The dissolution times of spherical particles

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The differential equation governing the rate of change of radius of a spherical particle dissolving or growing in a fluid has been numerically integrated by computer. The particle radius, as a function of time, can thus be calculated, and the dependence of the overall particle lifetime upon physical parameters obtained. The effects of high mass flux, change of solubility with particle size, and progressive saturation due to dissolution into a finite volume of liquid can all be taken into account during the integration process. Results are presented for salicylic, boric and citric acids dissolving in and crystallizing from water; these represent the behaviour of sparingly soluble, moderately soluble and very soluble compounds respectively.

The rate of dissolution of a particle in a liquid, the rate of growth of a crystal from a supersaturated solution, and the rate of evaporation of liquid from an atomized droplet in a spray drier or an aerosol spray, are all examples of high mass transfer rate processes. In this context high mass transfer rate means that the normal equations for the slow diffusion of a substance through a stagnant boundary layer do not apply, either because the movement of the transported substance itself disturbs the boundary layer, or because, as the phase change occurs, the surface of the particle recedes or advances relative to the instantaneous position of the interface between the phases. Ideally, for simulation calculation purposes, the particles should be spherical.

Differential equations governing the diffusion-controlled growth or dissolution of spheres in the absence of hydrodynamic instabilities have been derived by Readey & Cooper (1966). These authors assumed that the interface reaction was virtually instantaneous, i.e. that, for dissolution, the liquid adjacent to the surface was saturated with the solid. Composition-independent diffusion coefficients, and ideality of partial specific volumes of the solute and solvent with respect to concentration change, were also assumed.

Cable & Evans (1967) extended the work of the above authors and gave some computer solutions for dissolution by widening the ranges of the numerical factors, and by comparing their solutions with those of Scriven (1959) for growth from zero size. It became apparent that differences between the numerical computer solutions could easily arise, due to starting, iterative and discretization errors. Thus Duda & Vrentas (1969), who were interested in the growth and dissolution of bubbles, indicated that they disagreed in some quantitative respects with the results of Cable & Evans, whilst they in their turn have been criticized by Rosner (1969), for the same reason. Rosner has reviewed the earlier work, and has suggested an equation governing the rate of change of size; he has also obtained a solution for the overall particle lifetime, under dissolution conditions, in closed form for constant parameter

values. In a recent paper, Rosner & Epstein (1970) have included the effect of inter-face kinetic limitations, and have shown how to use the integral profile method (Goodman, 1964) in this field of non-linear moving-boundary problems.
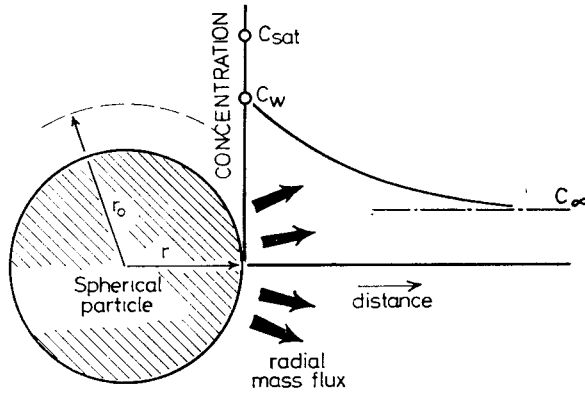

FIG. 1. Dissolution of a spherical particle. For explanation of symbols see text following equation (4).

Fig. 1 illustrates transfer of material, in dissolution, from the particle to the solvent phase (in growth, the transfer direction will be reversed). Dissolved material moves away into the bulk solution under the influence of the concentration gradient shown in the figure. If the rate of diffusional transport is large, the assumption of equili-brium at the solid–liquid interface may be incorrect, because dissolution rate may then become the controlling factor. Under such conditions Rosner (1969) has derived the equations which govern the behaviour of the particle. They are:

$$\frac{dr}{dt} = \frac{D\rho}{r\rho_s} \ln \left(\frac{1 - c_\infty}{1 - c_w}\right) \qquad .. \qquad .. \qquad .. \qquad .. \qquad (1)$$

and

$$k (c_{sat} - c_w)^p = \frac{D}{r} \ln \left(\frac{1 - c_\infty}{1 - c_w}\right) \qquad .. \qquad .. \qquad .. \qquad (2)$$

where r is the particle radius at any time t, D is the diffusivity of the solute, ρ is the density of the solvent and ρ_s that of the solute, k is the rate constant governing the interface kinetics, which may or may not be the same for dissolution and for growth, and p is the exponent on the mass transfer driving force, which has been shown to range from 1·0 to 1·8 (Strickland-Constable, 1968). Rosner dealt only with $p = 1·0$.

The remaining symbols are the concentration terms: c_{sat} is the concentration of a saturated solution, c_w the concentration at the interface between solid and liquid, and c_∞ the bulk concentration in the liquid phase at a large distance from the dissolving particle.

The logarithmic term is the concentration driving force, in a form suitable for diffusional transport at high mass flux (Spalding, 1963). Both equations must be satisfied together, that is, the instantaneous rate of change of r with t must be as given by equation (1) with the appropriate value of r and of c_w; the value of c_w must satisfy equation (2). In addition, the value of c_{sat} may be changed during the integration due to the increase in solubility caused by diminishing particle size: this

is discussed more fully later. The value of c_∞ will also change if the volume of solvent is finite, and this also must be allowed for.

The major restriction on computer simulations of the type considered here is the lack of data: solubility, density and diffusivity in a particular solvent are rarely all available for any but simple substances. However, empirical correlations exist from which diffusivities can be estimated, and which are usually accurate to within 10%, at least for dilute solutions of non-dissociating solutes.

Wilke & Chang (1955) give perhaps the best such equation:

$$D = 7 \cdot 4 \times 10^{-8} \frac{(\psi M)^{\frac{1}{2}} T}{\mu V^{0 \cdot 6}} \qquad .. \qquad .. \qquad .. \qquad .. \qquad (3)$$

where D is the required diffusivity of the solute in $cm^2\ s^{-1}$, the molar volume of the solute being $V\ cm^3$, M is its molecular weight, T is the absolute temperature, μ is the solvent viscosity (in cP), and ψ is an "association parameter" for the solvent, which has the values 2·6 for water, 1·9 for methanol, 1·5 for ethanol and 1·0 for benzene and non-polar solvents generally.

There are several pharmaceutical examples of particulate mass transfer relevant to the technique reported here. Gwilt, Robertson & others (1963) reported increased rates of paracetamol absorption *in vivo* when sorbitol was added to the tablets; Walters (1968) showed that no complex was formed between paracetamol and sorbitol and suggested that a higher dissolution rate must therefore be responsible for the increase. Any rapidly-dissolving adjuvant should increase the dissolution rate of a drug, by increasing the overall mass transfer rate out of the tablet, and such aided dissolution could be simulated using the method of the present paper.

Although dissolution-limited absorption rates are usually reported only for sparingly-soluble drugs, dissolution rate can control the absorption of sodium *p*-aminosalicylate and acetylsalicylic acid, and for aspirin formulations at least, *in vitro* dissolution rates can be correlated with rates of absorption (Levy, Leonards & Procknal, 1967). For griseofulvin, absorption rates increase with the addition of lactose to the tablet formulation, the mechanism of increase being either the improvement of wetting or increased mass transfer (M. H. Rubinstein, personal communication).

The dissolution of fat globules in the gut by the action of lipases may well be mass-transfer limited; it is known to be assisted by the presence of bile salts, proteins and soaps, but the difficulty here is to obtain data for the physical properties of such a complex system.

The most promising field for calculations of particle lifetime is in the Ostwald ripening process, whereby crystalline precipitates of small particle size can be altered so that they contain fewer, but larger particles. In a slightly supersaturated mother liquor, the small crystals, which are more soluble, tend to dissolve, and the larger crystals, which are less soluble, to grow. The relation between size and solubility is due to Ostwald, but a modern discussion is given by Mullin (1961). The basic equation is

$$\ln \frac{c_{sat}}{c^*_{sat}} = \frac{2M\sigma}{\mathbf{R}T\rho r} \qquad .. \qquad .. \qquad .. \qquad .. \qquad (4)$$

where c_{sat} is the concentration of a solution in equilibrium with crystals of radius r, c^*_{sat} is the equilibrium solubility of large crystals, M is the molecular weight, σ the surface energy, $\mathbf{R}$ the gas constant, T the absolute temperature, and ρ is the density

of the solid. The effect of Ostwald ripening is enhanced by "temperature cycling". The temperature of the crystals and mother liquor is increased and decreased at a slow rate, keeping the mean temperature at about the level required for crystallization; the dissolution of small crystals and the growth of larger ones then occur at an increased rate. Rate determinations have been made for sulphathiazole by Carless & Foster (1966) and by Varney (1967) for the same drug and for oxyclozamide. Varney describes an automatic cycling device for implementing the method. Carless & Foster noted the peculiar fact that the rate of particle growth was decreased by the addition of cetomacrogol to the solution, despite the resultant increase in the solubility of the drug. This could be due to a diffusivity change.

Computation

Equation (1) was integrated by the Runge-Kutta method, the inaccuracy due to truncation error being checked by doubling the integration step length. Apart from this control, the step length was adjusted as the dissolution (or growth) proceeded, to provide output information at appropriate intervals. At each radius considered, the equilibrium solubility c_{sat} was calculated from equation (4); c_∞ was calculated by a mass balance, assuming for this purpose that all the dissolved solute was distributed uniformly through the liquid bulk—an assumption reasonable enough in most cases but open to question where a highly soluble solute is present in a severely restricted volume of liquid.

The interface concentration c_w was calculated for each radius as follows: Equation (2) may be expressed, for dissolution, in the form:

$$\phi = \frac{-kr}{D}(c_{sat} - c_w)^p + \ln\left(\frac{1 - c_\infty}{1 - c_w}\right) = 0 \quad .. \qquad .. \quad (5)$$

a corresponding relation existing for the growth case where $c_{sat} < c_\infty$. By differentiation:

$$\left(\frac{\partial\phi}{\partial c_w}\right)_r = \frac{krp}{D}(c_{sat} - c_w)^{p-1} + \frac{1}{1 - c_w} \qquad .. \qquad .. \qquad .. \quad (6)$$

and an estimate of c_w may be improved by the use of the recurrence formula:

$$[c_w]_{n+1} = [c_w]_n - \left[\phi_r \middle/ \frac{\partial\phi}{\partial c_w}\right]_{n,r} \qquad\qquad .. \qquad .. \qquad .. \quad (7)$$

where n is the number of iterations. This formula was used repeatedly until both c_w and the relevant logarithmic term in equation (1) were constant within acceptable limits (a final relative correction $\leqslant 0.0005$ was accepted). Convergence was good; typically 10 to 20 iterations were required to find c_w initially, then 2 or 3 iterations for each value of r as the latter changed progressively.

RESULTS AND DISCUSSION

The physical properties of the pure compounds are listed in Table 1: diffusivities given are those calculated by using the Wilke & Chang equation; the solubilities are experimental values obtained from the literature (Mullin, 1961).

Table 2 lists the results of calculations of particle dissolution lifetimes, and Table 3 the times taken to grow to a radius of 1 mm from an initial size of 1·1 times the critical radius (defined as the radius at which the particle is just in equilibrium with the

Table 1. *Physical properties of the three compounds studied.*

	Molecular weight	Density kg m⁻³	Molar vol. m³ kmol⁻¹
Boric acid	61·9	1435	0·0393
Citric acid monohydrate ..	210·1	1542	0·1723
Salicylic acid	138·1	1443	0·1350

	Acid	Temperature °C					
		10	20	30	40	60	80
Solubility mass	Boric	0·0347	0·0476	0·0619	0·0800	0·1289	0·1922
fraction	Citric	0·5921	0·6492	0·7073	0·7466	0·8037	0·8621
	Salicylic	0·00150	0·00200	0·00279	0·00418	0·00902	0·0221
Diffusivity	Boric	1·212	1·632	2·119	2·672	3·977	5·544
m² s⁻¹ × 10⁹	Citric	0·499	0·673	0·873	1·101	1·638	2·284
	Salicylic	0·578	0·779	1·011	1·274	1·897	2·644
Viscosity	Water	1·308	1·005	0·801	0·656	0·469	0·357
kg m⁻¹ s⁻¹ × 10³							

Solvent association parameter for water $= 2·6$.

Table 2. *Particle lifetimes in dissolution for various values of the parameters which govern the dissolution rate.*

°C	k (m s⁻¹)	σ (J m⁻²)	p	Initial phase ratio	Lifetime Salicylic acid (s)	Lifetime Boric acid (s)	Lifetime Citric acid monohydrate (s)
10	25	0·2	1·0	infinite*	832 851	16 740	1722
20	25	0·2	1·0	infinite	463 807	9008	1094
30	25	0·2	1·0	infinite	255 341	5298	719
40‡	25‡	0·2‡	1·0‡	infinite‡	135 103‡	3219‡	510‡
60	25	0·2	1·0	infinite	41 989	1307	289
80	25	0·2	1·0	infinite	12 210	606	170
40	25	0·2	1·0	large*	202 011	4878	1007
40	25	0·2	1·0	medium*	463 325	11 357	2831
40	25	0·2	1·0	small*	1 250 312	30 941	8107
40	25	0·02–10	1·0	infinite	135 107–134 909	3219–3217	510–508
40	25	0·2	1·4	infinite	135 109	3219	510
40	25	0·2	1·8	infinite	135 293	3221	510
40	25	0·2	2·0	infinite	135 736	3225	511
40	25	0·2	3·0	infinite	161 372	3326	517
40	0·01	0·2	1·8	infinite	150 638	3374	525
40	0·01	0·2	2·0	infinite	171 103	3495	534
40	0·01	0·2	3·0	infinite	2 349 248	5155	604
40	0·10	0·2	2·0	infinite	145 502	3304	518
40	0·10	0·2	3·0	infinite	495 260	3974	554
40	0·50	0·2	3·0	infinite	275 713	3636	536
40	0·01–25	0·2	1·0	infinite	135 138–135 103	3221–3219	511–510

* The term infinite denotes that calculations were based on 10⁶ kg of water per particle.   Large, medium and small denote that the amount of water was such that, on complete dissolution of the particle, the water contained respectively 50%, 90% and 99% of the solute required to saturate it.   At the start of the dissolution process the water was free of solute.

‡ "Pivotal" case.

Table 3. *Times taken by spherical particles to grow from 1·1 × critical size to a radius of 1 mm.*

					Salicylic acid			Boric acid			Citric acid monohydrate		
°C	k ms⁻¹	σ Jm⁻²	p	Initial phase ratio	Critical radius m	Critical mass g	Growth time† s	Critical radius m	Critical mass g	Growth time† s	Critical radius m	Critical mass g	Growth time† s
10	25	0·2	1·0	infinite†	8·22 $\times 10^{-7}$	3·36 $\times 10^{-12}$	41 740 600	3·83 $\times 10^{-7}$	3·39 $\times 10^{-13}$	852 848	2·56 $\times 10^{-6}$	1·09 $\times 10^{-10}$	117 059
20	25	0·2	1·0	infinite	7·95	3·03	23 252 750	3·75	3·18	462 035	2·79	1·41	76 963
30	25	0·2	1·0	infinite	7·69	2·75	12 805 000	3·69	3·01	273 821	3·11	1·94	52 267
40‡	25‡	0·2‡	1·0‡	infinite‡	7·45	2·50	6 779 670‡	3·64	2·90	168 026‡	3·35	2·43	37 870‡
60	25	0·2	1·0	infinite	7·04	2·11	2 112 235	3·61	2·84	70 108	3·77	3·47	21 915
80	25	0·2	1·0	infinite	6·73	1·84	618 335	3·68	2·99	33 750	4·46	5·72	12 894
40	25	0·2	1·0	large†	7·45	2·50	8 819 050	3·64	2·90	218 516	3·35	2·43	45 958
40	25	0·2	1·0	medium†	7·45	2·50	14 610 800	3·64	2·90	361 704	3·35	2·43	59 603
40	25	0·2	1·0	small†	7·45	2·50	24 613 800	3·64	2·90	359 208	3·35	2·43	65 356
40	25	0·02	1·0	infinite	7·45 $\times 10^{-8}$	2·50 $\times 10^{-15}$	6 770 608	3·64 $\times 10^{-8}$	2·90 $\times 10^{-16}$	167 917	3·35 $\times 10^{-7}$	2·43 $\times 10^{-13}$	37 640
40	25	0·05	1·0	infinite	1·86 $\times 10^{-7}$	3·91 $\times 10^{-14}$	6 772 105	9·10 $\times 10^{-8}$	4·53 $\times 10^{-15}$	167 936	8·38 $\times 10^{-7}$	3·80 $\times 10^{-12}$	37 678
40	25	0·5	1·0	infinite	1·86 $\times 10^{-6}$	3·91 $\times 10^{-11}$	6 794 920	9·10 $\times 10^{-7}$	4·53 $\times 10^{-12}$	168 210	8·38 $\times 10^{-6}$	3·80 $\times 10^{-9}$	38 266
40	25	2	1·0	infinite	7·45 $\times 10^{-6}$	2·50 $\times 10^{-9}$	6 873 620	3·64 $\times 10^{-6}$	2·90 $\times 10^{-10}$	169 143	3·35 $\times 10^{-5}$	2·43 $\times 10^{-7}$	40 435
40	25	4	1·0	infinite	1·49 $\times 10^{-5}$	2·00 $\times 10^{-8}$	6 983 750	7·28 $\times 10^{-6}$	2·32 $\times 10^{-9}$	170 422	6·70 $\times 10^{-5}$	1·95 $\times 10^{-6}$	43 672
40	25	10	1·0	infinite	3·73 $\times 10^{-5}$	3·13 $\times 10^{-7}$	7 340 870	1·82 $\times 10^{-5}$	3·62 $\times 10^{-8}$	174 460	1·68 $\times 10^{-4}$	3·04 $\times 10^{-5}$	54 648
40	25	0·2	1·4	infinite	7·45 $\times 10^{-7}$	2·50 $\times 10^{-12}$	6 780 620	3·64 $\times 10^{-7}$	2·90 $\times 10^{-13}$	168 046	3·35 $\times 10^{-6}$	2·43 $\times 10^{-10}$	37 874
40	25	0·2	1·8	infinite	7·45	2·50	6 834 350	3·64	2·90	168 621	3·35	2·43	37 970
40	25	0·2	2·0	infinite	7·45	2·50	7 008 500	3·64	2·90	170 033	3·35	2·43	38 180
40	25	0·2	3·0	infinite	7·45	2·50	1·26 $\times 10^{8}$	3·64	2·90	276 211	3·35	2·43	48 905
40	0·01	0·2	1·8	infinite	7·45	2·50	12 536 700	3·64	2·90	220 868	3·35	2·43	46 598
40	0·01	0·2	2·0	infinite	7·45	2·50	33 167 200	3·64	2·90	307 832	3·35	2·43	57 825
40	0·01	0·2	2·5	infinite	7·45	2·50	2·38 $\times 10^{9}$	3·64	2·90	47 413 800	3·35	2·43	2 133 995
40	0·10	0·2	2·0	infinite	7·45	2·50	11 585 100	3·64	2·90	203 127	3·35	2·43	43 169
40	0·10	0·2	2·5	infinite	7·45	2·50	2·53 $\times 10^{9}$	3·64	2·90	5 173 760	3·35	2·43	296 790
40	0·50	0·2	2·5	infinite	7·45	2·50	2·69 $\times 10^{10}$	3·64	2·90		3·35	2·43	
40	0·50	0·2	3·0	infinite	7·45	2·50	62 609 200	3·64	2·90		3·35	2·43	
40	0·50	0·2	3·0	infinite	7·45	2·50	5·41 $\times 10^{9}$	3·64	2·90	1 371 872	3·35	2·43	116 890
40	0·01	0·2	1·0	infinite	7·45	2·50	6 781 400	3·64	2·90	168 125	3·35	2·43	37 903
40	0·10	0·2	1·0	infinite	7·45	2·50	6 779 850	3·64	2·90	168 036	3·35	2·43	37 873
40	0·50	0·2	1·0	infinite	7·45	2·50	6 779 700	3·64	2·90	168 028	3·35	2·43	37 870
40	1	0·2	1·0	infinite	7·45	2·50	6 779 670	3·64	2·90	168 028	3·35	2·43	37 870
40	5	0·2	1·0	infinite	7·45	2·50	6 779 670	3·64	2·90	168 027	3·35	2·43	37 870
40	125	0·2	1·0	infinite	7·45	2·50	6 779 670	3·64	2·90	168 026	3·35	2·43	37 870

† In every case the solution from which growth took place contained initially 2% more solute than that required to saturate the water present. The term infinite denotes that calculations were based on 10^{4} kg of water per particle. Large, medium and small denote that the amount of solution was such that, on completion of growth to 1 mm radius, respectively 50%, 90% and 99% of the excess solute had been deposited. The growth time is that from a nucleus of radius 1·1 r_{crit} to 1 mm radius.

‡ "Pivotal" case.

supersaturated solution, so that it neither grows nor dissolves; the increase in solubility caused by the curvature of its surface is just equal to the degree of supersaturation of its environment). For all the growth cases, the amount of solute initially was 2% more than the amount needed to saturate the water present.

For all these data the conditions for dissolution are for a stationary particle surrounded by solvent, and no relative motion between the solid and liquid phases is assumed. This is not a restrictive condition when comparing one substance with another, but in predicting actual dissolution times the data here yield the longest time that dissolution could be expected to take. Any stirring or other movement would effectively increase the diffusivity from the molecular motion figure used here to a value appropriate to the eddying turbulent conditions caused by the stirring. This change in effective diffusivity could have been predicted, although not very accurately, by using known correlations based upon the Reynolds, Sherwood, Schmidt and Prandtl dimensionless groups (see for example Treybal, 1955). But since the change in diffusivity would be dependent upon the system fluid dynamics
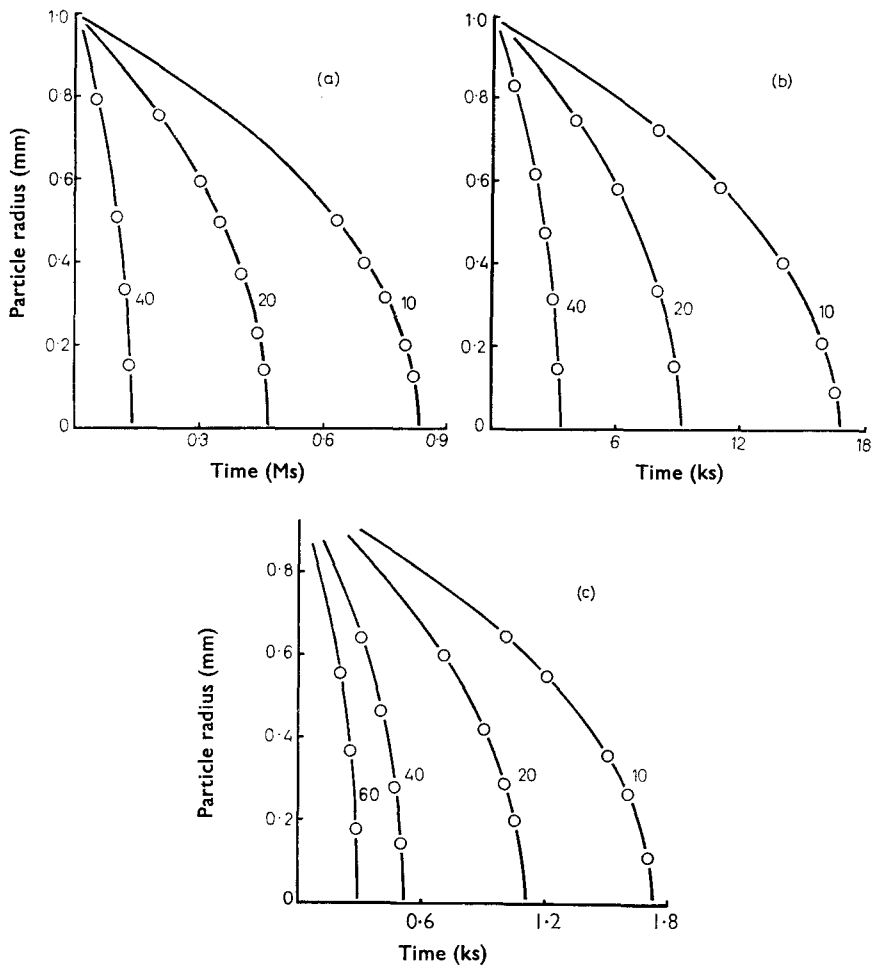
FIG. 2. Particle dissolution: (a) salicylic acid, (b) boric acid, (c) citric acid. Temperatures were as shown; other conditions "pivotal."

rather than upon what substances were being used, there would be little effect for comparative purposes. In consequence this parameter was not varied.

Because of the limited time available, all possible combinations of parameters were not inspected. For each substance, a "pivotal" case was chosen. This was at 40°, the middle of the temperature range, and the other factors were set at convenient levels in their ranges: σ at 0·2 J m^{-2}, k at 25 m s^{-1}, p at 1·0, c_∞ at zero for dissolution, and the phase ratio, the amount of solvent per unit mass of the solute, was made effectively infinite.

The dissolution rates of the three substances at various temperatures are plotted in Fig. 2, and Fig. 3 shows growth curves for boric acid only. The increased rate of reduction of radius near the end of the dissolution process is affected by the value of σ, the surface energy. This is not an easily-determined quantity for solids. It is analogous to the surface tension of a liquid, the presumption being that the surface tension does not disappear when a liquid solidifies, but is "locked in". The normal methods of surface tension determination are not applicable to solids, and the methods that are available are inaccurate. They are all based upon scratching, indentation or attrition. An account in detail is given by Kuznetsov (1957) who quotes values of a few hundred ergs cm^{-2} (mJ m^{-2}) for some substances, but rising to well over 1 J m^{-2} for results obtained by some of the methods. These are scarcely credible, as can be seen by an examination of the effects of varying σ, particularly in the case of the calculations performed for growth rates. In the present paper the initial size of the sphere considered has been taken to be a radius 10% greater than the critical size.

It was suggested by Strickland-Constable (1968), as a result of measuring the sublimation and deposition rates of benzophenone, that growth rates, and probably evaporation rates, were not first order processes. It is known (Mullin, 1961) that a
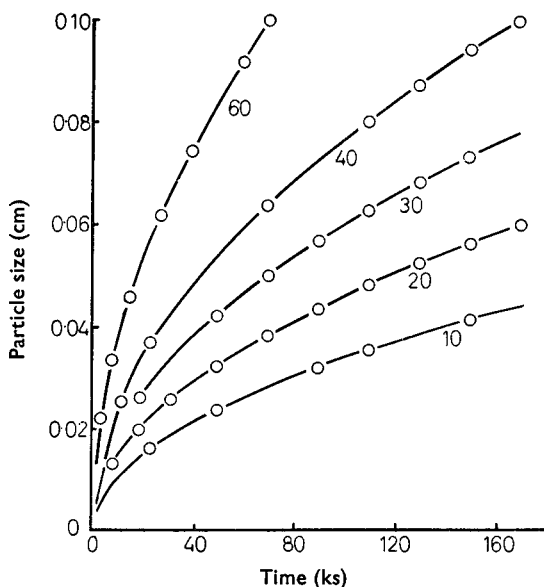

FIG. 3. Particle growth: spherical particle of boric acid in a 2% supersaturated solution. Radius of nucleus at $t = 0$ was 1·1 × the critical size. Temperatures were as shown; other conditions "pivotal."
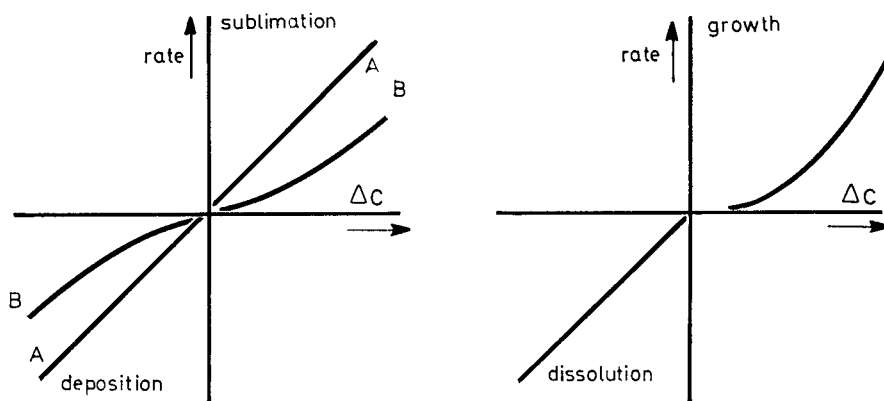
FIG. 4. The relation between growth or dissolution and concentration difference: (a) sublimation and deposition from the vapour phase (after Strickland-Constable)—AA linear (first-order) mechanism. BB higher-order mechanism. (b) dissolution, and growth from solution: dissolution is a first-order process, whereas solid deposition needs a finite concentration difference to begin, and then follows a power-law relation with exponent greater than unity.

finite degree of supersaturation is necessary to initiate crystal growth from solution, and that the growth rate is often proportional to the degree of supersaturation raised to a power of approximately 1·6.

These two types of behaviour lead to plots of the kind shown in Fig. 4. For sublimation and condensation on the Strickland-Constable model, the line AA in Fig. 4(a) shows the linear dependence of growth or evaporation upon concentration differences when first-order kinetics apply. For higher-order kinetics, curves such as BB are obtained. Crystallization behaviour usually resembles Fig. 4(b), where dissolution is a first-order process and yields a straight line, but the growth process requires a finite supersaturation for initiation; it then proceeds with a power-law relation in which the exponent is greater than unity. Both these types of behaviour are easily simulated by the numerical technique used in the present work, although such additions make it much more difficult to find an analytic solution to the differential equations which are being obeyed.

The effect of varying both the surface kinetics constant, k, and the exponent on the concentration difference term, p, is shown in Fig. 5. For values of k and p near the pivotal values of 25 m s^{-1} and 1·0, the curves of saturation concentration and interface concentration against particle radius follow one another closely down to the critical radius. With the higher values of p, however, there is a divergence, indicating that the rise in solubility at small particle size is less closely followed at the interface—as might be expected. When k also has a small value, the effect is enhanced. Even with the rise in solubility, interface concentration falls, because the surface kinetic step of removing a molecule from the crystal lattice into the solution is limiting. When k is reduced to 0·01, a value admittedly outside the normal range of 0·1–100, the effect of k overshadows that of p, so that the curves for $p = 2·0$ and $p = 3·0$ are less divergent from one another than both are from the c_{sat} curves.

Fig. 6 shows some plots of particle growth at extreme values of the parameters k and p. Those of Fig. 6(a) are for boric acid, and show the interface concentration and solubility as a function of particle radius during the growth process. Citric acid
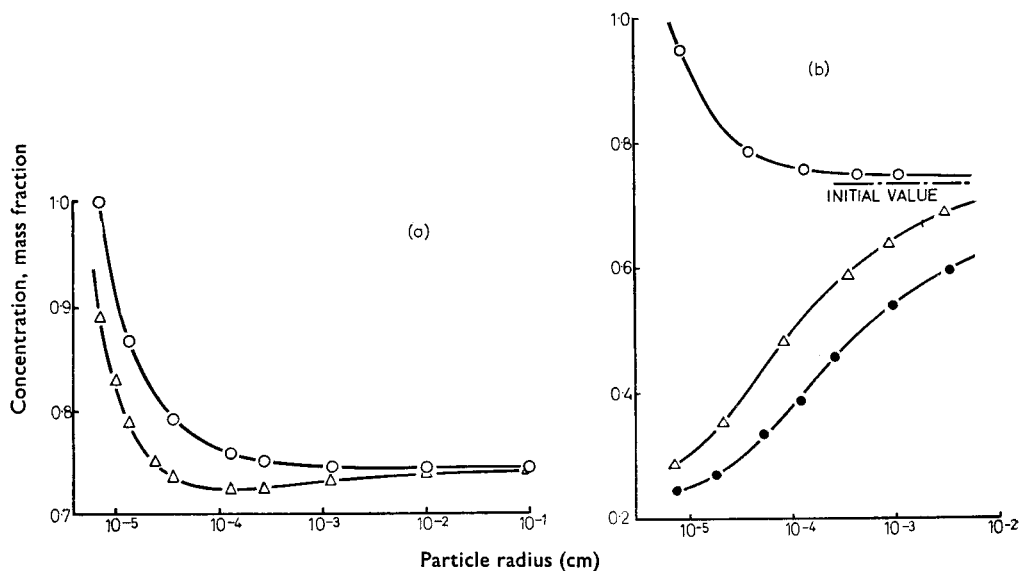
FIG. 5. Particle dissolution: solubility c_{sat} and interface concentration c_w *versus* particle radius. Conditions "pivotal" except where stated. (a) citric acid dissolution; $k = 25$ m s^{-1}, $p = 3\cdot0$— ◯ surface solubility, △ interface concentration. (b) citric acid dissolution; $k = 0\cdot01$ m s^{-1}— ◯ surface solubility, △ interface concentration, $p = 2\cdot0$, ● interface concentration, $p = 3\cdot0$.
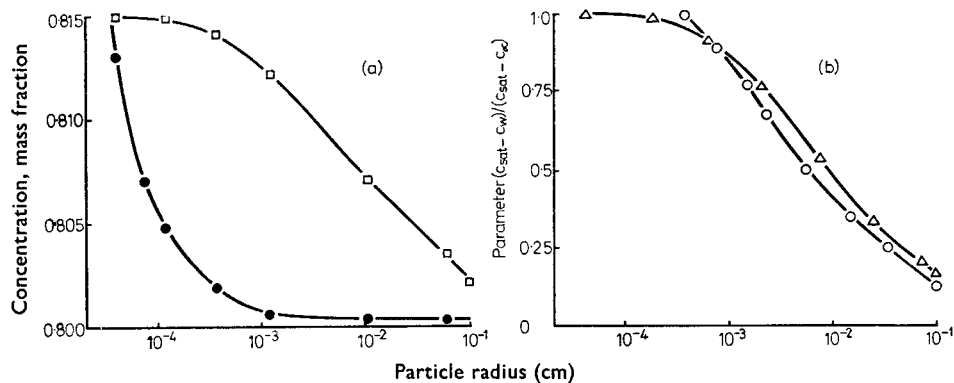

FIG. 6. Particle growth: conditions "pivotal" except where stated. (a) Solubility c_{sat} and interface concentration c_w *versus* particle radius; boric acid, $k = 1\cdot0$, $p = 3\cdot0$—● surface solubility, ☐ interface concentration. (b) The parameter $(c_{sat} - c_w)/(c_{sat} - c_\infty)$ *versus* particle radius. For values of the parameter near to unity, surface-kinetic control operates; for values near zero, diffusion is the limiting factor—◯ citric acid, △ boric acid.

behaves similarly, but the solubility of salicylic acid is so small that for values of p approaching $3\cdot0$ the growth time becomes extremely large ($> 10^6$ years). This reflects the fact that, because solute molecules are present only in very low concentrations, any process which is governed by third-order kinetics and so depends upon the occurrence of intermolecular collisions is bound to be extremely slow.

The variation of the quotient $(c_{sat} - c_w)/(c_{sat} - c_\infty)$ with particle radius is shown in Fig. 6(b). This quotient measures the division of the driving force, for either growth or dissolution, between the immediate neighbourhood of the solid surface, which is the kinetically-controlled region, and the boundary layer, which is the

diffusion-controlled region. Values near unity indicate surface control, and values near zero, diffusional limitation. For the cases shown here, both the boric acid and the citric acid growth processes change their limiting mechanism as the particle radius increases.

In conclusion, it appears that the simulation algorithm reported here is reliable over a wide range of the main parameters which influence the rate of the crystallization and dissolution processes. It should be useful in evaluating experimental data for various substances, particularly for nucleation phenomena and particle growth at small radii; in addition, extensions of the technique may in future prove valuable in the study of Ostwald ripening.

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