International Journal of Pharmaceutics, 39 (1987) 93–99
Elsevier

IJP 01312

Fatigue failure behaviour of direct compression excipients

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(Received 11 November 1986)
(Modified version received 20 April 1987)
(Accepted 24 April 1987)

Key words: Fatigue testing; Direct compression; Tablet testing; Work of failure; Acoustic emission

Summary

A test to determine the fatigue strengths of tablets compressed using pure direct compression excipients was developed to differentiate the ability of Avicel PH 102, Microtal, Dipac, Emcompress and Tablettose to relieve stress at crack tips. Monitoring acoustic emissions which occurred during fatigue testing showed that different modes of fatigue failure were produced prior to brittle fracture in Emcompress and ductile fracture in Avicel and Microtal tablets. It was concluded that such differences in fatigue behaviour were due to differences in fatigue crack propagation rates in the different materials.

Introduction

The most widely used method for characterizing tablet properties is the diametral crushing test, where the force required to cause tablet failure is measured. Such measurements are widely used both for in-process monitoring and quality assurance testing at the end of production. However, such a test does not give any direct quantitative assessment of powder compactibility, although various parameters are often derived from measurements performed during the diametral test, including tensile strength (Newton and Fell, 1968) and toughness (Rees and Rue, 1978). Unlike tensile strength determinations, toughness determinations (or work performed to cause tablet failure) take into consideration the fracture strain and measurement of work of failure has been shown to be a good parameter in the assessment of powder compactibility (Rees and Rue, 1978; Seager et al., 1980; Parrott and Jarosz, 1982; Patel, 1986). However, work of failure determinations do not take into account the rate of crack propagation in the tablet during the diametral test. In contrast, fatigue strength determinations (Patel et al., 1984) do take into account the rate of crack propagation.

Fatigue is a phenomenon in which a crack develops and extends under fluctuating stresses or strains. The kinetics of fatigue crack propagation (FCP) have been examined by measuring the change in crack length of a precracked sample as a function of the total number of loading cycles (Hertzberg and Manson, 1980) i.e. crack length increases with number of loading cycles and increasing the stress results in an increase in the fatigue crack growth (d_a/d_n) where a is the crack length and n is the number of cycles at any stage of the fatigue test.

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Using the principles of fracture mechanics, Paris (1964) postulated that the stress intensity factor, K, was a major controlling factor in the FCP process, where K is a function of stress and crack length, thus the relationship given in Eq. 1 can be inferred.

$$d_a/d_n = f(\sigma, a) \quad (1)$$

Paris found that the most important variable was the stress range (max–min) and therefore described fatigue crack growth rate per cycle in terms of a stress intensity factor range, according to Eq. 2:

$$d_a/d_n = A(\Delta K)^m \quad (2)$$

where ΔK is the stress intensity factor range, given by $K_{max} - K_{min}$ and test variables such as temperature, cycling frequency, stress ratio, nature of load application and material variables.

The rationale for performing a fatigue test on compressed tablets was to investigate differences in FCP rates which would result from differences in the viscoelastic behaviour of the excipients under constant test conditions.

Materials and Methods

Materials

Tablettose, a direct compression form of lactose (Meggle Milchindustrie GmbH, Reitmehring, F.R.G.); Dipac, a direct compression form of sucrose (Amstar Corp., New York, U.S.A.); Microtal, a direct compression form of sucrose (Tate & Lyle plc, Plaistow Wharf, U.K.); Avicel, type PH102, microcrystalline cellulose (FMC Corp., Philadelphia, U.S.A.); Emcompress, a direct compression form of dicalcium phosphate (Edward Mendell Co. Inc., Carmel, U.S.A.).

Tablet compression

The mass required to produce a tablet of 2.5 mm thickness at zero theoretical porosity was calculated from knowledge of the volume which the tablet should occupy and the true density of the powder. All powders were stored for 48 h at 25 °C, 55% relative humidity prior to manual compression using a reciprocating tableting machine (type E2, Manesty Machines, Speke, U.K.), fitted with 12.7-mm-diameter flat-faced punches, which had two pairs of strain gauges attached to the upper punch and lower punch holder. The reason for compressing the tablets manually was to reduce the deviations of individual compaction forces from the mean and to increase compaction force reproducibility. The complete system used for tablet compression and the necessary interfacing to determine the force applied during compaction have been previously described (Patel, 1986). The compressed tablets were stored for 48 h at 25 °C, 55% relative humidity prior to mechanical testing.

Fatigue testing procedure

Tablets compressed from each of 5 direct-compression excipients were examined by placing a tablet on edge between two platens. Each tablet was subjected to cyclic load application and removal at a constant frequency of 0.23 Hz between a maximum load equivalent to 80% of the mean peak crushing force, and a minimum load equivalent to 20% of the mean peak crushing force giving a constant stress ratio of 0.25. Crushing forces were obtained as the mean value of 10 tablets determined using a diametral test after Newton and Fell (1968). The cycling was performed using a sinusoidal waveform on a tensile tester (type T22K, J.J. Lloyd Instr., Southampton, U.K.). Fatigue failure was considered to have occurred when crack propagation had taken place vertically across the tablet diameter, usually splitting the tablet into halves. At this point the number of cycles required to cause fatigue failure was noted, using an automatic counter (type T5 08, J.J. Lloyd Instr.) interfaced to the tensile tester. The surfaces in contact with the tablet during the test were smooth and highly polished, thus eliminating possible indentations due to rough platen surfaces. Experimental work was performed at 15 ° ± 2 °C.

Normalized work of failure (NWF)

The area under the force vs tablet deformation curve was determined using the trapezoidal rule and was then normalized to account for changes

in cross-sectional areas between tablet specimens, caused by dimensional differences resulting from compression and storage. NWF was calculated according to Eq. 3 (Rees et al., 1977):

$$\mathrm{NWF} = 2/\pi Dt \int_0^x F \cdot \mathrm{d}x \qquad (3)$$

where D is tablet diameter, t is tablet thickness (m), F is the force applied during diametral testing and x is tablet deformation.

Acoustic emission

Part of the fatigue study was accompanied by a computer-based measurement of acoustic emission which occurred during fatigue failure testing. A miniature quartz piezo-electric acoustic sensor (type MAC 300, Acoustic Emission Consultants, Sacramento, U.S.A.) was attached to the centre of each tablet.

The complete system employed has been previously described elsewhere (Patel, 1986).

Results and Discussion

The relationship between normalized work of failure and compaction force for some direct compression excipients is illustrated in Figs. 1 and 2. Increase in the compaction force can be observed to increase the NWF values illustrating that the work performed to cause tensile failure increases. Tablet compression follows a volumetric die-filling step and the initial configuration of particles in the die will be of relatively low packing density. Thus initial volume reduction on contact of tablet machine punch with powder will probably be due to particle rearrangement to give a more closely packed unit. Further volume reduction can only occur through elastic deformation of particles and when the elastic limit of the particles is exceeded, destructive (irreversible) deformation will take place. However, irreversible deformation will be accompanied by an elastic deformation component which will be recovered on removal of force (Seelig and Wulff, 1946; Bricks and Muzzafar, 1971).

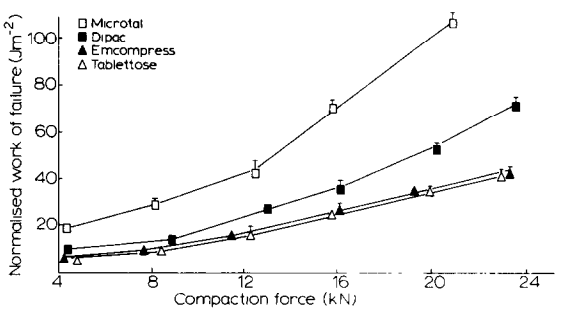

Fig. 1. Relationship between NWF and compaction force for some direct compression excipients. The points plotted are the mean of a minimum of 10 determinations and corresponding confidence interval at 95% level.

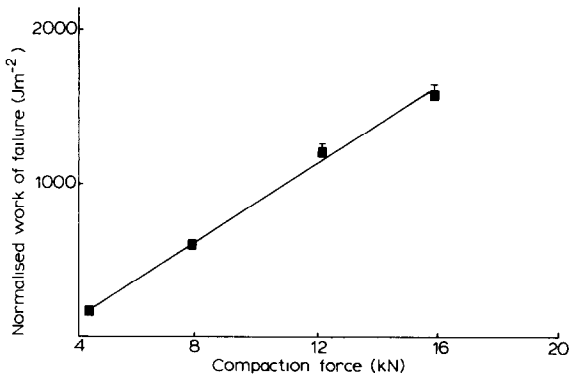

Fig. 2. Relationship between NWF and compaction force for Avicel PH102 tablets.

Two types of irreversible deformation can be identified: plastic deformation, due to imperfections or defects within the crystal lattice which causes movement of dislocations across the slip planes of crystals under the action of an applied force (Cottrell, 1953: Sinnott, 1958). The consequence of plastic deformation is that the particles come into closer proximity establishing areas of intimate contact over which strong attractive electrostatic forces lead to the formation of high inter-particle bonding. The second general type of irreversible particle deformation is that through brittle deformation (fragmentation) which takes place due to the incapacity of the particles to undergo strain sufficiently quickly to accomodate the load and thus particle fracture takes place (Griffith, 1920). This leads to an increase in the number of finer particles (Higuchi et al., 1953;

Armstrong and Haines-Nutt, 1970) with clean new surfaces which adhere with a strength equal to the bulk strength of the material (Bowden and Tabor, 1954). However, the increase in fines leads to a reduction in tablet porosity and at the same time, it leads to an increase in the number of interparticle contact points. This has the effect of decreasing the magnitude of the load at each contact point, consequently preventing the particles from coming into closer proximity and reducing the possibility of the establishment of intimate contact areas. All this will lead to the formation of weaker interparticle bonds.

It is the combination of high interparticle bond strength and plastic deformability of the powder which produces high NWF values. The results in Figs. 1 and 2 are in agreement with those reported by Rees and Rue (1978) and Seager et al. (1980) where high NWF values of tablets were associated with materials which underwent irreversible deformation by plastic flow during tablet compaction. Conversely, low NWF values were associated with materials which underwent irreversible deformation by brittle fragmentation. The results illustrated in Figs. 1 and 2 suggest that Avicel PH102 possesses the highest degree of plastic ductile characteristics. Of the two sucrose-based direct-compression excipients, Microtal and Dipac, the former was found to possess a greater degree of plasticity. It is thought that the co-transformation of sucrose with 3% maltodextrin 20 DE (Microtal) facilitates slippage to a greater degree than does modified dextrin in Dipac.

The fatigue failure data are illustrated in Figs. 3 and 4, where the numbers of cycles required for fatigue failure are plotted on a logarithmic scale, versus compaction force. For Avicel PH102, Microtal and Dipac tablets, the number of cycles required for fatigue failure was found to increase with increased in compaction force (Fig. 3). This is the result of an obvious relationship: increase in compaction force results in an increase in the areas of intimate interparticle contact, thus increasing the degree of interparticle bonding and consequently the tablet possesses greater resistance to mechanical damage. Fig. 4 shows that there was no influence of compaction force on the number of cycles for fatigue failure for either

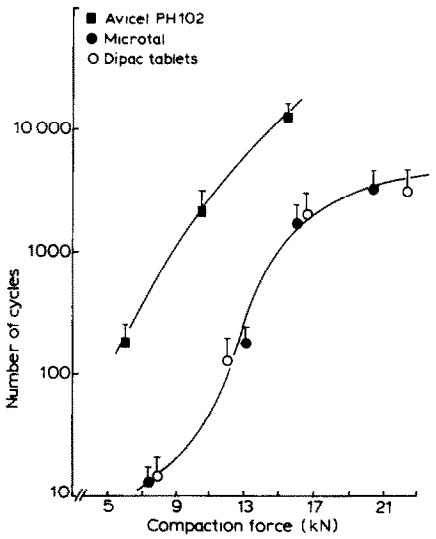

Fig. 3. Influence of compaction force on the number of cycles required for fatigue failure of Avicel PH102, Microtal and Dipac tablets. The points plotted are the mean of a minimum of 5 determinations and S.D.

Emcompress or Tablettose tablets. This behaviour was unexpected since the NWF value was previously found to increase with increase in compaction force for these tablets (Fig. 1), suggesting that

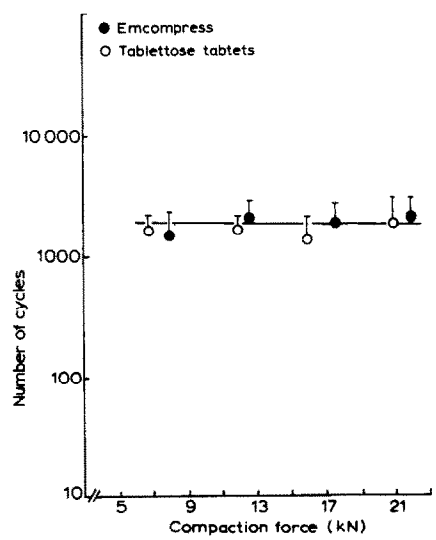

Fig. 4. Influence of compaction force on the number of cycles required for fatigue failure of two types of tablets.

the degree of interparticle bonding increased with compaction force. The different trends observed in Figs. 3 and 4 are a result of differences in the fatigue crack propagation (FCP) rates, since all variables except those of a physico chemical nature (material variables) of the powder in the Paris equation (Eqn. 2) were maintained constant.

Ganderton and Shotton (1961) have cited two types of failure of tablets during testing. (1) Where the interparticle bond is strong, fracture takes place across the particles. (2) Where the interparticle bond is weak fracture takes place at points of interparticle contact. As discussed above, for particles which can deform plastically, such as Avicel (Fox et al., 1963) the interparticle bonding will be extensive and strong, thus FCP in the tablet will be most likely to occur across the microcrystalline cellulose particles rather than at interparticle points of contact.

Griffith (1920) and Irwin (1960) have stated that the stress field at a crack tip is inversely proportional to the radius of curvature at the crack tip. Hence, the smaller the radius of curvature, the greater will be the stress concentration and the possibility of crack propagation will be thereby increased. It is thought that during fatiguing of Avicel tablets, these compacts undergo some degree of plastic deformation at the crack tip, reducing the maximum stress at the crack tip and FCP would thus be retarded. Results for Microtal and Dipac tablets (Fig. 3) show a similar trend to that for Avicel PH102 tablets, but were found to undergo fatigue failure at a lower number of cycles than Avicel, suggesting that the rate of FCP was much more rapid in Microtal and Dipac tablets and this is thought to be due to the lower degree of plastic deformation at the crack tip.

A probable explanation for the observed trend in Fig. 4 is that once the fatigue crack is initiated , its subsequent propagation may be extremely rapid since there may not exist mechanisms to increase the radius of curvature at the crack tip. Between 5 kN and 14 kN compaction force, the number of cycles required to cause fatigue failure of Dipac and Microtal tablets (Fig. 3) was lower than either Emcompress or Tablettose (Fig. 4), despite the fact that both Microtal and Dipac tablets apparently possessed a higher degree of interparticle bonding (Fig. 1). One possible reason for this observation is that the crack initiation in Emcompress and Tablettose tablets is the FCP rate-determining step and after crack initiation, the FCP rate will be rapid due to the absence of mechanisms to cause crack tip blunting. In the case of Microtal and Dipac tablets it is thought that the FCP rate-determining steps are most likely to be the radius of curvature of the crack tip and the degree of interparticle bonding. This will also be true for Avicel tablets.

Acoustic emission (AE) monitoring provides a means of following the damage and damage growth in a component, especially crack propagation (Engle and Dunegan, 1969). The formation of a crack and its subsequent propagation are associated with release of elastic energy, which can be detected by placing a sensitive piezo-electric sensor on the surface of the component. Fig. 5 shows the AE acquired during the fatigue test of a Microtal tablet compressed at 8 kN compaction force, where, after the point of loading, point L, which caused a burst of AE suggesting some fracture had taken place, there was a gradual increase in the AE up to the point of fatigue failure (point X). The AE data for an Avicel tablet compressed at 6 kN is illustrated in Fig. 6 and again, at the point of loading L, there was a burst of AE followed by a gradual increase until the point of fatigue failure of the tablet (point X). The profile was similar to that observed for Microtal tablets, suggesting the FCP was gradual up to the point of failure. The AE data for an Emcompress tablet compressed at a compaction force of 8 kN is illustrated in Fig. 7. After the point of loading, there was an increase in AE accompanied by sudden bursts of AE, which were observed to increase up to the point of failure. This profile is different from those obtained for Avicel and Microtal tablets. The sudden bursts of AE in the Emcompress tablet suggest that once a crack is initiated the subsequent propagation is rapid. This supports the hypothesis postulated earlier, that an absence of mechanisms for blunting the crack tip would cause the stress at the tip to be high. However, these bursts were short-lived (Fig. 7) indicating that the path of the crack was short. During compaction of Emcompress powder, the principle consolidation mecha-

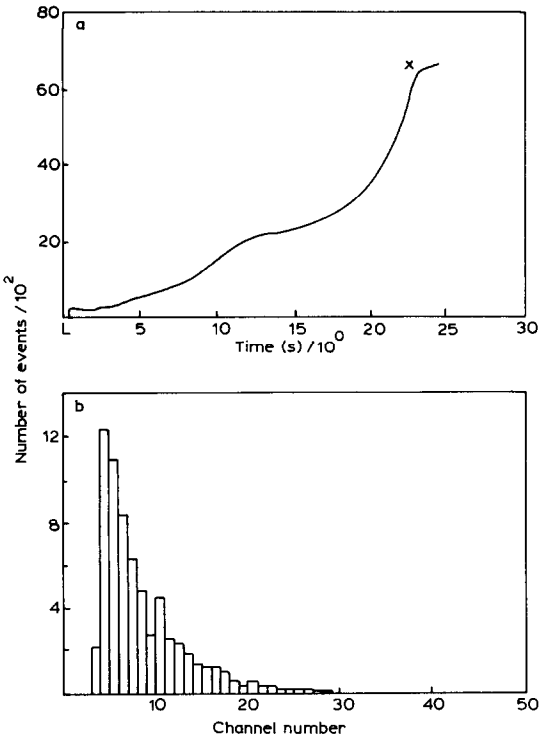

Fig. 5. A: cumulative number of events recorded with time during fatigue testing a Microtal tablet compressed at a compaction force of 8 kN. L, point of loading, X, point of fatigue failure. B: the distribution of energy levels of the acoustic emission during fatigue testing of a Microtal tablet compressed at a compaction force of 8 kN.

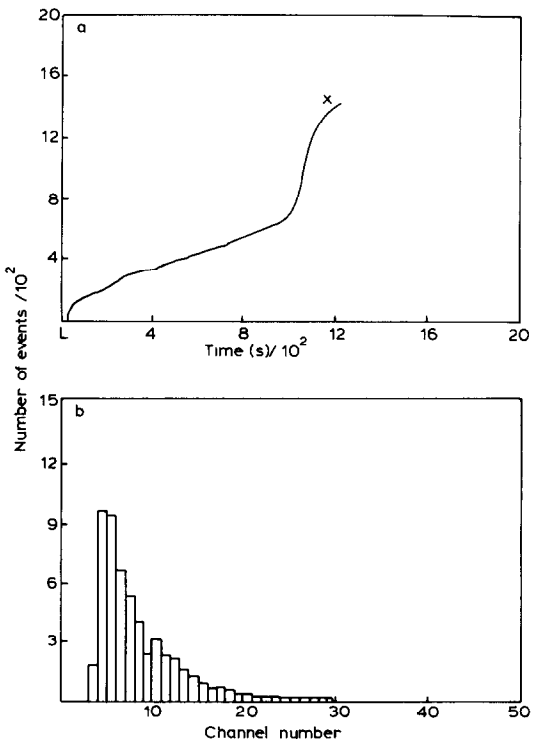

Fig. 6. A: cumulative number of acoustic events recorded with time during fatigue testing of an Avicel PH102 tablet compressed at a compaction force of 6 kN. B: the distribution of energy levels of the acoustic emission during fatigue testing of an Avicel PH102 tablet compressed at a compaction force of 6 kN.

nism is by brittle fragmentation, which will increase the number of fines thereby creating a closer packed structure. However, this will not be so effective a mechanism of reducing compact porosity as plastic deformation would have been. It is considered that the FCP in Emcompress tablets would be arrested when the crack intercepted a void. Such a void effectively increases the radius of curvature of the crack tip, temporarily arresting crack propagation. This explains the short-lived AE burst and the high number of cycles required to cause fatigue failure for Emcompress and Tablettose.

The AE profiles appear to indicate that two types of fracture are taking place during fatigue testing of tablets: Type 1 behaviour was that associated with Avicel and Microtal tablets, where the AE increased gradually with time, suggesting the FCP was retarted, presumably by plastic deformation. Type 2 behaviour was that found in Emcompress tablets where increase in AE occurred in a step-wise manner.

Conclusion

It is concluded that the differences in fatigue behaviour for Avicel PH102, Microtal, Dipac, Emcompress and Tablettose tablets were due to differences in the rates of crack propagation through the tablets. The fatigue test developed was found to distinguish between the two main causes of tablet fracture: ductile and brittle fracture. Differences in ductile fracture for Avicel PH102 and Microtal tablets were also found to be distinguishable. However, it was found that the

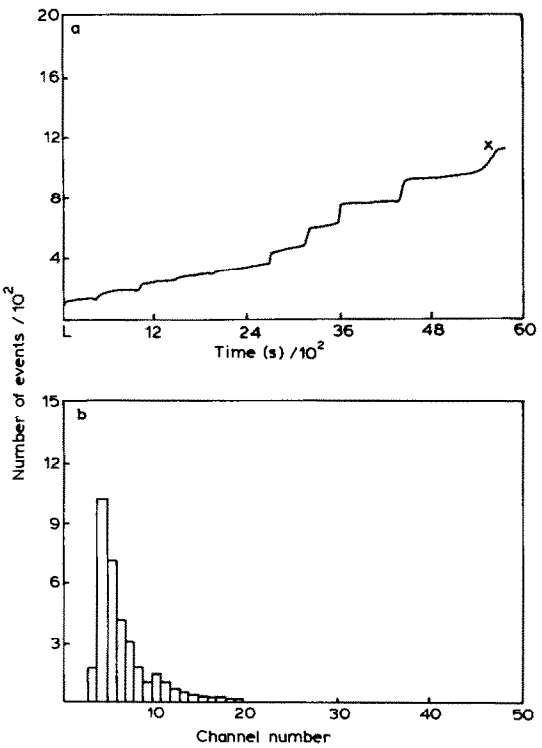

Fig. 7. A: cumulative number of acoustic events recorded with time during fatigue testing of an Emcompress tablet compressed at a compaction force of 8 kN. B: the distribution of energy levels of the acoustic emission during fatigue testing of an Emcompress tablet compressed at a compaction force of 8 kN.

fatigue test could not differentiate between the plasticity of Microtal and Dipac tablets - differences which were apparent using NWF determinations.

Acknowledgements

The authors would like to thank Professor B. Harris of the School of Materials Science, University of Bath, for use of the acoustic emission equipment.

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