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Formation and compression characteristics of prismatic polyhedral and thin plate-like crystals of paracetamol

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Abstract

Prismatic polyhedral crystals of paracetamol were prepared by cooling an aqueous saturated solution of paracetamol from 65 to 25°C. Thin plate-like crystals were prepared by adding a concentrated solution of paracetamol in hot ethanol to water at 3°C. Infrared (IR), X-ray powder diffraction (XPD) and differential scanning calorimetry (DSC) studies confirmed that these two forms of crystals were structurally similar, therefore polymorphic modifications were ruled out. The crystal habit influenced the compression properties during axial compression of paracetamol at different constant rates in a compaction simulator, the Heckel plots and their associated constants being dependent on the habits. The correlation coefficient of the initial part of the Heckel plots, and also the values of strain rate sensitivity (SRS), were lower for thin plate-like crystals, indicative of greater fragmentation for the thin plate-like as compared to polyhedral crystals. Compacts made from thin plate-like crystals exhibited higher elastic recoveries and elastic energies indicating that these crystals underwent less plastic deformation during compression than the polyhedral crystals. © 1999 Elsevier Science B.V. All rights reserved.

Keywords: Paracetamol; Crystallisation; Crystal habit; Compaction; Apparent mean yield pressure; Plastic deformation; Elastic deformation; Fragmentation

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1. Introduction

Crystallisation from solution is used widely for the purification of drugs during their final stages of manufacture. Crystallisation techniques can modify the crystal properties such as habit, polymorphism and size. The nature and extent of these changes depend on the crystallisation conditions, including the presence of impurities, type of solvent and cooling rate (Mullin, 1993).

The crystal habit of a drug is an important variable in pharmaceutical manufacturing. Different crystal habits of a particular drug possess different planes and thus differ not only in their

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specific surface, but also in their free surface energy. Therefore, they may exhibit different physico-mechanical properties (Hüttenrauch, 1983). Properties such as dissolution rate, powder flow and compressibility, which are of pharmaceutical interest, can differ for different habits of the same drug (York, 1983; Marshall and York, 1991). Attempts to change the morphology and the workability of drugs using alternative crystallisation procedures include modification of the crystal habits of drugs such as ibuprofen (Gordon and Amin, 1984), hexamethylmelamine (Gonda et al., 1985) and nitrofurantoin (Marshall and York, 1989, 1991).

Crystallisation of paracetamol from a wide range of solvents such as water, alcohols, esters, ketones, dioxane or acetone produced essentially prismatic polyhedral crystals (Fairbrother, 1974; Fachaux et al., 1992; El-Said, 1995). In fact, the prismatic polyhedral habit is the dominant form in paracetamol crystals. However, Fairbrother (1974) demonstrated that crystallisation of paracetamol from benzene, toluene and several chlorinated solvents such as dichloroethane produced slender rhombohedral needles.

One common method of crystallisation is by the addition of a second substance which reduces the solubility of the solute in the solvent. This method is known as salting-out. The added substance may be a liquid, solid or gas, although liquids (known as diluents) are most frequently used. The diluent must be miscible with the crystallisation solvent and the solute should be relatively insoluble in it. This process is commonly used during crystallisation of organic substances from water-miscible organic solvents, by controlled addition of water to the solution. The term watering-out is used in this case.

The aim of this study was to produce paracetamol crystals of different habit, using a watering-out crystallisation technique from ethanolic solutions. The effect of crystallisation conditions such as ethanol/water combination or cooling temperature on the crystal habit were studied. The solid state characteristics and compression properties of the modified crystals were also investigated.

2. Materials and methods

Paracetamol powder, was obtained from Sterling Organics, Northumberland, UK. Absolute ethanol BP, containing not less than 99.5% v/v of C_2H_5OH, was obtained from Hayman Ltd., Witham, Essex, UK.

2.1. Crystallisation procedures

In every case, the precipitated crystals were collected by filtration using a sintered glass funnel no. 3 under vacuum after 15 min, with no agitation. They were dried for 24 h at 55°C and stored in a dessicator at room temperature before use in tightly closed jars. This was to remove any moisture that might affect the compaction properties of paracetamol (Garr and Rubinstein, 1992).

2.1.1. Crystallisation of paracetamol using a watering-out method at 3°C

Samples of paracetamol (5 g) were dissolved in 12 ml of ethanol at 75°C. The temperature was reduced to 65°C and the solutions were rapidly added to 50 ml water at 3°C. The resultant solutions were mixed by means of a glass rod and maintained at 3 ± 1°C.

2.1.2. Alternative crystallisation procedures

Crystallisation of paracetamol by a watering-out method at 25°C was carried out as explained above but maintaining 50 ml water at 25 ± 1°C.

Paracetamol was crystallised from an ethanol/water mixture by dissolving 5 g paracetamol in a mixture of 12 ml ethanol and 50 ml water (the same quantities as used in the watering-out methods) at 65°C. The solutions were then cooled to 3 ± 1 or 25 ± 1°C.

Paracetamol was also crystallised directly from water by dissolving 1.5 g paracetamol in 60 ml water at 65°C. The solutions were cooled to 3 ± 1 or 25 ± 1°C.

2.2. Scanning electron microscopy (SEM) and particle size measurements

Electron-micrographs of crystals were obtained using a scanning electron microscope (Jeol model

JSM T200, Tokyo, Japan). The specimens were mounted on a metal stub with double sided adhesive tape and coated under vacuum with gold in an argon atmosphere prior to observation. The particle sizes of crystals were estimated from the electron micrographs. For polyhedral crystals the longest dimension was taken as the length and the shortest dimension as the width. The thickness of polyhedral crystals was approximately equal to their width. The thickness was only determined for plate-like crystals. Each determination was carried out on a minimum of 60 crystals.

2.3. Differential scanning calorimetry (DSC)

A differential scanning calorimeter model DSC7 (Perkin Elmer, Beaconsfield, UK), controlled by a Perkin Elmer TAC7, was used. The equipment was calibrated using indium and zinc. Samples of paracetamol crystals (2–4 mg) were heated at 10°C min^{-1} in crimped aluminium pans under nitrogen atmosphere. The onsets of the melting points and enthalpies of fusion of samples were automatically calculated by the instrument.

2.4. X-ray powder diffraction (XPD)

X-ray diffraction spectra of paracetamol samples were obtained using a Phillips PW 1729 X-ray generator fitted with PW 1710 diffractometer (Phillips, Almelo, Netherland). The cavity of the metal sample holder was filled with the ground sample powder and then smoothed with a spatula. A scanning rate of 0.04° 2θ s^{-1} over the range of 10–70° 2θ was used to produce each spectrum.

2.5. Infrared spectroscopy (IR)

Infrared spectra were recorded using a Perkin Elmer FTIR 1600 spectrophotometer (Norwalk, Connecticut, USA) utilising potassium bromide discs.

2.6. Compression

Sieved fractions of paracetamol (105–210 μm) were used to achieve approximate equivalency of particle size. Compression was carried out using the High Speed Compaction Simulator (ESH Testing Ltd., Brierley Hill, West Midlands, UK) modified by the Liverpool School of Pharmacy and Chemistry, fitted with 12.5 mm flat faced punches. A sawtooth time-displacement profile was used to control the movement of both upper and lower punches. The die wall was cleaned with acetone and prelubricated with 4% w/w magnesium stearate in acetone before each compression. Paracetamol samples were hand filled into the die. Four tablets were produced at compression speeds of 10, 50, 100 or 250 mm s^{-1} up to a maximum 30 kN compaction force. A constant weight of 400 mg was maintained for all the samples. During compression, upper punch load and punch separation were monitored to an accuracy of 0.05 kN and ±12 μm, respectively (Bateman, 1988).

2.7. Analyses of compaction data

During a compression cycle, force and displacement data from the upper and lower load cells and linear variable differential transformers (LVDTs) were captured and analysed.

2.8. Measurement of elastic and plastic energy

For a system in which both punches are mobile, the punch separation may be plotted against upper punch force. The area under this curve will be the work done or energy. The net work of compaction (plastic energy) and expansion work of compaction (elastic energy) were measured using energy analysis on force–punch separation plots.

Fig. 1 illustrates a typical force–punch separation plot, where A is the punch separation when the compression force is first recorded. B is the peak force at minimal punch separation, C represents the minimum punch separation and D is the separation after decompression when the compression force is zero, giving the tablet thickness. The area ABC gives the gross energy, and the area under curve CBD corresponds to the decompression energy or elastic energy. The net compaction energy or plastic energy (the area under curve ABD) was determined from the difference between area ABC and area CBD. A computer

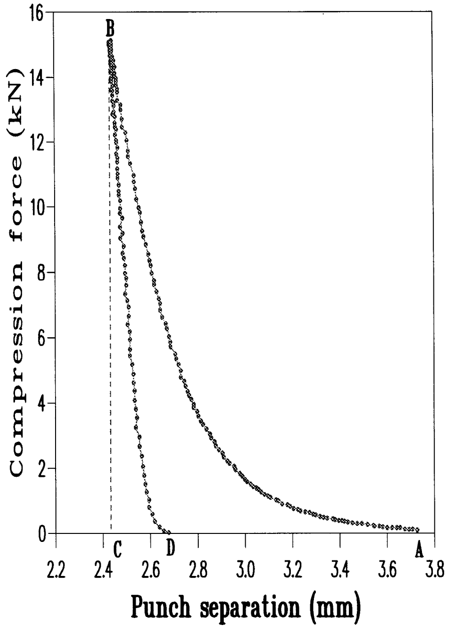

Fig. 1. A typical force-punch separation plot for untreated paracetamol (particle size 105–210 μm) obtained at a compression speed of 10 mm s^{-1}.

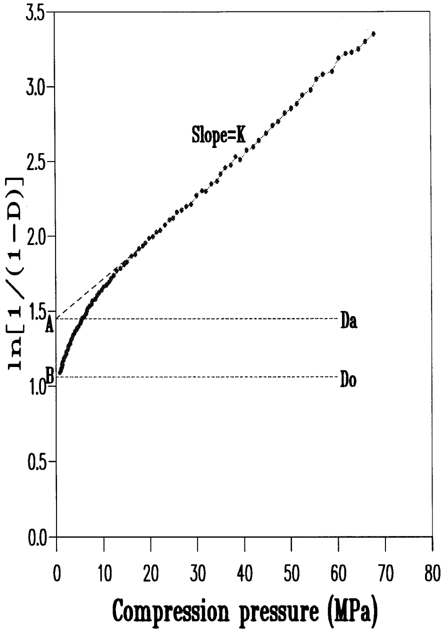

Fig. 2. Typical Heckel plot for untreated paracetamol (particle size 105–210 μm) obtained at a compression speed of 10 mm s^{-1}.

programme was employed to calculate plastic and elastic energies from data obtained during compaction.

2.9. Heckel analysis

A computer programme was employed to fit data obtained during compaction to the Heckel equation (Eq. (1)) (Heckel, 1961a,b).

$$\ln[1/(1-D)] = KP + A \quad (1)$$

Fig. 2 illustrates a typical Heckel plot. In Eq. (1), D is the relative density of tablet (the ratio of tablet density to true density of powder) at applied pressure P. K is the slope of the straight line portion of the Heckel plot and the reciprocal of K is the mean yield pressure, and since the tablet dimensions were measured in the die, it is referred to as apparent mean yield pressure. From the intercept of the linear portion of this plot, A, the total densification of the powder bed due to die filling and particle rearrangement, D_a, was obtained using Eq. (2).

$$D_a = 1 - e^{-A} \quad (2)$$

From B, the place where the Heckel plot intercepts the $\ln 1/1-D$ axis (Fig. 2), the density of powder at zero pressure, D_o, is obtained (Eq. (3)). D_o can be defined as the densification due to die filling or to initial powder packing.

$$D_o = 1 - e^{-B} \quad (3)$$

2.10. Determination of elastic recovery of the tablet in the die

Tablets made from paracetamol samples were too weak and capped after ejection, so that it was impossible to handle them and monitor their thickness outside the die. Therefore, the percentage of elastic recovery in the die of each tablet was calculated using Eq. (4), (Armstrong and Haines-Nutt, 1972).

$$\%\ \text{Elastic recovery} = [(H - H_c)/H_c] \times 100 \quad (4)$$

where H_c and H are the thickness of tablet under maximum pressure and after the compression force was removed, respectively. The values were determined from the compaction simulator displacement measurements.

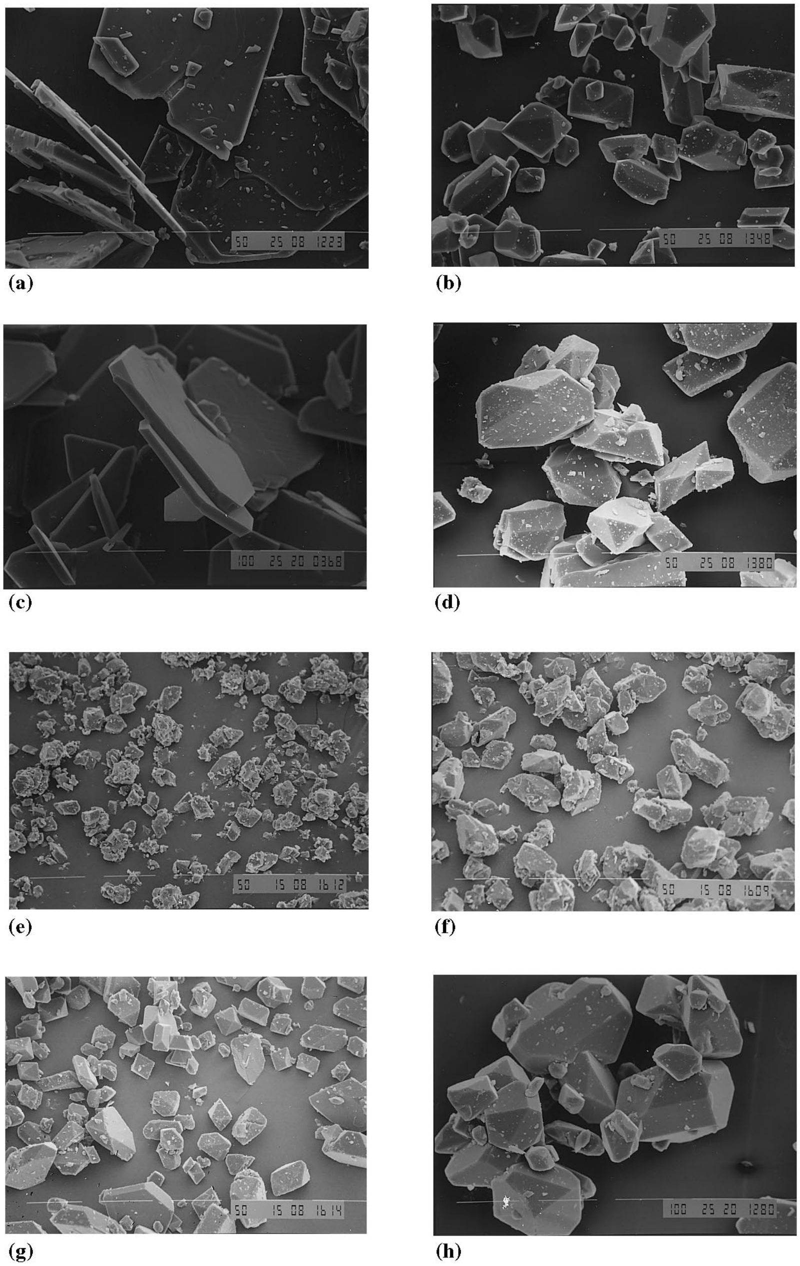

Fig. 3. Scanning electron micrographs of paracetamol particles crystallised by the (a) watering-out method at 3°C; (b) watering-out method at 25°C; (c) from a mixture of ethanol/water at 3°C; (d) at 25°C; (e) from ethanol at 3°C; (f) at 25°C; (g) from water at 3°C and (h) at 25°C (all magnifications × 200).

3. Results and discussion

Fig. 3a shows the scanning electron micrographs of paracetamol crystals obtained by the watering-out method at 3°C. These crystals were very thin and flaky. Fig. 3b shows the scanning electron micrographs of paracetamol crystals obtained by the watering-out method at 25°C. These were prismatic polyhedral crystals. Crystallisation of paracetamol from a mixture of ethanol/water at 3°C produced thin plate-like crystals (Fig. 3c), while at 25°C it produced polyhedral crystals (Fig. 3d). Crystallisation of paracetamol from ethanol or water at 3 or 25°C, produced prismatic polyhedral crystals (Fig. 3e, f, g and h).

The polyhedral habit is the dominant form of paracetamol crystals and crystallisation of paracetamol from different solvents such as water, ethanol or dioxane (Fachaux et al., 1992), isopropanol, dioxane or acetone and their mixtures with water (El-Said, 1995), alcohols, esters, ketones or acetonitrile (Fairbrother, 1974) produced prismatic polyhedral crystals. The results clearly indicate that a combination of ethanol and water as crystallisation solvent and a low crystallisation temperature (3°C), i.e. rapid cooling, was required to produce thin plate-like crystals of paracetamol. In the absence of one of these two factors, polyhedral crystals were produced. The formation of thin plate-like crystals of paracetamol is probably attributed to an interaction between paracetamol and the binary system during crystallisation in conjunction with rapid cooling (at3°C).

Cooling rate has also a major influence on the degree of supersaturation of a system. The extent of supersaturation may cause preferential growth of crystals in one particular direction, leading to the formation of a different crystal habit (Mullin, 1993). For instance, naphthalene was crystallised as thin-plates from methanol by rapid cooling, but when it was slowly crystallised, it yielded compact (grain-like) crystals (Haleblian, 1975). Garti and Tibika (1980) demonstrated that by increasing the cooling rate during crystallisation of nitrofurantoin from a formic acid/ethanol mixture, more elongated crystals were produced, i.e. with increase in the cooling rate the ratio of length to width increased.

Table 1
The onsets of melting point (T_m) and enthalpies of fusion (ΔH_f) for thin plate-like and polyhedral crystals of paracetamol[a]

Crystal type	Onset of T_m ($\pm$S.D.) (°C)	ΔH_f ($\pm$S.D.) (J g^{-1})
Thin plate-like crystals	171.87 ± 0.14	179.35 ± 10.47
Polyhedral crystals	171.91 ± 0.21	176.75 ± 4.82

[a] Results are the means and standard deviations of four determinations.

3.1. Solid state characteristics of polyhedral and thin plate-like crystals of paracetamol

Since the compression properties of polyhedral crystals of paracetamol obtained from water at 25°C (Fig. 3h) and thin plate-like crystals obtained by the watering-out method at 3°C (Fig. 3a) were investigated in this study, the solid state characteristics of these two forms of paracetamol crystals were assessed. DSC scans of the thin plate-like crystals and polyhedral crystals were similar showing only the melting endotherm of paracetamol. The mean values of the onsets of the melting point and the enthalpies of fusion for these two forms of crystals are presented in Table 1. No events such as hydration, solvation or polymorphic modification, had occurred during crystallisation.

Fig. 4 shows the size distributions of polyhedral crystals and thin plate-like crystals of paracetamol. There is a large difference between the size dimensions of these two forms of crystals. This indicates a strong inhibition of crystal growth at some crystal faces and the inducement to more growth at other faces for the thin plate-like as compared to the polyhedral crystals.

The X-ray powder diffraction spectra for the thin plate-like and polyhedral crystals of paracetamol are presented in Fig. 5. X-ray powder diffraction is a very useful method in determining whether a pair of crystals of a particular drug are polymorphs. In general for two forms of crystals, when the patterns (peak positions) are identical, the particles have the same internal structures. If the patterns are different, then the crystals have different internal structures and are polymorphs (Byrn, 1982). Here both samples exhibited spectra with similar positions of peaks (2θ values) (Fig.

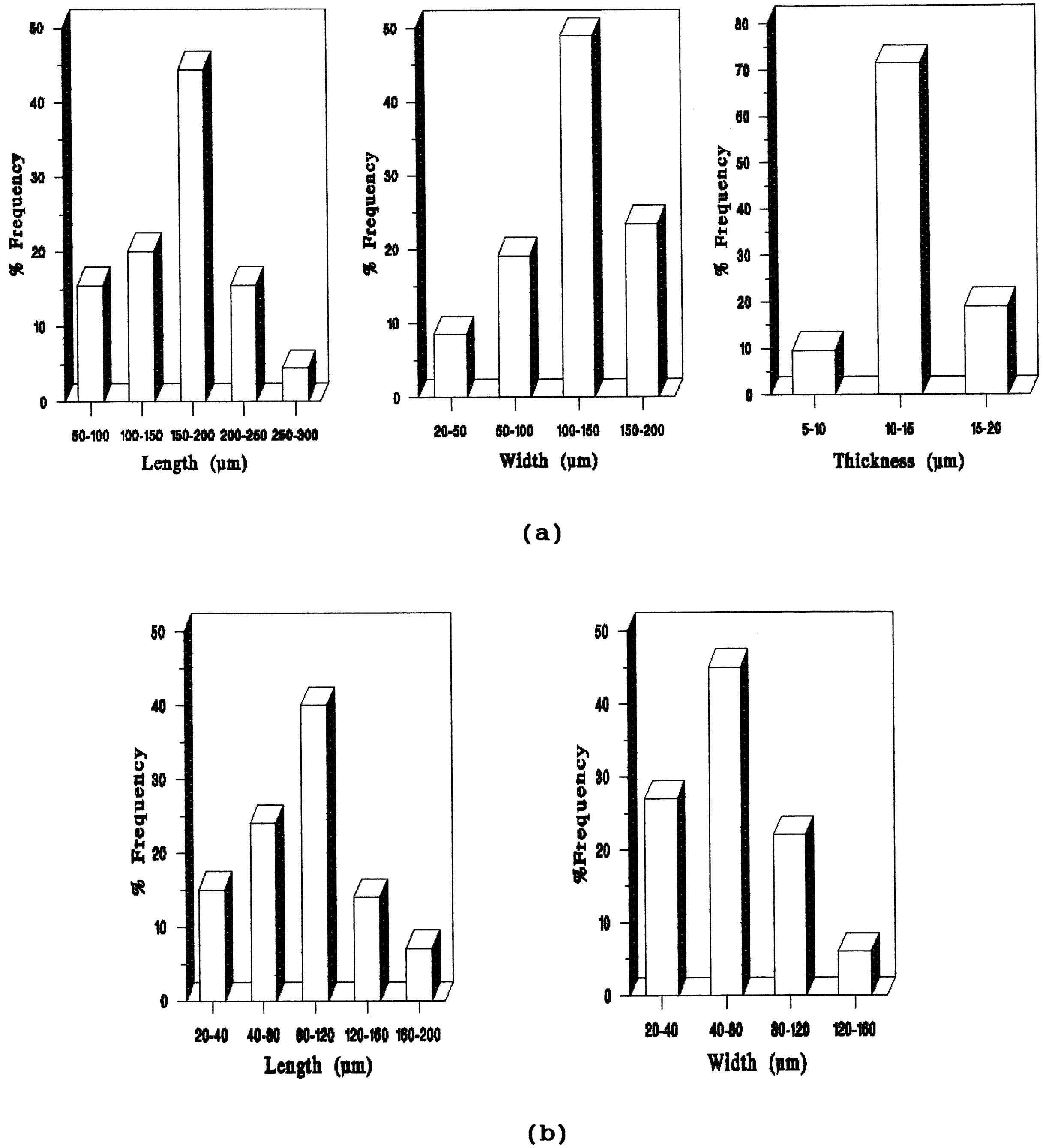

Fig. 4. Size distributions of (a) thin plate-like and (b) polyhedral crystals of paracetamol. The thickness of polyhedral crystals were approximately equal to their width.

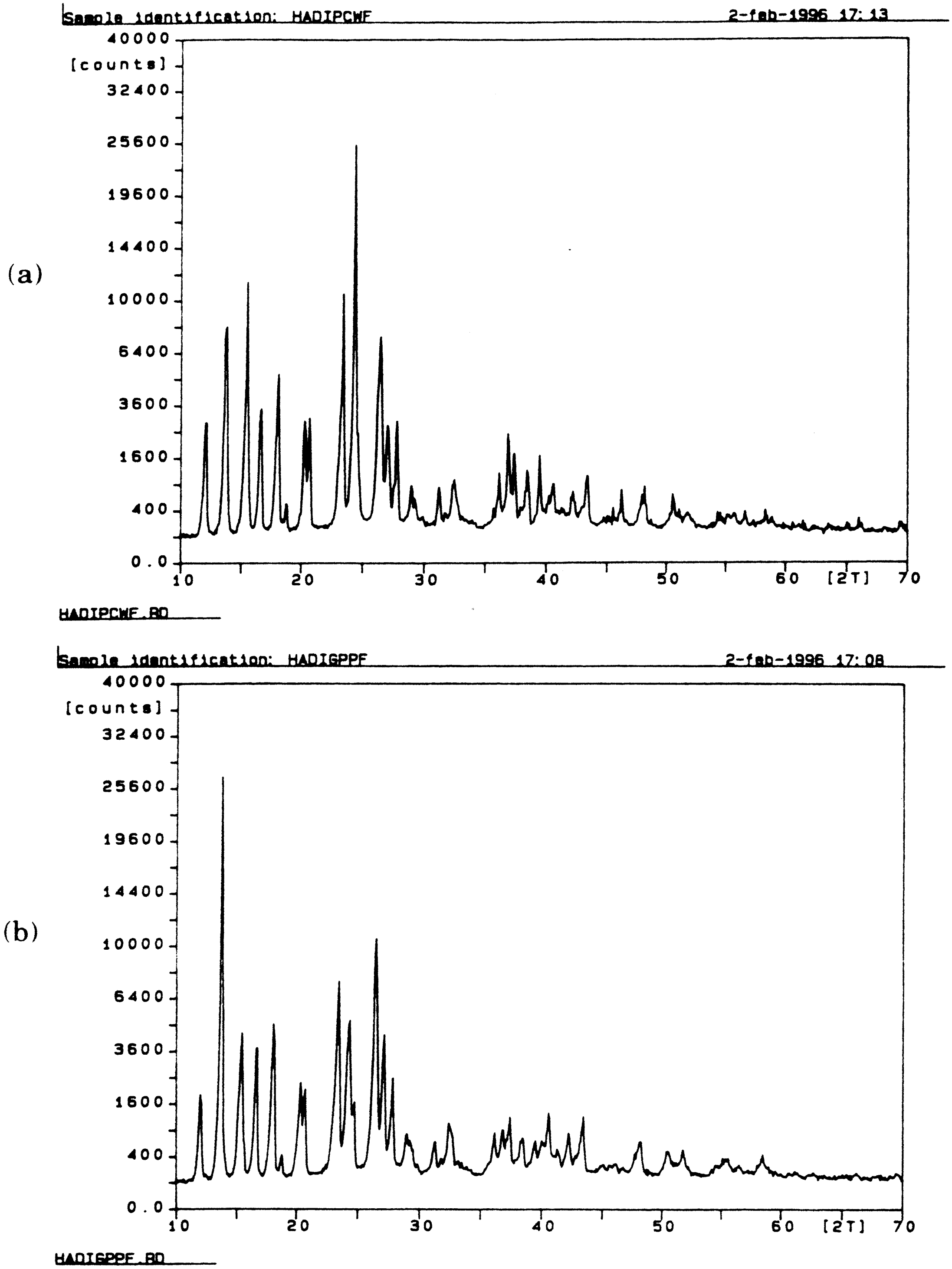

Fig. 5. The X-ray powder diffraction spectra of (a) polyhedral and (b) thin plate-like crystals of paracetamol.

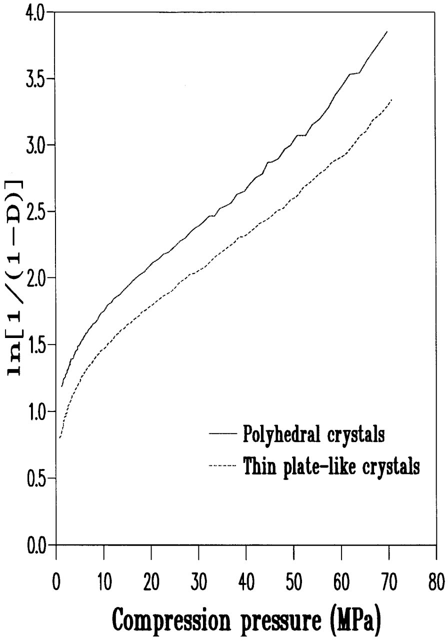

Fig. 6. Typical Heckel plots of polyhedral or thin plate-like crystals of paracetamol obtained at a compaction speed of 10 mm s^{-1}.

5). Therefore polymorphism can be ruled out. However, the relative intensities of their peaks were different. This may be because the crystals exhibited preferred orientations within the sample holder due to their markedly different crystal habits. Therefore, the relative abundance of the planes exposed to the X-ray source would have been altered, producing the variations in the relative intensities of the peaks (Marshall & York, 1989). El-Said (1995) has also reported that paracetamol crystals obtained from different solvents exhibited similar X-ray diffraction patterns, but different intensities. This was attributed to differences in crystal size.

The principal absorption bands in the infrared spectra of thin plate-like and polyhedral crystals of paracetamol were similar, suggesting there were no differences between the internal structure and conformation of these samples. The infrared spectrum is extremely sensitive to structure and conformation of a compound and thus can be used to compare the structure of a compound in different solid states (Byrn, 1982).

3.2. Compression properties of polyhedral and thin plate-like crystals of paracetamol

Compression of polyhedral and thin plate-like crystals of paracetamol at all compression forces (even at the lowest compression speed), produced extremely weak compacts which had no measurable strength and a high tendency to cap.

Fig. 6 shows individual typical Heckel plots of the polyhedral and thin plate-like crystals of paracetamol, obtained at a compaction speed of 10 mm s^{-1}. This figure indicates that the polyhedral crystals exhibited higher relative densities for given applied pressure than thin plate-like crystals. Therefore, the degree of densification that occurred during compression was greater for the polyhedral crystals. This can be attributed to increased frictional and cohesive forces between thin plate-like crystals, due to their large and flat surfaces (Fig. 3a) which would increase the contact points between them, restrict particle sliding and thus reduce densification. Additionally fragmentation, or easier packing or rearrangement occurred at lower pressure. It has been reported that the degree of densification that occurs during compression depends on the surface structure, size

Table 2
The values derived from the Heckel plots of Fig. 6 of polyhedral and thin plate-like crystals of paracetamol compressed at a compression speed of 10 mm s^{-1} to a maximum 30 kN compression force

Crystal type	*K* (slope)	1/*K* = apparent mean yield pressure (MPa)	D_a	D_o	*r**	r**
Polyhedral	0.0367	27.5	0.71	0.66	0.965	0.9989
Thin plate-like	0.0285	35.3	0.69	0.53	0.925	0.997

* Correlation coefficient of initial curve of Heckel plot (0–20 MPa).

** Correlation coefficient of straight line portion of Heckel plot (20–65 MPa).

Table 3
The values derived from the Heckel plots of polyhedral and thin plate-like crystals of paracetamol compressed at 10, 50, 100 or 250 mm s^{-1} up to a maximum 30 kN compression force

Compression speed (mm s^{-1})	Polyhedral crystals			Plate crystals		
	D_a	D_o	D_b	D_a	D_o	D_B
10	0.703 ± 0.009	0.650 ± 0.005	0.050 ± 0.005	0.693 ± 0.005	0.525 ± 0.006	0.165 ± 0.013
50	0.070 ± 0.007	0.650 ± 0.077	0.050 ± 0.007	0.665 ± 0.005	0.515 ± 0.005	0.150 ± 0.010
100	0.680 ± 0.005	0.640 ± 0.004	0.040 ± 0.004	0.657 ± 0.004	0.515 ± 0.011	0.143 ± 0.008
250	0.660 ± 0.004	0.620 ± 0.005	0.037 ± 0.004	0.598 ± 0.001	0.505 ± 0.005	0.088 ± 0.008

and shape of particles (York, 1978; McKenna and McCafferty, 1982; Roberts and Rowe, 1985, 1986). The values of D_o and D_a (Table 2) also indicate that densification due to die filling and particle rearrangement for the polyhedral crystals was higher than for plate-like crystals.

The slope of the plot for polyhedral crystals was greater than that of the thin plate crystals (Fig. 6). Table 2 indicates that the value of slope (K) was greater for the polyhedral crystals and therefore the reciprocal of K, which is the apparent mean yield pressure, was lower. The first and second derivatives of the Heckel plots (Fig. 6) were calculated and it was found that the change of function from non-linear to a linear curve occurred at 12 and 14 MPa, for polyhedral and plate-like paracetomol crystals, respectively. The root mean square analysis of the residuals for the non-linear portion of both Heckel plots (0–12 MPa for polyhedral and 0–14 for plate-like crystals) were calculated and they were 0.044 and 0.052, respectively. These results indicate a 15.4% differences in goodness of fit in the non-linear regions of the curves. Table 2 also indicates that the correlation coefficient of the initial part of Heckel plot was lower for the plate-like crystals. This is indicative of extensive fragmentation of the plates as compared to the polyhedral crystals. The initial part of Heckel plot can be a useful index in estimating the degree of particle fragmentation, with a linear segment for non-fragmenting materials, while a non-linear curve corresponds to materials which consolidate by fragmentation (Humbert-Droz et al., 1983; Duberg and Nystrom, 1986). Table 3 gives the values of D_o, D_a and D_b for the polyhedral and thin plate-like crystals of paracetamol and for compaction speeds which confirm the trends seen in Table 2 and Fig. 6.

The effects of compression speed on the apparent mean yield pressure of polyhedral and thin plate-like crystals were also investigated and the results are shown in Table 4. Two way analysis of variance showed that there were significant differences ($P < 0.05$)eckel plot can be a useful index kkk between the apparent mean yield pressures of polyhedral and thin plate crystals. However, Tukey's test revealed that there were no significant differences ($P > 0.05$) between the apparent mean yield pressures obtained at 250 mm s^{-1} for polyhedral and thin plate crystals, suggesting that changes in the crystals induced under compression became similar, irrespective of the crystal habit.

Table 4
The effect of compression speed on apparent mean yield pressures of polyhedral and thin plate-like crystals of paracetamol[a]

Compression speed (mm s^{-1})	Apparent mean yield pressure (MPa)	
	Polyhedral crystals	Thin plate-like crystals
10	28.2 ± 1.6	35.1 ± 1.8
50	30.5 ± 1.4	37.3 ± 2.6
100	36.9 ± 1.4	41.9 ± 1.3
250	38.9 ± 0.8	40.8 ± 1.6

[a] The apparent mean yield pressures are the reciprocals of the Heckel plots. Results are the mean and standard deviations of four determinations.

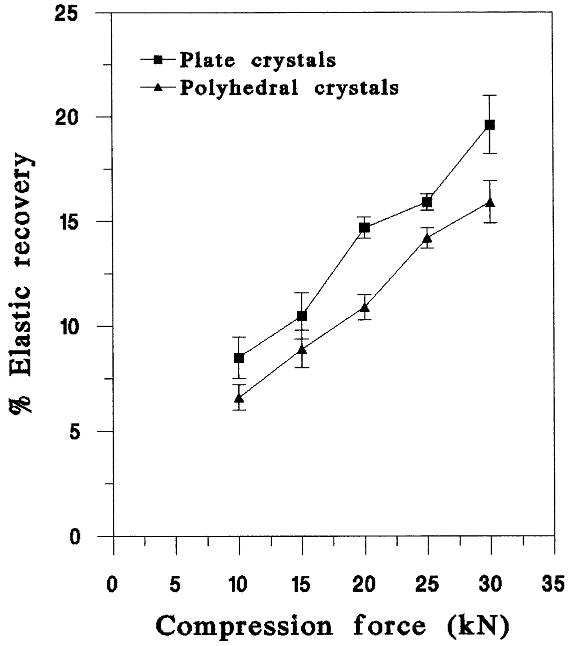

Fig. 7. Effect of compression force on the elastic recovery in the die of tablets made from polyhedral or thin plate-like crystals of paracetamol, at a compression speed of 10 mm s^{-1}.

As the compression speed increased, the apparent mean yield pressure of both samples increased but polyhedral crystals were more sensitive to changes in compaction speed. The changes of apparent mean yield pressure with different compression speeds were calculated as strain rate sensitivity (SRS) using Eq. (5) (Roberts and Rowe, 1985).

$$SRS = [(P_{Y_2} - P_{Y_1})/P_{Y_2}] \times 100\% \quad (5)$$

P_{Y_1} and P_{Y_2} are the apparent mean yield pressure at 10 and 250 mm s^{-1} speed, respectively. The calculated values of SRS for polyhedral and thin plate-like crystals were 27 and 14%, respectively. It has been reported that, due to the time dependent nature of plastic flow, the apparent mean yield pressures increase with increasing punch velocity for plastic materials which consequently show higher value of SRS (Roberts and Rowe, 1985, 1986). Therefore these results indicate that polyhedral crystals were more sensitive to compression speed suggesting that they were more plastic than the thin plate-like crystals which were more brittle.

The effect of compression force on the elastic recoveries in the die of tablets made from polyhedral and thin plate-like crystals (Fig. 7) indicate that tablets made from thin plate-like crystals exhibited higher elastic recoveries than polyhedral crystals. However, Tukey's test showed that the difference between the elastic recoveries of compacts made from the two crystal habits at 15 kN were not significant ($P > 0.05$).

The effects of compression force and compression speed on the elastic energies of compacts are illustrated in Figs. 8 and 9. At different compression forces or speeds, the compacts made from polyhedral crystals exhibited lower elastic energies than compacts made from thin plate-like crystals. However, Tukey's test revealed that there were no significant differences between the elastic energies of compacts made from polyhedral or thin plate-like crystals at 10, and at 15 kN compression forces (Fig. 8) and also at 50 mm s^{-1} compression speed (Fig. 9). The low forces and speeds probably allowed reorganisation of the crystals during the early stages of compression diminish-

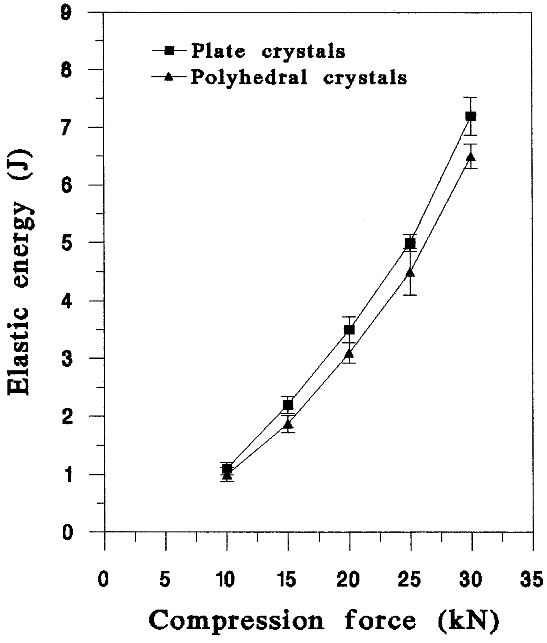

Fig. 8. Effect of compression force on the elastic energies of tablets made from polyhedral or thin plate-like crystals of paracetamol, at a compression speed of 10 mm s^{-1}.

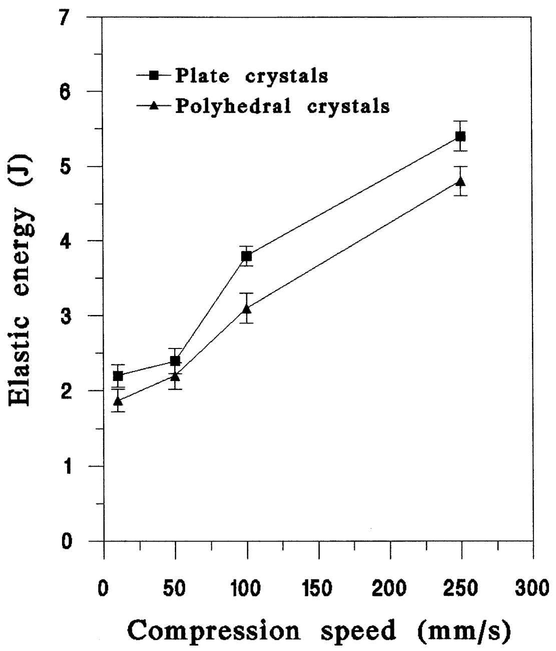

Fig. 9. Effect of compression speed on the elastic energies of tablets made from polyhedral or thin plate-like crystals of paracetamol, at a compaction force of 15 kN.

ing any differences seen in the crystals. The results of elastic energies supported the elastic recoveries (Fig. 7) which indicated that thin plate-like crystals underwent more elastic deformation during compaction than polyhedral crystals.

It has been reported that poor compressibility of a specific crystal habit of a particular drug can be attributed to the presence of crystal faces that gives poor adhesion to each other and the absence of the faces that are required for optimal adhesion (Milosovich, 1963). It is obvious that for thin plate-like and polyhedral crystals (Fig. 3a, h) the relative abundance of the different faces within the crystals were modified. This can affect the interparticulate bonding between these crystals resulting in different elastic recoveries for these two habits of paracetamol. Several studies have reported that crystal shape affects the compaction properties of drugs. Hong-Guang and Ru-Hue (1995) investigated the compaction properties of paracetamol of different crystalline shapes obtained from different manufacturers. They reported that needle-like crystals of paracetamol exhibited poorer compressibility and tablets made from them showed a greater extent of capping and lamination compared to tablets made from polyhedral crystals. This was attributed to greater elastic deformation of the needle-like form. Marshall and York (1991) reported that needle-like crystals of nitrofurantoin underwent more elastic deformation than plate-like crystals. They showed that the elastic recoveries of tablets made from needle-like crystals of nitrofurantoin were greater than those of thin plate-like crystals.

4. Conclusions

Crystallisation of paracetamol by a combination of watering-out from an ethanolic solution and rapid cooling caused marked modification to the crystal habit and produced thin plate-like crystals indicative of strong inhibition of crystal growth at different crystal faces. It was found that crystallisation solvent (ethanol/water) and crystallisation temperature (3°C), i.e. rapid cooling, are both critical in the production of thin plate-like crystals and elimination of either of these factors inhibited the production of these crystals. It was shown that this modified form of paracetamol (thin plate-like) is a habit modification and not due to polymorphism.

Crystal habit had a great influence on the compaction behaviour of paracetamol. Heckel plots and their constants, strain rate sensitivities, elastic recoveries and elastic energies were affected by the different crystalline habits of paracetamol. The results of the Heckel analysis and strain rate sensitivity indicated that polyhedral crystals underwent a greater plasticity during compression than thin plate-like crystals which were more brittle in nature during compression. The results of elastic recoveries and elastic energies indicated that thin plate-like crystals underwent more elastic deformation during compaction than the polyhedral crystals.

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