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Mathematical Description of Solute Velocities during Dissolution from a Horizontal Surface

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Abstract □ A mathematical analysis of solute flow in a descending column following dissolution is presented. The acceleration of a solute particle from zero velocity, when it is in the solid phase, to its final equilibrium descending velocity was analyzed. The maximum velocity for *N*-(3-methylphenyl)acetamide developed essentially at the solid–liquid interface, contradicting the postulate of a microsize diffusional layer. The possibility of a diffusional layer existing for solids of lower solubility than *N*-(3-methylphenyl)acetamide is discussed.

Keyphrases □ Solute velocities—in descending column during dissolution from a horizontal surface, mathematical analysis □ Velocities, solute—in descending column during dissolution from a horizontal surface, mathematical analysis □ Dissolution—from a horizontal surface, mathematical analysis of solute velocities in descending column

Studies utilizing a descending column model to investigate the dissolution of a solid showed that convective transport of solute rather than molecular diffusion is the primary means of mass transfer for such a model (1, 2). Interfacial effects such as solvent penetration, wetting, and solvation of the solid seem to control the rate of mass transfer when dissolution from the solid surface occurs in the descending direction. Under such conditions, one would not anticipate the presence of a finite "diffusion layer." Calculations based on measurements of the rate of movement of a solute front in a descending dissolution column (1) are presented here to show that steady-state velocities are established within microseconds and essentially begin at the interface, thus eliminating the possibility of a microsize diffusion layer.

THEORY AND DISCUSSION

The velocity of solute flow in a vertical dissolution column was determined from observations of the movement of the solute front down the column (1). Since a linear relationship was observed between the solvent front location and time, the velocity appears to be independent of time. There must, however, be a time-variant laminar flow velocity profile, on a molecular basis, for molecules in the bulk fluid stream at times close to zero. A molecule in the solid phase obviously has a zero-velocity component contributing to its flow down the column.

Following the solvation step in a dissolution process, the solvated solute molecule descends from rest in a stationary fluid under the action of gravity. The molecule first accelerates as it would in a vacuum; but unlike the situation in a vacuum, its acceleration is retarded due to friction with the surrounding solvent medium. As the frictional force increases with an increase in velocity, this force eventually reaches a value equal to that of the gravitational force. From that point on, the two forces are balanced and the molecule continues to fall at a constant velocity. The exponentially increasing velocity of such a molecule descending from rest under the influence of gravity represents an interesting first-order system, because the dynamics are defined completely by the steady-state velocity and the time constant for the approach to steady state can be predicted from this velocity.

Consider the fall of a solvated solute molecule through an aqueous medium when the solvated solute and solvent differ in density and viscosity. Under the action of gravity, the downward force, F, acting on the molecule depends on the relative magnitudes of the forces of gravity and buoyancy. The gravitational force, F_w, acts on the molecule even when it is at rest and remains constant during the entire period of descent. The buoyancy, F_b, is dependent on the solvent medium. From Newton's second law of motion:

$$F = F_w - F_b \qquad \text{(Eq. 1a)}$$

$$F = (\rho - \rho_0)gV \qquad \text{(Eq. 1b)}$$

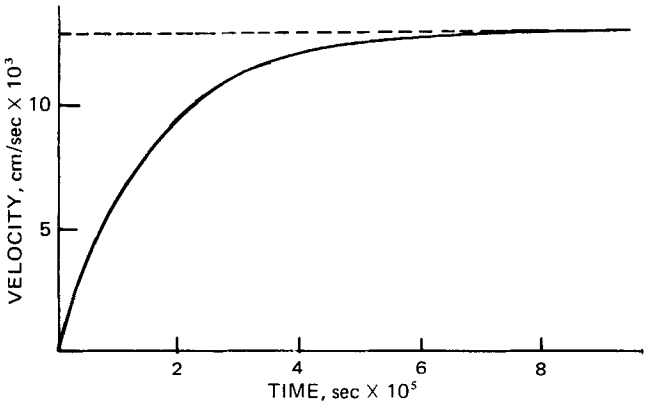

Figure 1—*Plot of velocity* versus *time for I using Eq. 9. The dashed line is the limiting maximum velocity:* v_{max} = *0.013 cm/sec.*

where g is the gravitational acceleration; ρ and ρ_0 are the densities of solvated solute and solvent, respectively; and V is the volume of the solvated solute molecule. The force F_w in Eq. 1*a* is the downward force of gravity acting on the solute molecule in the stationary medium. The term $\rho_0 gV$ represents the buoyancy effect. Although it is difficult to determine the volume of a molecule with an irregular shape, shape is an important factor contributing to the forces acting on a falling molecule. For the sake of simplicity, the solvated molecules are assumed to be spherical. If D is the diameter of a molecule, then:

$$V = \frac{\pi D^3}{6} \qquad \text{(Eq. 2)}$$

Substituting Eq. 2 into Eq. 1*b* yields:

$$F = \frac{\pi D^3 g}{6}(\rho - \rho_0) \qquad \text{(Eq. 3)}$$

The force resisting motion is generally referred to as the drag, R. It is assumed that its magnitude is a function of the diameter of the molecule, its velocity, v, and the viscosity of the surrounding fluid. On the basis of these assumptions, Stokes derived an equation for flow resistance in laminar flow systems (3):

$$R = KD\eta v \qquad \text{(Eq. 4)}$$

where η is the dynamic viscosity of the solvent medium, K is a shape factor for the solute and has been determined experimentally for a number of shapes, and v is velocity. For a spherical object, K has a value of 3π, so Eq. 4 takes the form:

$$R = 3\pi D\eta v \qquad \text{(Eq. 5)}$$

The net driving force, DF, acting on a molecule is:

$$DF = F - R \qquad \text{(Eq. 6)}$$

From Newton's law (3):

$$DF = \frac{F}{g}(dv/dt) \qquad \text{(Eq. 7}a\text{)}$$

$$DF = \frac{\pi D^3}{6}(\rho - \rho_0)dv/dt \qquad \text{(Eq. 7}b\text{)}$$

Substituting Eqs. 3, 5, and 7*b* into Eq. 6 yields:

$$\frac{\pi D^3}{6}(\rho - \rho_0)dv/dt = \frac{\pi D^3 g}{6}(\rho - \rho_0) - 3\pi D\eta v \qquad \text{(Eq. 8)}$$

Table I—Solubilities, Effective Interfacial Concentrations, and Velocities[a]

Solid	Saturation Solubility, C_s, $M \times 10^2$	Interfacial Concentration, C_i, $M \times 10^3$	Steady-State Velocity, V_{max}, cm/sec $\times 10^2$
Phenacetin	0.53	0.32	0.48
Salicylamide	2.0	1.1	1.6
I	4.1	2.8	1.3
Benzamide	12.5	4.0	4.2

[a] From Ref. 4.

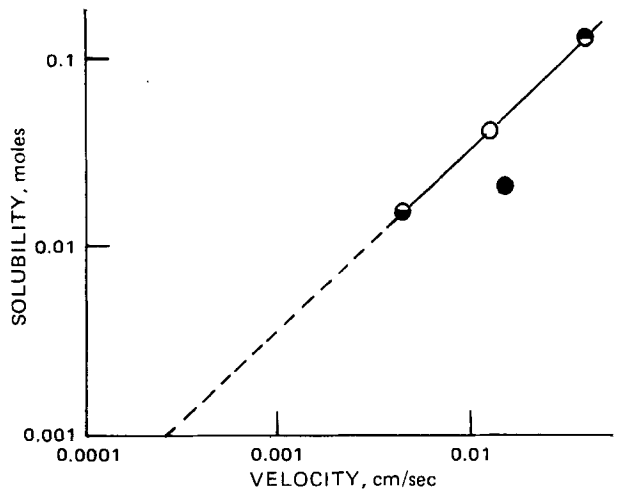

Figure 2—*Logarithmic plot of solubility* versus *velocity of flow. Key:* ○, *I;* ◓, *benzamide;* ◒, *phenacetin; and* ●, *salicylamide.*

By letting $v = 0$ at $t = 0$ since the molecules are initially at rest, the solution of Eq. 8 becomes:

$$v = \frac{D^2 g(\rho - \rho_0)}{18\eta}\left[1 - e^{-(18\eta/D^2)(\rho-\rho_0)t}\right] \qquad \text{(Eq. 9)}$$

As time increases, v approaches a constant limiting velocity, v_{max}, where:

$$v_{max} = \frac{D^2 g(\rho - \rho_0)}{18\eta} \qquad \text{(Eq. 10)}$$

In the descending dissolution of *N*-(3-methylphenyl)acetamide (I) in water, a v_{max} of 0.013 cm/sec was observed (1). A graph of the velocity of flow, v, as a function of time can be constructed according to Eq. 9 (Fig. 1). The descending molecules start at rest, exponentially gain velocity due to the effects of gravity, and reach their limiting velocity in an extremely short period (about 80 μsec).

The distance from the solid surface at which the maximum velocity is first attained is of particular interest. Since the solute velocity increases from 0 to 0.013 cm/sec, it is conceivable that diffusional velocities exist in the approximately 50-μm region usually described by diffusion layer theory. Equation 9 may be written as:

$$dx/dt = v_{max}\left[1 - e^{-(g/V_{max})t}\right] \qquad \text{(Eq. 11)}$$

where $v = dx/dt$ = the change in distance x with time for a solute front moving in the x direction. The solution of this equation for x with the initial condition $x = 0$ at $t = 0$ is:

$$x = v_{max}\left\{t + \frac{V_{max}}{g}\left[e^{-(g/V_{max})t}\right] - \frac{V_{max}}{g}\right\} \qquad \text{(Eq. 12)}$$

The solution of Eq. 12 at $t = 80$ μsec is 9.26×10^{-7} cm. As might be expected from the short time required, the maximum velocity for I is established essentially at the interface, contradicting any postulate of a microsize diffusional layer.

Since the steady-state velocity in the descending column is related to the solubility of the solid (Table I), the question arises as to the possibility of a diffusional layer existing for solids of a lower solubility than I. By using the solubility and descending solute front velocity values reported (2–4) for the solids I, benzamide, phenacetin, and salicylamide, a logarithmic plot of solubility *versus* velocity was constructed (Fig. 2) and an extrapolation was made to lower velocities. Since the velocity of solute flow down the column is related to the density difference between the solution at the interface and the bulk solution and since this density difference should, in general, decrease with the decreasing solubility of the solid, the extrapolation in Fig. 2 should reasonably reflect solute velocities at low solubilities.

The diffusional velocity of I can be estimated from reported ascending dissolution experiments (examining a true diffusion process) (1). When using the I diffusion coefficient of 1.25×10^{-5} cm^2/sec as representative of most solutes and a 60-min time period, a diffusion velocity of 2×10^{-4} cm/sec was obtained. The extrapolation in Fig. 2 indicated that velocities in the diffusional range are reached when the solubility falls below 0.001

M. Variations from Fig. 2 occur due to the fact that not all solids and their resulting solutions have the same density and convective velocity. For example, salicylamide has a lower solubility than I but a higher solution mass transfer velocity.

Finally, it must be stressed that a diffusional mass transfer step does not mean a diffusion-controlled mechanism for dissolution. While the dissolution of solids having solubilities below 0.001 M appears to be diffusion controlled, this does not mean that the interfacial rate is now fast compared to the diffusion rate. Certainly, the rate of interaction at the solid–liquid interface decreases as the solubility decreases, as indicated by the data in Table I showing that the effective interfacial concentration decreases with decreasing solubility. This phenomenon is not likely to change at even lower solubilities. Consequently, regardless of solubility or the approach to diffusional mass transfer, the interfacial rate will remain slower than the diffusion rate and dissolution must be considered as an interfacially controlled process.

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GLC–Mass Spectral Analysis of Psilocin and Psilocybin

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Abstract □ With the combined technique of GLC–mass spectrometry, psilocin and psilocybin, two hallucinogenic indoles, were analyzed as their trimethylsilyl derivatives. The method was applied to these two components in an extract of *Psilocybe cubensis* (Earle) Sing.

Keyphrases □ Psilocin—GLC–mass spectral analysis in extract of mushroom *Psilocybe cubensis* □ Psilocybin—GLC–mass spectral analysis in extract of mushroom *Psilocybe cubensis* □ GLC–mass spectrometry—analysis, psilocin and psilocybin in extract of mushroom *Psilocybe cubensis* □ Hallucinogenics—psilocin and psilocybin, GLC–mass spectral analysis in extract of mushroom *Psilocybe cubensis*

Psilocin and psilocybin, two hallucinogenic principles found in certain agarics (1), have aroused considerable interest since their isolation and characterization in the late 1950's (2, 3). The mushrooms in which they occur have been known and revered in southern Mexico for centuries. Their rediscovery in 1939 (4) and their subsequent study (5, 6) and popularization ultimately led to legislation to control their use (7).

BACKGROUND

Psilocin (3-[2-(dimethylamino)ethyl]indol-4-ol) and psilocybin, its dihydrogen phosphate ester, are unique in nature as indoles having a 4-substituent and a phosphate group. Both qualitative and quantitative methods have been utilized for their analysis. Paper chromatography (2) and TLC (8) have been used in conjunction with colorimetric reagents as well as UV spectroscopy. When pure samples are available, IR spectrometry can be used (9). Mass spectrometry (10) has been relied upon for identification of these compounds in various pharmaceutical preparations. Various fluorescence and phosphorescence techniques (11) as well as other emission spectral techniques (12) have also been used.

In an investigation of the genus *Psilocybe* and related genera, the need for a sensitive and accurate quantitative method for the analysis of psilocin and psilocybin became apparent. This method would have to be applicable to extracts of minute amounts of scarce herbarium material and vegetative mycelium obtained from liquid culture.

Previously, GLC was applied to the analysis of psilocin (13) and psilocybin (14), both as the free bases and their trimethylsilyl derivatives. GLC–mass spectrometry has been successfully applied to the bis(trimethylsilyl) derivative of bufotenine, the 5-hydroxy positional isomer of psilocin (15).

The possibility of utilizing GLC for the separation of organic molecules containing a phosphate group was suggested by work with trimethylsilyl derivatives of ribonucleotides (16).

EXPERIMENTAL[1]

Fifty milligrams of freeze-dried pileus tissue of *P. cubensis*[2] was ground to a fine powder with sand and transferred to a screw-capped vial. Methanol (5 ml) was added, and the tube was shaken at room temperature for 24 hr. The mixture was filtered, and the solid was washed with 5 ml of methanol. The filtrate was concentrated *in vacuo* to 0.5 ml, transferred to a 1.0-ml vial[3], and concentrated to dryness in a nitrogen stream. All traces of solvent were removed by evacuation on the oil pump. In an anhydrous nitrogen atmosphere, 100 μl of bis(trimethylsilyl)trifluoroacetamide[4] was added to the vial, which was then closed with a septum-lined aluminum seal[5].

The vial was heated at 140° for 15 min. Prolonged reaction periods (up to 2.5 hr) showed that this length of time was sufficient for quantitative

[1] GLC was carried out using a Hewlett-Packard model 402 gas chromatograph equipped with hydrogen flame-ionization detectors. The column used was a 1.6-m × 2.8-mm i.d. glass U-tube with 1.5% SE-30 on 100–120-mesh Chromosorb W. Chromatography conditions were: injection block, 220°; detector, 280°; oven, temperature programmed from 150 to 250° at 7.5°/min; chart speed, 0.64 cm/min; and helium carrier gas, 50 ml/min. TLC utilized glass plates with 0.25-mm layers of silica gel GF using 1-propanol–5% ammonium hydroxide (5:2) (17).

GLC–mass spectrometry was carried out with a Finnigan model 9500 gas chromatograph coupled to a Finnigan model 3100 D quadrupole mass spectrometer through a single-stage glass jet separator. A System/250 data system (Systems Industries) was used to control the mass spectrometer and acquire data. The mass spectrometer parameters were: interface temperature, 200–225°; transfer line, 150–175°; manifold temperature, 100°; and ion source potential, 70 ev. Two sets of chromatography conditions were employed: (*a*) essentially the same as those listed for GLC, and (*b*) a 0.75-m × 2-mm i.d. glass U-tube with 3% OV-101 on 100–120-mesh Gas Chrom Q temperature programmed from 200 to 275° at 10°/min with a helium flow rate of 20 ml/min.

[2] Carpophores of *Psilocybe cubensis* (Earle) Singer (= *Stropharia cubensis* Earle) (Strophariaceae) were obtained by aseptic cultivation of a strain of this fungus on sterile horse manure. The strain was isolated from pileus tissue of a fresh carpophore of *P. cubensis* collected Aug. 31, 1974, in Huautla de Jimenez, Oaxaca, Mexico, and was maintained on malt extract agar. The origin and maintenance of the culture and the production of fruiting bodies were similar to those reported previously (5, 6, 18). Carpophores were authoritatively identified by Dr. Gastón Guzmán, Escuela Nacional de Ciencias Biológicas (ENCB), I.P.N., Mexico, D.F., Mexico. Herbarium material is on deposit at the ENCB herbarium and the University of Michigan herbarium as LESLIE 1902 and at the Institute for Fermentation herbarium, Osaka, Japan, as IFO-H 11703. Subcultures are on deposit at the Institute for Fermentation (IFO 30176) and the Centraalbureau vorr Schimmelcultures, Baarn, The Netherlands (CBS 134.76).

[3] Hewlett-Packard 5080-8712.

[4] Regisil, Regis Chemical Co.

[5] Hewlett-Packard 5080-8713.