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Report

Evaluating the Deformation Kinetics of Sucrose Crystals Using Microindentation Techniques

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The deformation kinetics of sucrose crystals were evaluated using the Vickers microindentation technique. A (100) face of a crystal of sucrose was indented for varying lengths of time at temperatures ranging from 23 to 103°C, and the deformation kinetics analysis proposed by Verrall *et al.* (1) was employed to calculate the strain rate and stress from the indentation time and the size of the indentation. Two kinetic parameters, the activation volume and the activation energy, were calculated from the experimental data and compared to those of other materials on normalized scales. The results suggest that the deformation kinetics of sucrose resemble those of ice, the crystal lattice of which is highly hydrogen-bonded, similar to that of sucrose.

KEY WORDS: deformation kinetics; microindentation; sucrose.

INTRODUCTION

To a large extent, whether a material is called "plastic," "elastic," or "brittle" will depend upon the rate at which it is stressed. The relative amount of plastic deformation decreases with increasing rate of deformation. At the rates at which modern tableting machines run, many materials do not deform in a sufficiently plastic manner to permit the formation of strong tablets: if they do not literally fall apart, then failures such as capping and lamination may be observed. It is not surprising, then, that so much effort has been expended in an attempt to understand the kinetics of tableting. Nevertheless, data obtained from the study of the relationship between stress, deformation, and time during tableting are not necessarily fundamental. To understand the origins of tableting kinetics, the behavior of single crystals must be understood first. This paper discusses a study in which the deformation kinetics of a common pharmaceutical excipient, sucrose, are evaluated by microindentation techniques.

Kinetic analyses of deformation behavior of crystals are useful since they may reveal the nature of the obstacles to deformation. The fundamental assumptions of the rate theory of plastic deformation are as follows: (i) in the process of flow, energy barriers must be overcome which are similar to those which limit the rate of a chemical reaction; and (ii) the applied traction (in the simplest case a shear stress) does work; it effectively decreases the height of the energy barrier in the forward direction and increases the height of the energy barrier in the backward direction. The activation parameters which result from a kinetic analysis indicate the nature of the obstacle to flow (through the activation volume or activation area) and the height of the barrier (activation energy).

The most fundamental information is obtained from a study of dislocation mobility in crystals subjected to a stress pulse (2). The relationship between dislocation velocity and temperature and stress may then be studied. Many theories of dislocation mobility have been proposed which attempt to relate the macroscopic strain rate to the contribution of each flow mechanism (3). Often the kinetics of plastic flow are complex, but the simplest model which provides an adequate fit to the experimental data is sought.

Unfortunately, satisfactory techniques have not been developed to study individual dislocation motion in many crystals, and indirect measurements must be found. Typically these measure the average velocity of all the mobile flow units within the specimen. The concentration of mobile flow units may change with stress and strain and this limits the usefulness of the indirect techniques. Stress relaxation experiments are often preferred in this regard, since the change in strain which occurs during the test is small.

Two experimental quantities may be derived from the relationships between strain rate and temperature and strain rate and stress. These are

$$\Delta H^* = k \cdot T^2 \cdot [\partial \ln(d\epsilon_s/dt)/\partial T]\tau,\ \text{struct} \tag{1}$$

$$\Delta V^* = k \cdot T \cdot [\partial \ln(d\epsilon_s/dt)/\partial \tau]T,\ \text{struct} \tag{2}$$

where ΔH^* is the experimental activation enthalpy, k is the Boltzmann constant, replaced by R, the gas constant, for molar quantities, T is the absolute temperature (K), $d\epsilon_s/dt$ is the shear strain rate, τ is the applied shear stress, V^* is the experimental activation volume derived from the stress de-

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pendence of the rate of deformation, and struct (i.e., structural factors) is a measure of the extrinsic factors which limit dislocation mobility such as dislocation tangles or impurities.

The experimental activation enthalpy is an apparent value, since it includes the effect of the applied work. At high stresses, where the probability of activation in the forward direction is much greater than that in the backward direction, a simple relationship exists between the theoretical activation energy and the experimental value:

$$\Delta H^* = \Delta H^\dagger - W(\tau) \tag{3}$$

where $\Delta H^\dagger$ is the theoretical activation enthalpy and $W(\tau)$ is the work of applied shear stress.

At high stresses, the experimental activation volume is an order-of-magnitude estimate of the theoretical activation volume (4). These volumes are usually related to the Burgers vector. Typical ranges of activation volumes are listed in Table 1 [from Krausz and Eyring (3)].

The microindentation test has been employed to investigate the deformation kinetics of various materials at high levels of stress (e.g., Refs. 1 and 5). It is quite useful in this regime, since fracture is suppressed by the relatively high compressive hydrostatic stress associated with this test configuration and the change in the absolute strain is very small. The test possesses the drawback that the strain rate is difficult to define, and many different approximations are employed. For example, Roebuck and Almond (6) defined the strain rate as the rate of change of the logarithm of the diameter of the indentation. This approach is not realistic since the inherent assumption is that the diameter of the indentation represents the total strain. A. G. Atkins (7) developed a complex relationship between loading rate, time, and diameter of the indentation. Unfortunately, this approach requires prior knowledge of the stress sensitivity of the strain rate. Therefore, while it is not useful in the present case, it may be used to check values derived by other methods. Verrall *et al.* (1) used a particularly simple relationship. Noting that $\epsilon \sim 0.08$ for a Vickers indentation, they suggested that the strain rate could be approximated by Eq. (4); the shear strain rate by Eq. (5); and the shear stress by Eq. (6).

$$d\epsilon/dt = 0.08/t \tag{4}$$

$$d\epsilon_s/dt = 0.08 \cdot \sqrt{3}/t \tag{5}$$

$$\tau = H/(3\sqrt{3}) \tag{6}$$

where $d\epsilon/dt$ is the strain rate, $d\epsilon_s/dt$ is the shear strain rate, t is time, τ is the shear stress, and H is the hardness.

Equation (6) arises from the relationship between the hardness and the shear strength of a material, assuming a constraint factor of 3 and the Von Mises yield criterion. These relationships arise naturally if the change in hardness with time is equivalent to a creep process. Empirically, a linear relationship between strain and the logarithm of time is often observed: the first derivative of this relationship possesses the same form as Eq. (4). The factor of 0.08 is somewhat arbitrary. Assuming that it is independent of temperature, its magnitude does not affect the results of subsequent kinetic analyses. Yet its magnitude must always be reported since it provides information about the structural factors which could limit dislocation mobility. The density of dislocations with a crystal increases with increasing strain: the kinetics evaluated from Vickers indentation data will apply only to crystals strained to 8%. To evaluate the kinetics of deformation at different strain levels it would be necessary to employ an indenter of a different geometry.

Table I. Activation Volumes Associated with Various Deformation Mechanisms (2)

Mechanism	Volume ($\times b^3$)
Climb of dislocations	1
Peierls–Nabarro barrier to dislocation motion	10–10^2
Cross-slip of dislocations	10–10^2
Intersection of dislocations	10^2–10^4
Nonconservative motion of jogs	10^2–10^4

It must be emphasized that a spherical indenter would not be appropriate for this purpose, since as the indentation enlarges its geometry and consequently the average strain changes. Conversely, the indentations produced by conic or pyramidal indenters are similar regardless of their size so that the average strain will be constant as indentation proceeds. Only the volume of deformed material increases.

The flow which accommodates the indenter in the hardness test is complex. The operation of at least five independent slip systems (flow along defined planes in defined directions) is required to produce an arbitrary deformation pattern. The indentation behavior is also complicated by elastic anisotropy: crystals of sucrose, for example, are monoclinic and possess 13 elastic constants. The deformation kinetic information derived from microindentation tests is necessarily an average, nevertheless, the information is useful with respect to tablet compaction where average kinetics are also observed.

MATERIALS AND METHODS

Crystal Preparation

Small crystals of sucrose (0.25–0.75 mm in diameter, Fisher Scientific, Lot 99258/2085) were tested as received. The as-received crystals were often multiply twinned, but single crystals were selected for testing. These possessed a platy habit, in which the (100) and (001) faces predominated. Large crystals of sucrose (1–4 mm) were prepared by slowly evaporating a saturated aqueous solution of sucrose (Fisher Scientific, Lot 99258/2085) at 23°C for a period of 3–6 months. The crystals were collected and washed for 1min in with pure methanol to remove traces of crystallization solution. The purity of the crystals was verified using melting point determinations (melting range for all crystals, 185–193 ± 2°C). The washing procedure was assumed to be complete when the surfaces of the crystals were optically smooth, and minute etch pits began to appear.

Microindentation Testing

Microindentation testing was performed using a Leitz-Wetzlar Miniload hardness tester (Ser 4762) equipped with a 136° pyramidal, diamond (Vickers) indenter. A crystal was

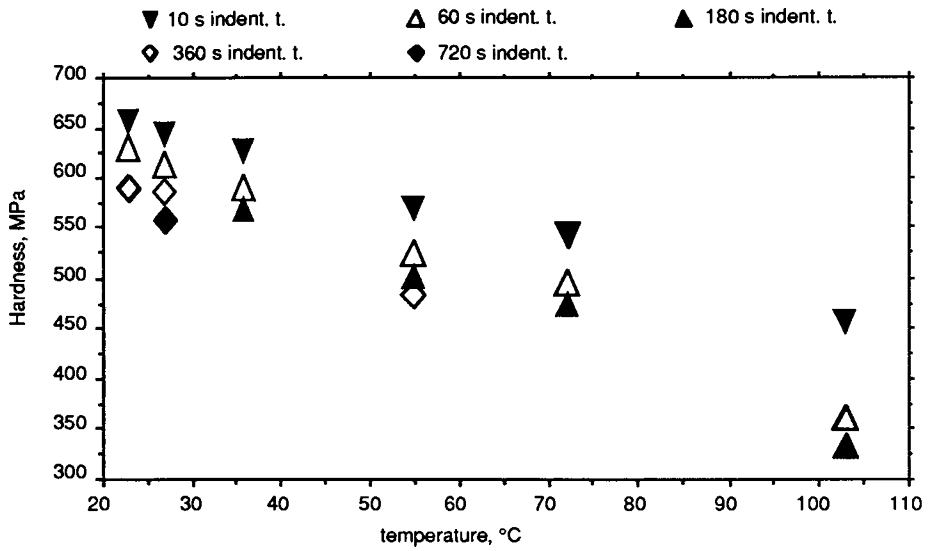

Fig. 1. Plot of hardness of sucrose crystals vs temperature. Each symbol represents the average of at least five determinations. The average confidence interval (95%) for the hardness values was independent of temperature and was equal to ±29 MPa.

mounted in plasticene[4] so that the surface to be indented (100 face) was normal to the indentation direction. This was achieved by maximizing the intensity of light reflected from the surface when the crystal was viewed under the microscope attachment. The 40× objective was then used to select an indentation site.

The indenter was cleaned with acetone, allowed to dry, and lowered slowly onto the surface of the crystal, over a period of 15 sec. The full load, normally maintained for 10 sec in a standard Vickers microindentation test, was maintained from 10 sec to 12 min to investigate creep effects. At the end of the test, the indenter was raised almost instantaneously. Vibrations, which could give rise to false low hardness values (8), were avoided throughout the testing procedure. A 147 mN load, the minimum possible with this instrument, was employed. The indentations and cracks which resulted were measured using the scale in the eyepiece of a Leitz microscope which was calibrated daily.

Hardness measurements were made at temperatures ranging from 23 ± 0.2 to 103 ± 5°C at ambient relative humidity (30%) to evaluate the change in hardness with temperature. Hardness determinations at temperatures other than 23°C were made by controlling the temperature with a Reichert hot stage which was mounted on the stage of the hardness tester. A crystal of sucrose was mounted in thermal conductive gel and a (100) face was prepared for indentation as described previously. Barriers were erected to minimize air flow around the testing area. The temperature was allowed to increase at a rate no greater than 0.5°C/min to avoid fracture due to thermal shock. A crystal was equilibrated at a defined temperature ranging from 27 to 10°C for 10 minutes, then indented. While the attached thermometer was calibrated to ±1°C, it measured the temperature of the support on which the crystal was mounted. Therefore the experimental error in the temperature reading was larger and was calculated from an approximate heat conductivity of $17 \cdot \mathrm{J\ m^{-3} \cdot sec^{-1}}$, a melting time of approximately 1 min for a crystal weighing 0.012 g, with steady state assumed. Hardnesses at ambient temperatures were determined both before and after heating to determine whether the hardness had changed due to an annealing process. The indentations produced at temperatures ≥50°C were examined periodically under the microscope for 30 min while the temperature was maintained.

Further discussion of the microindentation test procedure and its application to the evaluation of the flow and fracture behavior of pharmaceutical crystals can be found in an earlier publication (9).

RESULTS

In the temperature range between 20 and 103°C, the hardness of sucrose crystals appeared to decrease significantly (Fig. 1). The hardness at ambient temperature determined before and after heating were identical, suggesting that little annealing had occurred. The rate of enlargement of the indentations due to creep increased with temperature as well. This is expected, since these temperatures are well above 0.45 T_m, the temperature at which diffusion processes are expected to become important (T_m, i.e., the melting point of sucrose, is 461 K). When the indentations on crystals which were indented and stored at 75°C were observed over time, the bottoms of the indentations flattened and the edges of the cracks associated with the indentations became rounded, while narrow cracks appeared to heal, albeit imperfectly. These effects were visible under the microscope within 15 min for freshly harvested crystals which were indented at 30% r.h. and within 30 min to 1 hr for crystals which had been stored over phosphorus pentoxide for 2 weeks prior to indentation under the same conditions.

Such phenomena, which appeared to be related to diffusion or creep, were much more obvious in the areas of the

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[4] Plasticene is recommended as a mounting material if the indentation site remains sharply in focus during the indentation procedure, as was the case in the present study.

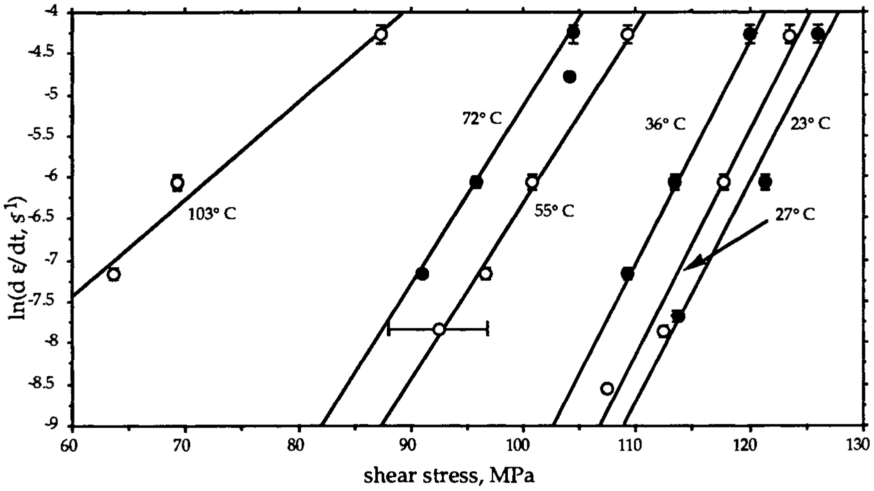

Fig. 2. Plot of the logarithm of strain rate vs shear stress from data obtained from microindentation experiments at various temperatures. The 95% confidence intervals are shown for the strain rate data. For the sake of clarity, the average error associated with the shear stress values is shown for one point only.

crystal which contained a very high initial density of dislocations. Decomposition began to occur in these areas at temperatures above 75°C in agreement with the observations of Thomas and Williams (10). It was also extremely difficult to produce *permanent* indentations in these regions. At temperatures between 36 and 72°C and after relatively short contact times (10–60 sec), large indentations remained (~50% larger than those in the regions of the crystal which possessed relatively few dislocations). The size of these indentations was extremely variable, and above 72°C no impressions appeared to remain after longer contact times. Instead, patterns similar to the bending and indentation figures described by Votava *et al.* (11) remained.

As the crystals were heated, the surface water was removed. Above 72°C the crystals invariably began to decompose and to exhibit anomalous behavior, and at temperatures greater than 103°C the surfaces appeared to be covered with a thin layer of liquid since it exhibited interference patterns, and permanent indentations could not be produced, even with loads as high as 0.98 N.

A kinetic analysis of the experimental data is permitted by the fact that the indentation creep of sucrose crystals appeared to be independent of the relative humidity below r.h. = 55%.

Calculation of Activation Volumes

The values of ln(shear strain rate) calculated using the Verrall *et al.* approach (1) are plotted vs the shear stress in Fig. 2. While curvature of this plot is possible, there are insufficient data to justify more complicated regressions. Because the applied stress is large during indentation (~3 times

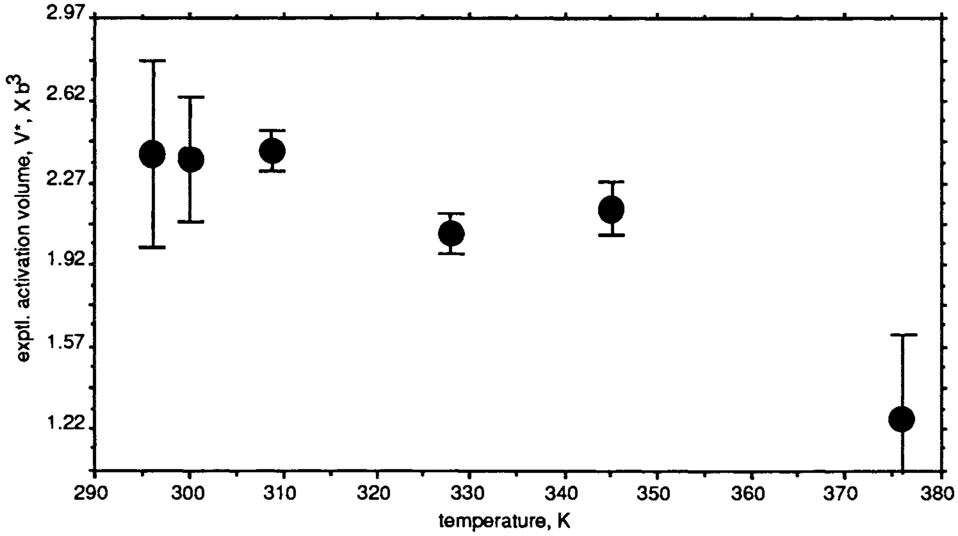

Fig. 3. Experimental activation volumes determined as a function of temperature from microindentation experiments. These are expressed as multiples of the volume of the unit cell for sucrose ($7.4 \cdot 10^{-28}$ m^3). The 95% confidence intervals are shown.

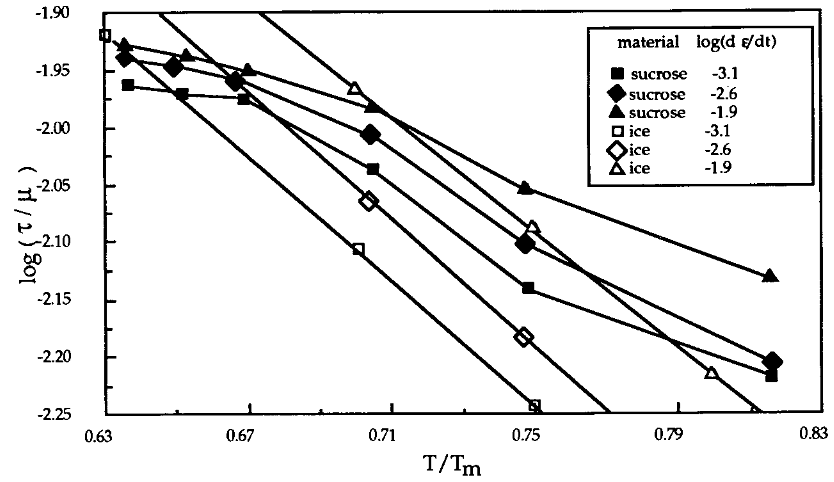

Fig. 4. The deformation parameters of sucrose superimposed on the deformation mechanism map of ice (region of proton-rearrangement-controlled glide). The values on the axes are normalized and are therefore dimensionless.

the yield stress), the slope of the plot of $\ln(d\epsilon_s/dt)$ vs shear stress should give an order-of-magnitude approximation of the activation volume associated with flow in the forward direction. From the slopes of these plots, the experimental activation volume appears to remain approximately constant to 72°C (Fig. 3). The activation volumes, calculated using Eq. (2), ranged from $1.2 \times 2.4 \times b^3$[5] and suggest, in the absence of other evidence, that a climb mechanism controls flow at these temperatures.

The crystal structure of ice consists of a lattice of hydrogen-bonded water molecules and therefore resembles that of sucrose, which is formed by a lattice of hydrogen-bonded sucrose molecules. The activation volume for the deformation of ice at similar homologous temperatures is approximately $6 \times b^3$, which is of the same order of magnitude as those listed above (5). While the values of the activation energy and volume for the deformation of ice are similar to those associated with climb, it is believed that the deformation of ice is glide-controlled via proton rearrangement, since glide creates defects in its wake. It is easy to imagine that sucrose would behave in the same manner, since the unbonded hydroxyl group in the core of each dislocation has some rotational freedom. This hypothesis could be tested in the future by doping sucrose crystals with HF, which lowers the creep activation energy in ice (12). By assuming that μ, the elastic shear modulus, is 10,800 MPa at 23°C and that it varies with temperature in proportion to the bulk modulus (13), the stress/strain rate/temperature data for sucrose are superimposed on the deformation mechanism map for ice (5) in Fig. 4. Such deformation mechanism maps are normalized so that materials which exhibit similar deformation behaviours possess similar maps. The similarity between the two materials is especially striking if their behavior is contrasted to those of other crystals (14).

Experimental Apparent Activation Energy

The activation energy may be calculated from the strain-

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[5] *b*, the average Burgers vector, was assumed to be the average of the unit cell dimensions for sucrose: 0.91 nm.

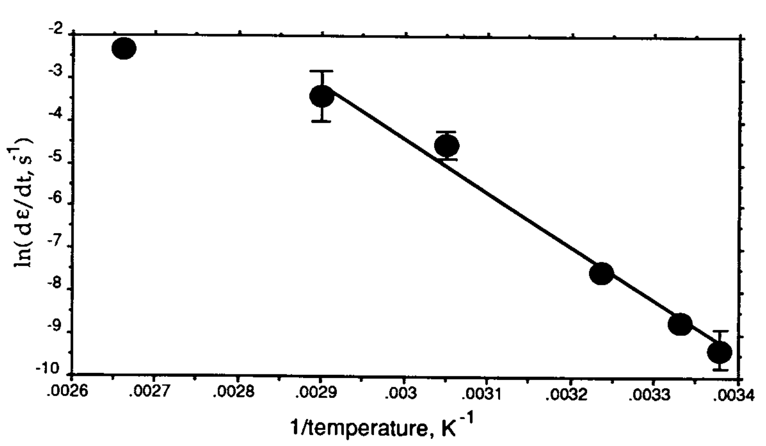

Fig. 5. Arrhenius plot for the constant shear stress of 108 MPa. The structure is assumed to be constant. The linear regression of the mean predicted strain rates is shown. The regression is weighted by the variance of the logarithms of the predicted strain rates and includes the effect of extrapolation at 23 and 72°C.

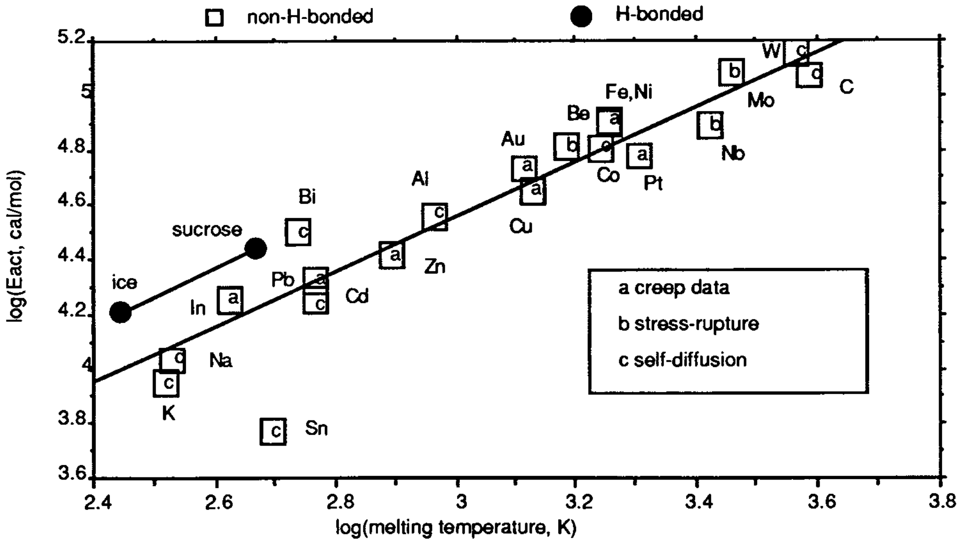

Fig. 6. Comparison of the experimental activation energy for the deformation of sucrose crystals during microindentation with those of other materials.

rate and temperature at constant stress using Eq. (1). One shear stress value, 108 MPa, was chosen for this purpose since it required only minor extrapolation of the data determined at 72 and 23°C.

The Arrhenius plot, illustrated in Fig. 5, is linear with experimental error. From the slope of the curve, the apparent activation enthalpy for deformation is 106 ± 29 kJ/mol. The apparent strain rate data at 103°C were omitted from the linear regression since the observed chemical decomposition could alter the deformation processes at high temperatures.

The relatively high local stresses associated with indentation ensure that activation is almost exclusively in the forward direction (cf. creep, where the thermal energy is sufficient to permit some activation in the opposite direction to the applied stress). A theoretical activation enthalpy cannot be estimated from the experimental data, however, since an Arrhenius plot has been constructed at one stress only. It would be dangerous to attempt a regression of values interpolated at several levels of stress, since these values might be correlated.

Dorn (15) found a strong correlation between the activation energies of creep, stress-rupture, and self-diffusion and the melting temperature of many materials. This correlation is useful to assess the generality of this method of deformation analysis, since activation energies for sucrose, other than those associated with crystallization, have not been determined. The values for sucrose and for ice are compared to other materials in Fig. 6. While the value for sucrose lies above the regression line for most materials, it is in the same relative position as ice, which suggests that the value obtained using the microindentation technique is of approximately the correct magnitude.

The activation energy for viscous flow of a supersaturated sucrose solution is 42–63 kJ/mol (16). Sucrose solutions are partially structured by hydrogen bonds, and these bonds must be broken for flow to occur. The activation values for the flow of sucrose solutions and crystals are of the same order of magnitude, as expected.

CONCLUSIONS

The kinetics of deformation of sucrose crystals were evaluated using microindentation techniques and compared to those of other materials on normalized scales such as the correlation between activation energy and melting temperature suggested by Dorn (15) and deformation mechanism maps described by Frost and Ashby (14). While these comparisons suggest that the microindentation approach is useful and valid, more fundamental studies are required to elucidate the exact mechanism of yielding in sucrose crystals.

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REFERENCES

1. R. A. Verrall, R. J. Fields, and M. F. Ashby. *J. Am. Cer. Soc.* 60:211–216 (1977).
2. J. J. Gilman and W. G. Johnston. In F. Seitz and D. Turnbull (eds.), *Solid State Physics, Advances in Research and Applications, Vol. 13,* Academic Press, New York, 1962, p. 147.
3. A. S. Krausz and H. Eyring. *Deformation Kinetics,* John Wiley and Sons, New York, 1975.
4. B. Escaig. In B. Escaig and G. G'Sell (eds.), *Plastic Deformation of Amorphous and Semicrystalline Materials,* Les Editions de Physique, France, 1982, p. 187.
5. D. J. Goodman, H. J. Frost, and M. F. Ashby. *Phil. Mag.* A43:655–695 (1981).
6. B. Roebuck and E. A. Almond. *J. Mater. Sci. Lett.* 1:519–521 (1982).
7. A. G. Atkins. In J. H. Westbrook and H. Conrad (eds.), *The Science of Hardness Testing and its Research Applications,* ASM, Metals Parks, Ohio, 1973, pp. 223–240.

8. D. Tabor. *The Hardness of Metals,* Clarendon Press, Oxford, 1951.
9. W. C. Duncan-Hewitt and G. C. Weatherly. *Pharm. Res.* (in press).
10. J. M. Thomas and J. O. Williams. *Trans. Faraday Soc.* 63:1922–1928 (1967).
11. E. Votava, S. Amelinckx, and W. Dekyser. *Acta Metal.* 3:89–94 (1955).
12. J.-P. Poirier. *Creep of Crystals, High Temperature Deformation Processes in Metals, Ceramics, and Minerals,* Cambridge University Press, Cambridge, 1985.
13. P. W. Bridgman. *Proc. Am. Acad. Arts Sci.* 68:27–93 (1933).
14. H. J. Frost and M. F. Ashby. *Deformation-Mechanism Maps,* Pergamon Press, New York, 1982.
15. J. E. Dorn. In *Creep and Fracture of Metals at High Temperatures, Proc. Symp. Mat. Phys. Lab., 1954,* H.M.S. Office, 1956.
16. B. M. Smythe. *Aust. J. Chem.* 20:1087–1095 (1967).