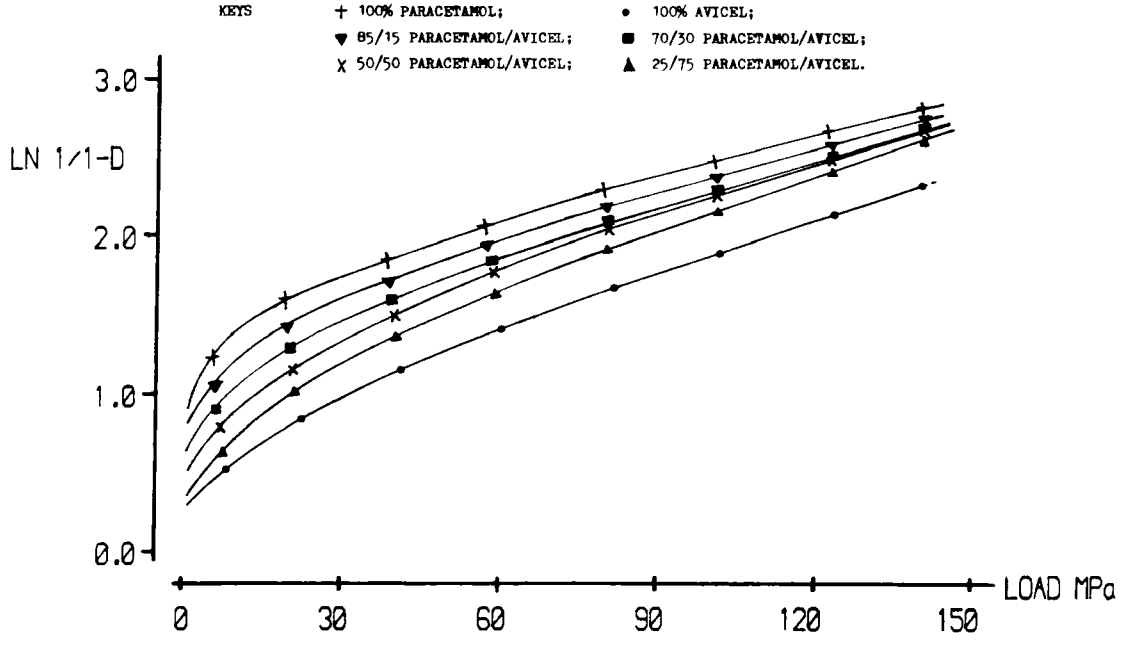

FIG. 7 THE RELATIONSHIP BETWEEN LOGe(1/1-D) AND THE APPLIED PRESSURE FOR THE AVICEL/PARACETAMOL COMPACTS.

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composition, as adding an extra amount of Avicel would not affect the mode of tablet consolidation, besides improving the tensile strength. An initial non linear section was observed with all the mixture (fig. 7) which indicated that particle slippage and rearrangement occurred at low applied pressures. Avicel exhibited the smallest Db value (Db = 0.192, table 1) indicating the particles achieve good packing during die filling. This may be attributed to the self lubricating property claimed to be possessed by this material, and hence it only required little rearrangement at the initial stage of compression. Paracetamol displays very poor flowability, and therefore packs loosely, resulting in a larger degree of particle slippage and rearrangement which was expected (Db = 0.3327).

Although other workers [8,9] have reported a deviation from linearity at low pressure, when using the Kawakita equation, the present study did not reveal such observations (fig. 8). From table 2, an increase of the 1/b value was noticed as the amount of Avicel in the mixture increased. Since the value of 1/b is related to the amount of change in compact volume during compaction, compressing Avicel involved a larger volume reduction compared with the compression of pure paracetamol. As mentioned previously Avicel consolidates by plastic flow and therefore, the observation is easily explained. As the applied pressure increases beyond the elastic limit of the

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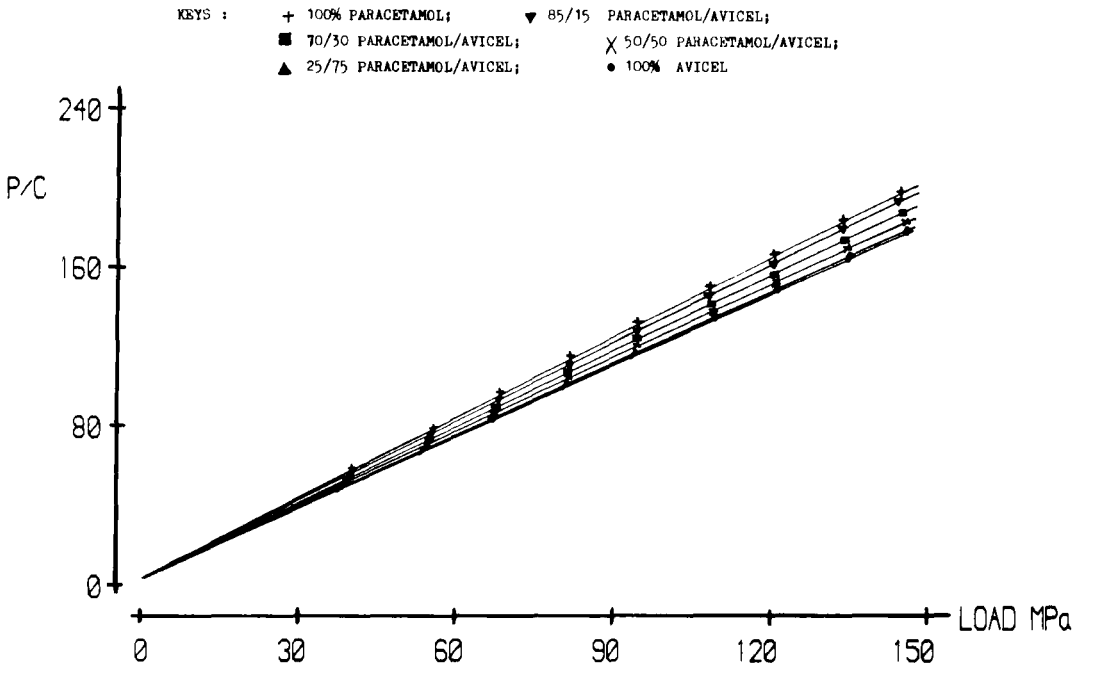

FIG. 8 THE KAWAKITA PLOTS FOR THE AVICEL/PARACETAMOL COMPACTS.

Table 2. The Kawakita analysis of the compaction data over the range 1-140MPa.

Mass fraction of Avicel	Bulk Density (g/cc)	Initial Apparent Volume (ml)	Slope (1/a)	1/b (MPa)
0	0.31	0.39	1.35	0.8106
0.15	0.30	0.42	1.32	0.9785
0.3	0.28	0.45	1.28	1.0046
0.5	0.26	0.52	1.24	1.1558
0.75	0.24	0.55	1.21	1.2319
1.0	0.25	0.57	1.21	2.1776

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material, Avicel particles start to deform plastically; the mechanism involving particle shearing and squeezing and is believed to facilitate the filling of gaps and pores. Air trapped in the powder bed can also escape more readily. On the other hand, paracetamol crystals fracture and create a lot of finer particles during compression. The increased surface area within the powder bed reduces the pressure exerted on each particle and thus allows less contact points for the support of the powder column. The smaller particles are also able to seal those small pores that exist in the compact and air entrapment ensues. Both mechanisms affect the change in volume during the application of pressure and allow the formation of a relatively porous compact.

Both Heckel and Kawakita equations are derived from the same principle, which is based on the relationship between the applied pressure and the density of the compact. However, The Heckel plot is more commomly employed than the Kawakita equation. As seen in equation (2), the C value of the Kawakita equation is very much depended on the Vo value (the initial apparent volume). Therefore, factors such as the die filling method, that can affect the initial powder packing are able to influence the 1/b value of the Kawakita analysis. The Heckel 1/k value is however determined after the rearrangement stage, and therefore, the value is unaffected by the fashion of initial powder packing. No

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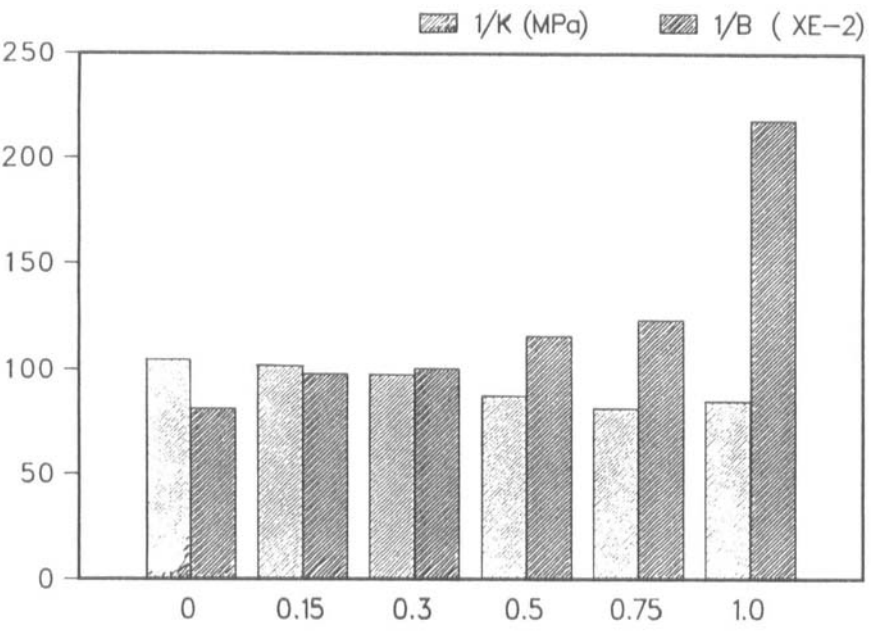

FIG. 9 THE RELATIONSHIP BETWEEN 1/K (HECKEL); 1/B (KAWAKITA) VALUES WITH THE MASS FRACTION OF AVICAL IN THE COMPACTS.

obvious relationship can be identified between the 1/k and 1/b values (fig. 9).

Stress relaxation is considered as a post compression measurement used for studying the compaction mechanism. Measurements are taken after the peak pressure has been applied and is very much time dependent. Increasing the amount of Avicel in the mixture increased the percentage stress relaxation (table 3), and therefore reflects the degree of plasticity of the materials under study. Also, by examining the rate of percentage stress decay that occurred after different time intervals (table 5), Avicel

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Table 3. The stress relaxation data for the mixtures of Avicel and paracetamol.

Mass fraction of Avicel	Stress relaxation (N)	Percentage stress relaxation
0	211.41	4.51
0.15	404.77	7.31
0.3	494.64	8.56
0.5	586.44	10.00
0.75	713.93	11.93
1.0	863.26	13.94

Table 4. The porosity analysis of the compaction data during compression, holding period and decompression.

Mass fraction of Avicel	% change in porosity (compression)	% change in porosity (holding)	% change in porosity (decompression)
0	-406.47	-44.1	144.35
0.15	-606.03	-42.56	104.27
0.3	-866.35	-46.99	109.00
0.5	-1195.08	-49.2	104.42
0.75	-1636.42	-53.47	94.6
1.0	-1965.66	-85.95	34.02

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relieved stress faster than paracetamol. This latter observation confirms the finding of Hiestand et al [10]. Analysing the percentage change in porosity during different phases of the compression cycle (table 4) revealed a massive decrease in porosity of Avicel during compression which was almost five times that of pure paracetamol. Since the effect is not due to particle rearrangement, it must only be attributable to the visco-elastic flow of the material. However, during the holding period, the percentage change in porosity of Avicel was only double that of paracetamol. For Avicel, it is therefore suggested that the majority of the plastic flow occurred during the loading period. For paracetamol, as mentioned previously, air is probably trapped within the small pores and thus during the holding time, slow visco-elastic movements would facilitate the collapse of those voids and give a reasonable amount of stress relaxation. A high percentage change in porosity during decompression (Pd) for paracetamol indicates a more elastic nature of the material, and would account for the poor compactibility of paracetamol.

Table 6 shows the results from the Shott analysis. The treated data fitted a series of straight lines (Fig. 10) and the gradient of the lines (n) signifies the degree of stress relaxation, as well as the rate of stress decay during the holding period. Paracetamol compacts exhibited the biggest slope value, which indicated the least amount

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Table 5. The rate of % stress decay over the period of (i) 25ms; (ii) 50ms; (iii) 75ms & (iv) 100ms

Mass fraction of Avicel	25ms $X10^{-2}$ (ms^{-1})	50ms $X10^{-2}$ (ms^{-1})	75ms $X10^{-2}$ (ms^{-1})	100ms $X10^{-2}$ (ms^{-1})
0	-1.498	-2.710	-2.717	-2.303
0.15	-2.247	-3.867	-3.815	-3.429
0.3	-2.201	-4.151	-4.330	-3.925
0.5	-4.443	-5.276	-5.151	-4.508
0.75	-4.828	-7.587	-6.857	-5.399
1.0	-14.693	-13.008	-9.004	-6.771

Table 6. The Shott's analysis of the stress relaxation data of the Avicel/paracetamol compacts.

Mass fraction of Avicel	Slope (n)	Y-intercept	Correl. coeff. %
0	213.75	-3998.00	93.0
0.15	131.73	-2460.80	97.4
0.3	105.89	-1975.40	97.8
0.5	90.83	-1691.62	98.4
0.75	85.21	-1585.65	98.1
1.0	79.64	-1478.95	97.4

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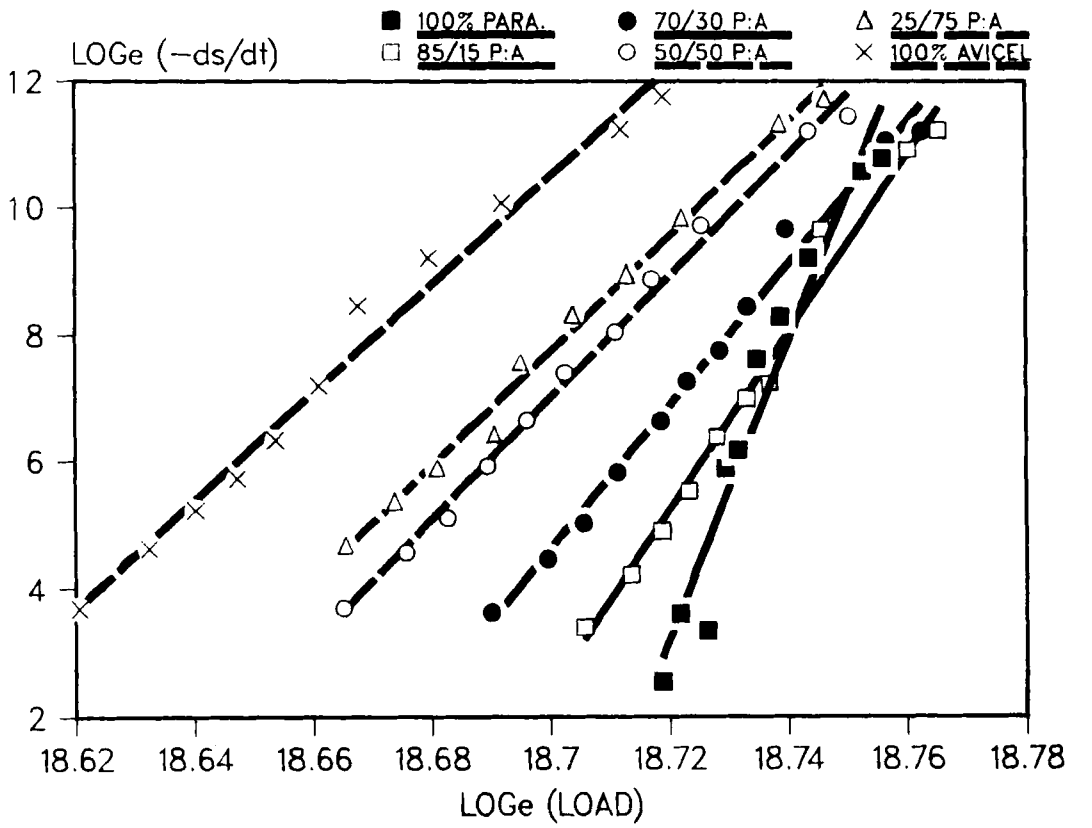

FIG. 10 THE RELATIONSHIP BETWEEN LOGe(-ds/dt) AND LOGe(LOAD) FOR AVICEL/PARACETAMOL COMPACTS.

of stress relaxation and the slowest rate of stress decay. The slope (n) decreased with increasing amount of Avicel in the compacts, thus showing the usefulness of this parameter as an index of post compressional plastic flow. A similar method of analysing the stress relaxation data is used in the mathematical treatment of the Maxwell model under constant strain (equation 8). A complicated plot (fig. 11) displayed lines with an initial curve, which

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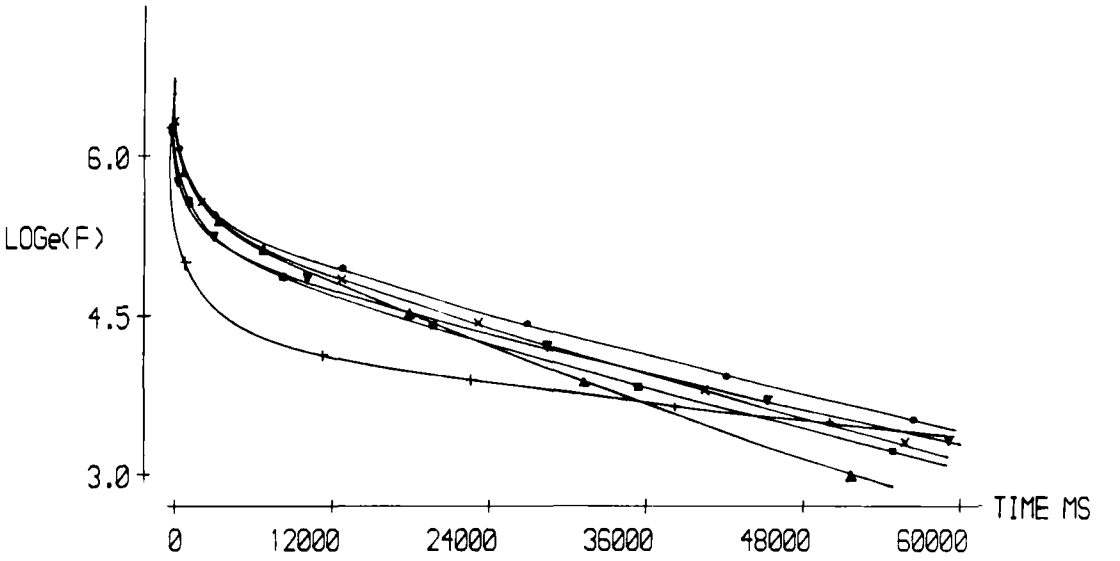

FIG. 11 THE RELATIONSHIP BETWEEN THE LOGe(F) AND THE HOLDING TIME FOR AVICEL/PARACETAMOL COMPACTS.
KEYS : as figure 7.

gradually became linear. Hence, the viscoelastic slope cannot be determined. Holding the compacts under stress for 60s may not be sufficient to allow complete stress relaxation to take place. However, more than 80% of the total plastic flow should be achieved by the end of that period. Therefore, incomplete stress relief does not seem to be the sole cause for the deviation from the linearity. The nature of deformation of the studied material is considered too complicated to be described by a linear viscoelastic model, ie. a combination of a linear elastic (Hookean) element and a linear plastic (Newtonian) element. Also, in a binary system interaction between heterogeneous materials may , to a minor extend, affect the deformation of the system.

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CONCLUSION

Compression and stress relaxation data from powder mixtures of Avicel and paracetamol have been analysed using various treatments, such as the Heckel and the Kawakita equation, the Shott equation and the Maxwell model treatment. Scanning electron micrographs were also utilised to characterise the compacts. No direct relationship was found between the 1/k value of the Heckel plots, and the 1/b value of the Kawakita equations. However, the compaction mechanism of a material can be elucidated more readily if both methods are used together. The slope value (n) of the Shott equation was shown to be a useful parameter for measuring the amount of stress relaxation and the rate of stress decay. The use of David & Augsburger's equation was limited to certain materials, which undergo Maxwell deformation. For binary systems and those materials showing deviation from the David & Augsburger plot, a more complicated model is required for describing the deformation mechanism.

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