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Elucidation of the compressive deformation behaviour of α-lactose monohydrate and anhydrous α-lactose single crystals by mechanical strength and acoustic emission analyses

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Summary

Compressive deformation studies on single α-lactose crystals by mechanical strength and acoustic emission analyses revealed a distinct difference in the deformation behaviour of α-lactose monohydrate and anhydrous α-lactose. α-Lactose monohydrate monocrystals were found to exhibit greater mechanical strength when compared with the anhydrous α-lactose crystals. The acoustic emission data show that the fragmentation process of the monohydrate crystals is acoustically more active and energetic. Amplitude distribution analysis of the acoustic signals further confirmed that the nature of fragmentation during the deformation of the two types of lactose was different. This is attributed to fundamental differences in the internal crystal structure of the two lactose types. This work shows that mechanical strength and acoustic emission analyses provide an insight into the fundamental deformation characteristics of these two types of lactose.

Introduction

In the field of tabletting technology, it is still not possible to predict with certainty how a given material will behave during compression. Substantial literature exists on different techniques and methods of analysis to elucidate the deformation mechanisms of pharmaceutical materials. Much of this research has been of an empirical nature in which the role of the fundamental mechanical properties and the deformation characteristics of many pharmaceutical materials have not been fully clarified.

Using α-lactose monohydrate and anhydrous α-lactose monocrystals, Wong and Aulton (1987) and Wong et al. (1988) have shown that fundamental mechanical and compression characteristics of single crystals can be assessed by microindentation and compressive deformation, providing both visual and quantitative confirmation of the well documented bulk compression characteristics of these two types of lactose (Lerk et al., 1983; Vromans et al., 1985). Recently, Waring et al.

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(1987a–c) have used an acoustic emission technique for the evaluation of pharmaceutical materials during tablet compression. This present work describes the use of acoustic emission information together with the mechanical data generated during compressive deformation of monocrystals of α-lactose monohydrate and anhydrous α-lactose to gain a better insight into the deformation and fragmentation process of single crystals of these lactose types.

Materials and Methods

Materials

Lactose monohydrate (Sigma, Poole, U.K.) was used as the starting material. For this work, macroscopically well-formed α-lactose monohydrate monocrystals of a range of sizes were grown by an agar-gel suspension technique (Wong and Aulton, 1987) and anhydrous α-lactose monocrystals were obtained by refluxing the monohydrate crystals in specially dried methanol (Wong et al., 1988).

Equipment

The single crystal compression rig developed by Wong et al. (1988) was modified by mounting an acoustic wave guide onto the static platen which was attached to a 50 N load transducer (Type U4000, Manwood Instruments Ltd, Basingstoke, U.K.). Attached to the other end of the wave guide was a differential acoustic transducer (Model D140B, Dunegan PAC, Cambridge, U.K.) with a bandwidth of 40–320 kHz. Acoustic coupling gel was used to enhance the acoustic signals from the static platen to the wave guide. The transduced acoustic signals were logged and analysed by a LOCator ANalyser (LOCAN) (Dunegan PAC, Cambridge, U.K.). This set-up enables simultaneous monitoring of the acoustic activity and the force-displacement profile. A schematic diagram of the arrangement is shown in Fig. 1.

Crushing procedure and monitoring of acoustic signals during single crystal compressive deformation

Selected well-formed single crystals of α-lactose monohydrate and anhydrous α-lactose of size range 2.5–4.5 mm were individually mounted onto interchangeable crystal holders using cyanoacrylate adhesive. The adhesive was allowed to cure for 7 days. The mounted monocrystals were then subjected to a compressive rate of 8.5 $\mu m\ s^{-1}$ under load as described previously (Wong et al., 1988), during which the force-displacement was recorded. The transduced acoustic signals emitted during the deformation process were simultaneously monitored using the LOCAN. These signals were conditioned by a set of parameters initiated in the LOCAN by the onboard computer. The settings of these parameters are given in Table 1. These parameters are explained with reference to Fig. 2 which shows all idealised acoustic signal. Superimposed on this diagram are various terms used in this work.

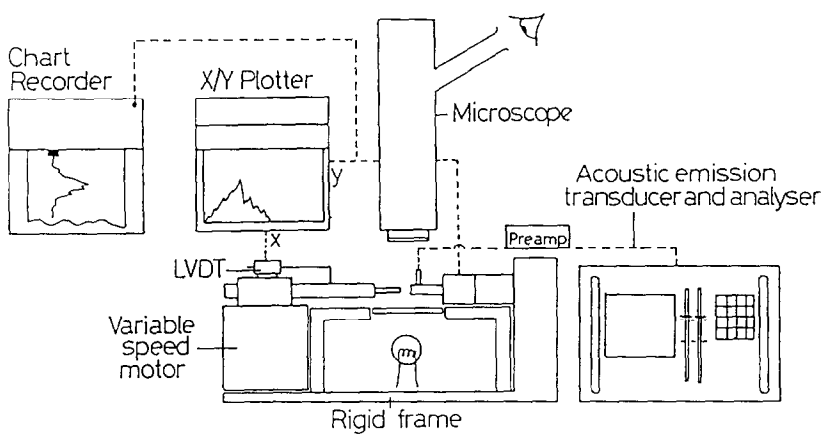

Fig. 1. The single crystal compression rig and acoustic transducer analyser set-up.

TABLE 1

Initiation parameter set up in the LOCAN acoustic signal analyser

Gain	53 dB
Threshold	36 dB
PDT	50 s
HDT	100 s
HLT	100 s

Prior to quantitative measurements, the acoustic analyser was calibrated using the Hsu-Nielson test which involved fracturing a standard 2H 0.5 mm pencil lead on the surface of the static platen. For this study, a peak amplitude of 90 dB was used as the reference calibration. The settings of all machine parameters were maintained unchanged throughout the study. The data acquired was processed by the onboard computer software and made available on a real-time data display and stored on floppy disc for further analysis.

Results and Discussion

Single crystals of α-lactose monohydrate and anhydrous α-lactose of a size range 2.5–4.5 mm in length were subjected to compressive deformation during which the force-displacement curve was recorded. Most of the crystal samples were also monitored simultaneously for acoustic emissions.

Crushing data

The crushing data of both types of lactose are summarised in Table 2. The data shown are in general agreement with previously published work (Wong et al., 1988). However, the present data were generated from a greater number of crystals (50) with a wider range of crystal sizes. The mean crystal length for the two lactose types was about the same.

The force-displacement data for α-lactose monohydrate monocrystals and anhydrous α-lactose are also illustrated graphically in Figs 3a–

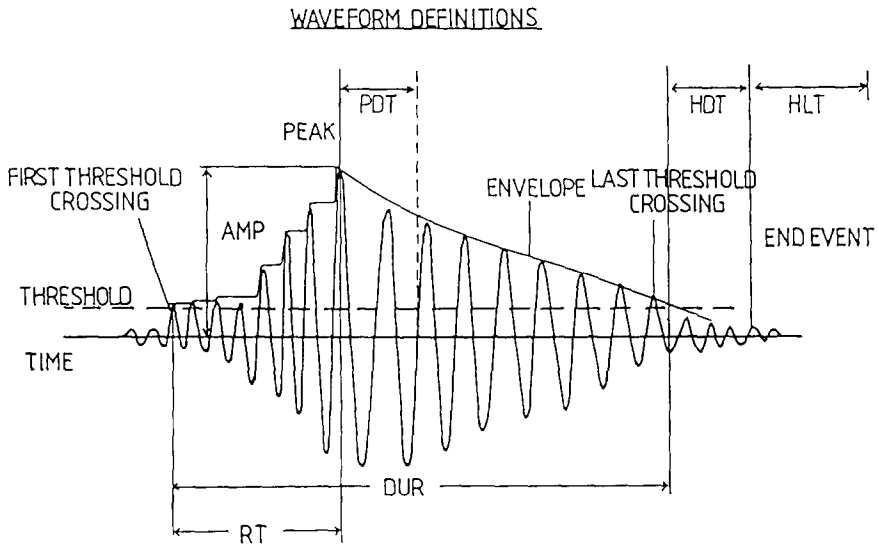

Fig. 2. Diagram of an idealised acoustic emission signal with waveform definitions. Terms used to characterise the acoustic signals: RT: *Rise time*: Time from first threshold crossing to peak of signal. HDT: *Hit definition time*: When no threshold crossing has occurred for the duration of the HDT, the acoustic event is presumed to have ended. PDT: *Peak definition time*: Time interval used to determine the peak of the waveform. Should the acoustic signal not increase during this time, the last highest value will be recorded as the peak. HLT: *Hit lockout time*: Time between end of HDT and the enabling of a channel for the next acoustic signal. This can be used to eliminate reflections of the signals. Threshold: Detected threshold in dB with reference to 1 μV at sensor. Other terms: Event: An event is defined as a detected acoustic emission burst from the first threshold crossing until the end of the HDT. DUR: Duration of events in microseconds. AMP: Amplitude: Rectified peak signal in dB. Counts: Number of threshold crossings in the event. Energy: Area under the signal envelope from the first to the last threshold crossing (dB μs).

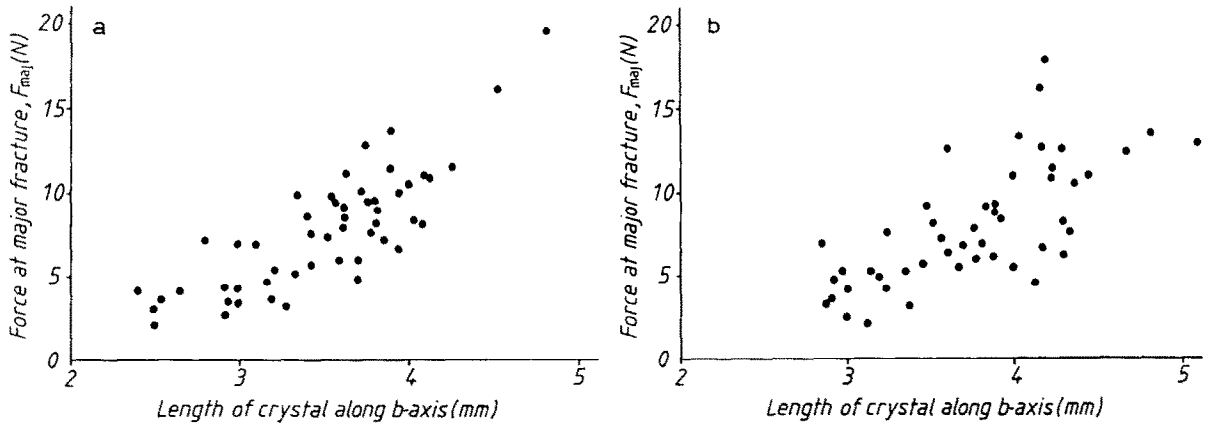

Fig. 3. Mechanical data (force at major fracture) from the compressive deformation of monocrystals of α-lactose monohydrate (a) and anhydrous α-lactose (b).

5a and 3b–5b, respectively. The scatter of the force-displacement data as seen on these diagrams is indicative of brittle fracture. These diagrams show that the force up to major fracture, displacement up to major fracture and work done up to major fracture all increased with an increase in crystal size. This is due to an increase both in the bulk of the crystal and the contact area between the deforming crystal tip and the load transducer platen as the crystal size increases.

The data show that the crushing force for similar sized crystals is only slightly higher for monohydrate crystals. This may be explained by the fact that monohydrate crystals which constantly undergo spalling fracture have in fact dissipated the stress exerted at the crystal tip as it is being crushed. Thus the recorded force is not a continual increment of the stress exerted but fluctuates as shown by the jagged force-displacement curve reported in our previous study (Wong et al., 1988).

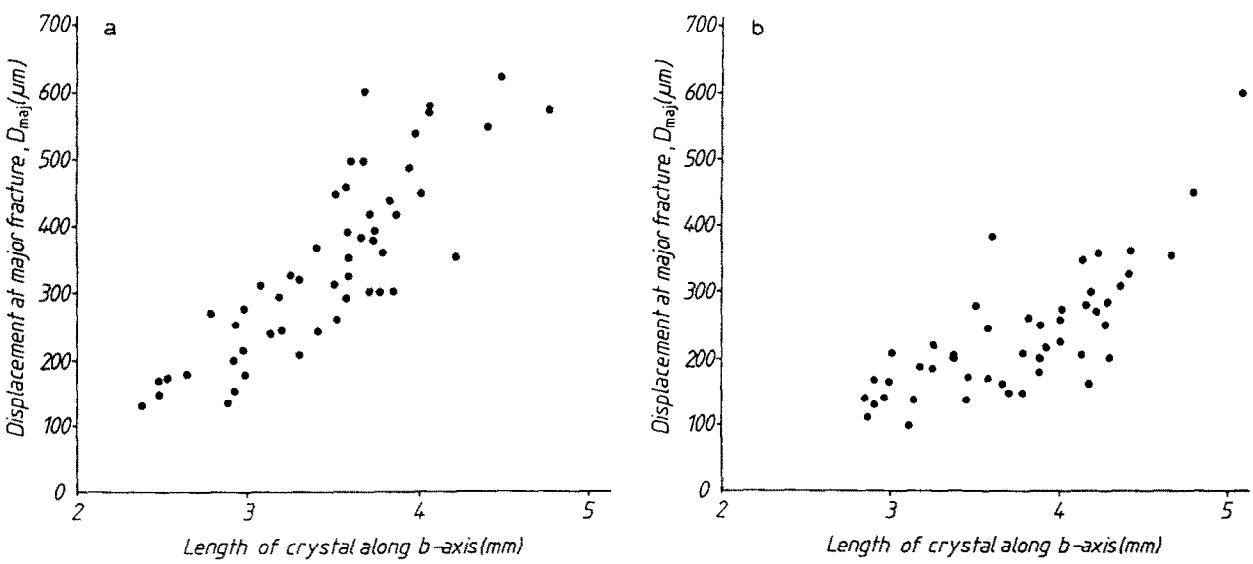

Fig. 4. Mechanical data (displacement at major fracture) from the compressive deformation of monocrystals of α-lactose monohydrate (a) and anhydrous α-lactose (b).

TABLE 2

Summary of the crushing data for α-lactose monohydrate and anhydrous α-lactose

Property	α-Lactose monohydrate	Anhydrous α-lactose
Mean length of crystal tested (mm)	3.50	3.64
Mean width of crystal at base of tip (mm)	1.56	1.60
Cross-sectional area of crystal at base of tip (mm^2)	0.272	0.268
Force at major fracture (F_{maj}) (N)	7.78	7.71
Stress at base of crystal tip at major fracture (MPa)	33.29	29.84
Displacement at major fracture (D_{maj}) (μm)	354.0	227.0
% Strain ($100 \times \delta L/L$) at major fracture (%)	10.1	6.2
Work done up to major fracture (W_{maj}) (mJ)	1.415	0.986

Furthermore, due to the constant spalling fracture of the monohydrate crystal, which resulted in breakage of large crystal fragments from the main crystal, the actual contact area between the crushed monohydrate crystal and the load transducer platen is much smaller than if the crystal tip was to remain intact and in full contact with the platen, which is the case for the anhydrous lactose. Consequently, one would expected to register a lower crushing force at major fracture for the monohydrate crystals. However, the displacement and work done up to major fracture are much larger for the monohydrate crystals.

The best measure of the mechanical strength of the crystal is the stress at fracture. However, this requires an accurate measurement of the true area of contact. Due to the difficulty in measuring the actual contact area, the stress at major fracture was calculated, using the cross-sectional area of the crystal at the base of the tip as an arbitrary contact area. By this method, one has to assume that the base of the crystal tip remains intact and in full contact with the platen. In reality, this criterion is only fulfilled in the case of the anhydrous crystal. As a consequence of the propagative fracture of the monohydrate crystal, the real area of contact for the monohydrate crystal is in fact much smaller than the calculated area. Therefore, the stress experienced by these crystals will be much larger than estimated by this method.

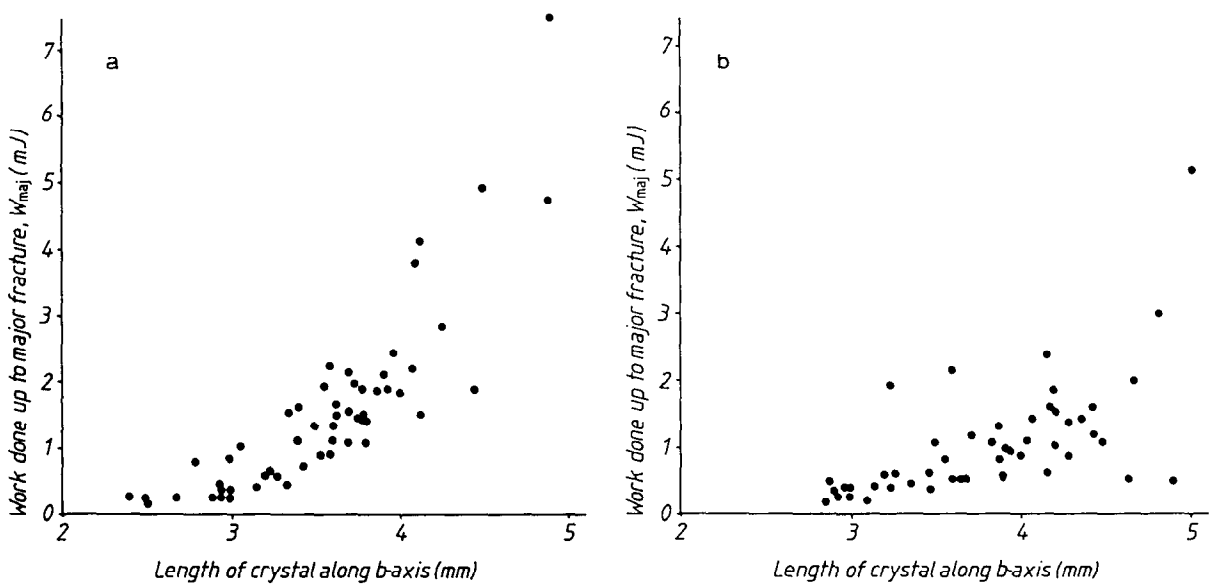

Fig. 5. Mechanical data (work done up to major fracture) from the compressive deformation of monocrystals of α-lactose monohydrate (a) and anhydrous α-lactose (b).

Nevertheless, the calculated stress at major fracture for the monohydrate crystal is still higher, even though only marginally, than the anhydrous crystal.

Theoretically, one would expect an increase in fracture stress with decreasing particle size because larger crystals have a greater incidence of defects which facilitate brittle fracture; in smaller particles deformation will be mainly by plastic deformation (Roberts and Rowe, 1987). However, such observations may only be made with much smaller crystals. The crystals used in this study are probably in the size range where such observation would not be so evident. For this reason and also because of the difficulty in measuring the true contact area, no attempt was made to correlate the relationship between fracture stress with particle size for these crystals.

In general, the monohydrate crystals exhibit greater mechanical strength when compared with the anhydrous crystals. The anhydrous lactose withstood a lower maximum recorded load, exhibited a lower displacement prior to the large destructive crack and thus required less work to break than the monohydrate crystals. It was previously observed (Wong et al., 1988) that the types of lactose have very different fragmentatory characteristics. Analysis of the acoustic activity monitored during compressive deformation of these crystals was carried out so as to differentiate the fragmentation process of the two lactose types.

Acoustic emission data

In this present study, the captured acoustic emission data were analysed as follows: (a) total acoustic counts up to major fracture; (b) total acoustic energy up to major fracture and (c) amplitude distribution analysis.

A comparison of the total acoustic emission counts and total energy of acoustic emission up to the point of major fracture during the crushing of monohydrate and anhydrous crystals was carried out. These results are shown in Figs 6 and 7, respectively. These figures show clearly that the monohydrate crystals exhibited far greater acoustic emission than anhydrous crystals during deformation. The results also showed that the acoustic

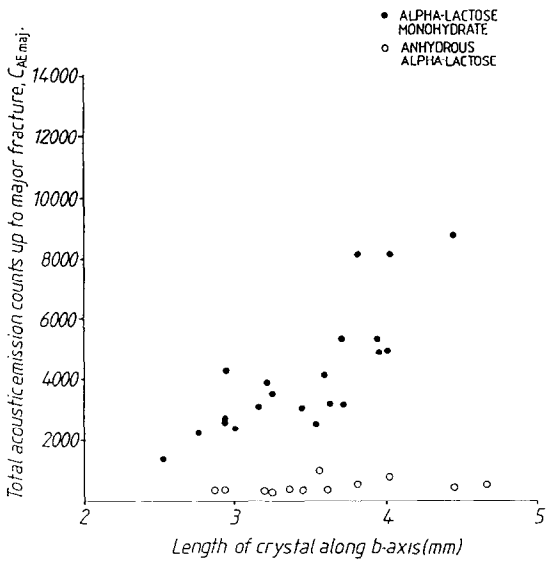

Fig. 6. Comparison of the total acoustic emission counts from the compressive deformation of monocrystals of α-lactose monohydrate and anhydrous α-lactose.

counts and acoustic energy increased with an increase in crystal size for the monohydrate crystal whereas with the anhydrous crystal there is little

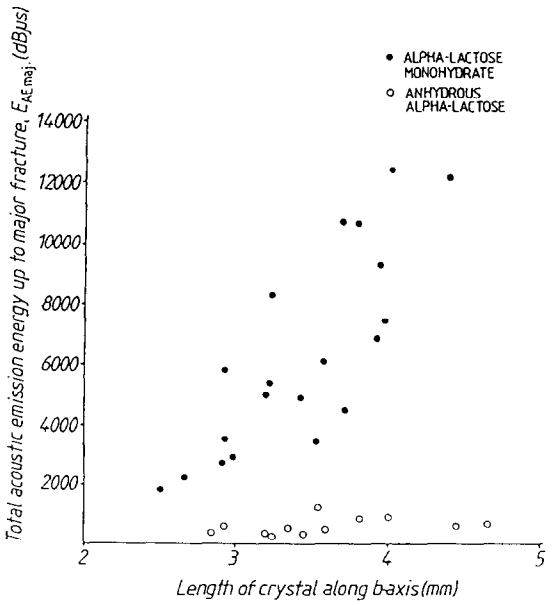

Fig. 7. Comparison of the total energy of acoustic emission from the compressive deformation of monocrystals of α-lactose monohydrate and anhydrous α-lactose.

difference in the amount of detectable acoustic activity for crystals of different sizes.

The results of the acoustic activity described above correlated with the crushing strength data and visual confirmation which showed that the two types of lactose differed in the degree and nature of their fragmentation mechanism. This difference was further characterised using amplitude distribution analysis which involves plotting the log of cumulative number of events which exceed a particular amplitude vs that amplitude (in dB). The slope of this plot is known as the *b* value (Pollock, 1981); *b* values are calculated in terms of decade per decade, remembering that dB is itself a log scale. A low *b* value is exhibited by materials which undergo brittle fracture whereas a high *b* value is indicative of less brittle mechanisms. The amplitude distibution curves for both types of lactose are shown in Fig. 8.

For anhydrous α-lactose, the amplitude distribution curve yields one slope with a *b* value of 0.62. The single slope indicates that a single fracture mechanism occurred during compressive deformation of the anhydrous crystals. This confirmed the observations that most of the acoustic signals were in fact generated as the anhydrous crystals underwent terminal fracture into two halves. For the monohydrate crystal, the situation is more complex. The deformation of these crystals involved spalling fracture of the tip followed by a terminal fracture (Wong et al., 1988). This is confirmed by the amplitude distibution curve which shows two slopes. Slope 1 with a *b* value of 0.50 is attributed to spalling fracture whereas slope 2 with a *b* value of 0.77 is due to terminal fracture. For comparative evaluation of the two lactose, a single *b* value of 0.57 was also obtained for the monohydrate crystal.

The *b* values confirmed the deformability of the two types of lactose. The lower *b* value of the monohydrate crystal indicates that it is more brittle. On the other hand, the higher *b* value of the anhydrous crystals suggested that they are more deformable than the monohydrate crystals which is in accordance with the crushing strength data. If ductile flow was to occur for the anhydrous crystal, the acoustic activity would be of continual emissions of low amplitudes and high frequencies. The

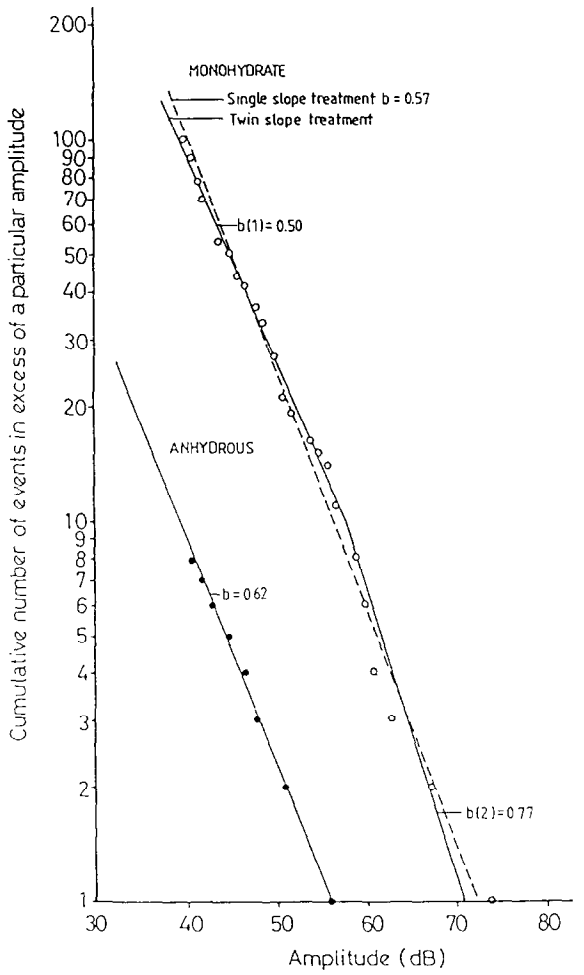

Fig. 8. A plot of cumulative events vs amplitude for α-lactose monohydrate and anhydrous α-lactose.

low acoustic activity with a few abrupt high amplitude acoustic emissions is the reason for the steeper slope and higher *b* value for the amplitude distribution curve of the anhydrous crystals. This suggested deformation by fragmentation of a different character rather than deformation by ductile flow. Therefore, the amplitude distribution analysis helps to identify the nature of the fragmentation during the deformation of these two lactose types.

The difference in acoustic activity of the two types of lactose can best be explained in terms of the internal structure of the lactose crystals. The anhydrous crystal is composed of an aggregate of

smaller crystal fragments which are loosely bound. The dehydration process results in extensive internal fragmentation, transforming the single monohydrate crystal into a polycrystalline particle whilst retaining its original shape and form. Lerk (1984) illustrated this observation with an SEM photomicrograph of a section of a partially dehydrated monohydrate crystal. The SEM photomicrograph revealed a monohydrate core with a smooth surface texture which was surrounded by loose aggregates of anhydrous α-lactose crystal fragments.

During the crushing of the anhydrous crystals, compressive deformation probably occurred by void coalescence and rearrangement of crystal fragments by sliding of these fragments over each other. This is followed by the crumbling of materials during which the displaced fragments broke away from the overall crystal without undergoing any propagative fracture themselves and ultimately the collapse of the whole anhydrous crystals. Therefore, the anhydrous crystals also undergo brittle failure with relatively few major fractures rather than ductile flow, hence accounting for the low acoustic activity observed. It also explained the small differences in acoustic activity monitored for crystals of different size, since most of the fractures will have occurred during the dehydration process. Therefore, no new or relatively few fractures were created during the crushing of these crystals. In fact, the only significant acoustic activity of the anhydrous form was detected at terminal fracture as the crystal collapsed.

On the other hand, the monohydrate crystals exhibited spalling brittle fracture as they deformed. The propagative nature of the fracture emitted high amplitude acoustic signals and this coupled with the high incidence of fractures accounted for the high acoustic counts and acoustic energy emitted by α-lactose monohydrate crystals. Larger crystals underwent more spalling fractures compared with crystals of smaller size before the final collapse of the crystals, hence greater acoustic activity was detected.

Conclusion

Generally, α-lactose monohydrate crystals exhibit greater mechanical strength when compared with the anhydrous α-lactose crystals. The anhydrous lactose withstood a lower maximum recorded load, exhibited a lower displacement prior to the large destructive crack and thus required less work to break than the monohydrate crystals.

α-Lactose monohydrate crystals which fractured by spalling emitted acoustic signals of high amplitude thus accounting for the high acoustic count and high energy detected. The low acoustic activity detected for the anhydrous α-lactose can be explained by the fact that the crystals were already fragmented internally and that the deformation of these crystals only resulted in localised displacement of materials without large internal cracking as with the monohydrate form.

This work shows that the correlation of acoustic emission with the crushing strength data provides valuable information regarding the microprocesses which take place within single crystals during deformation, thus providing a further opportunity to gain a better picture of the deformation mechanisms involved. Fundamental studies of this nature are important in providing a better understanding of material behaviour during bulk compression.

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References

Lerk, C.F., The effect of thermal and mechanical treatment on the physicopharmaceutical properties of lactose. *Proc. 4th Pharm. Tech. Conf.*, Edinburgh, 3 (1984) 87–106.

Lerk, C.F., Andreae, A.C., De Boer, A.H., Bolhuis, G.K., Zuurman, K., De Hoog, P., Kussendrager, K. and Van Leverink, J., Increased binding capacity and flowability of alpha-lactose monohydrate after dehydration. *J. Pharm. Pharmacol.*, 35 (1983) 747–748.

Pollock, A.A., Acoustic emission amplitude distribution. *Int. Adv. N.D.T.*, 7 (1981) 215–239.

Roberts, R.J. and Rowe, R.C., Brittle/ductile behaviour in pharmaceutical materials used in tabletting. *Int. J. Pharm.*, 36 (1987) 205–209.

Vromans, H., De Boer, A.H., Bolhuis, G.K., Lerk, C.F., Kussendrager, K.D. and Bosch, H., Studies on tabletting properties of lactose. Part 2: Consolidation and compaction of different types of crystalline lactose. *Pharm. Weekbl. Sci. Edn.*, 7 (1985) 183–186.

Waring, M.J., Rubinstein, M.N. and Howard, J.R., Acoustic emission of pharmaceutical materials during compression. *Int. J. Pharm.*, 36 (1987a) 29–36.

Waring, M.J., Rubinstein, M.N. and Howard, J.R., Acoustic emission of pharmaceutical materials: the effect of compression speed, ejection, lubrication and tablet weight. *Int. J. Pharm.*, 40 (1987b) 15–22.

Waring, M.J., Rubinstein, M.N. and Howard, J.R., Amplitude analysis of the acoustic emissions from pharmaceutical materials during compression. *J. Pharm. Pharmacol.*, 39 (1987c) Suppl. 131P.

Wong, D.Y.T. and Aulton, M.E., Modification of the mechanical properties of alpha-lactose monohydrate crystals by adjustment of growth conditions. *J. Pharm. Pharmacol.*, 39 (1987) Suppl. 124P.

Wong, D.Y.T., Wright, P. and Aulton, M.E., The deformation of alpha-lactose monohydrate and anhydrous alpha-lactose monocrystals. *Drug Dev. Ind. Pharm.*, 14 (1988) 2109–2126.