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COMPARISON OF SEVERAL DIFFUSION EQUATIONS IN THE CALCULATION OF VISCOSITY AND ITS RELATION TO DISSOLUTION RATE

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ABSTRACT

The viscosity of polymeric solutions as measured by a rotational viscometer may not be the viscosity of the environment through which a solute molecule diffuses. By use of the Stokes-Einstein equation a viscosity, which is not affected by the mechanics of the viscometer, may be calculated if the size and diffusivity of the solute molecule are determined. The values of such viscosity calculated by using several diffusion equations compare favorably with the value calculated with the Stokes-Einstein equation. The dissolution rates of benzoic acid in aqueous solutions of three non-ionic suspending agents is related to the viscosity.

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INTRODUCTION

Viscosity is one of several factors that affect the dissolution rate of a solid. An empirical relationship between the dissolution rate and viscosity raised to some power is

$$R = k\eta^{-\alpha} \qquad \text{(Eq.1)}$$

where R is the rate, η is the viscosity of the medium, and k and α are constants which depend on the system (1-4). There is no unanimity for this expression as reported values of α vary from 0.25 to 0.8 (5). The purpose of this study was to compare the values of these constants obtained from experimental dissolution rates and viscosities calculated from experimental diffusion coefficients using several diffusion equations.

EXPERIMENTAL

Dissolution Rate Determinations. The method of tablet production and the dissolution apparatus have been described previously (6). Spherical benzoic acid tablets with a diameter of 1.273 ± 0.0005 cm were compressed at 2,270 kg of force by a hydraulic press[1]. Determinations were made in triplicate at 25 ± 0.1° and at a stirrer speed of 324 rpm. The 2 l. of dissolution medium in the dissolution beaker was changed at appropriate intervals so that the concentration of the dissolved benzoic acid was not permitted to exceed 3% of its solubility. With each change of dissolution medium the sphere was weighed and its diameter was measured with a micrometer. Solutions were prepared by a conventional method and allowed to stand 24 hours before use as the dissolution

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[1] Carver press, model D

media. Dissolution rates were determined in various concentrations of aqueous methycellulose[2], hydroxypropyl cellulose[3] and guar gum[4] solutions.

Other Measurements. The densitites of the solutions were measured by pycnometer. Viscosity was measured by a rotational viscometer[5]. The diffusion coefficients were determined by use of a diffusion cell previously described (7); the value of the diffusion coefficient in Table I is the average of three determinations for each concentration.

RESULTS AND DISCUSSION

A plot of the logarithmic form of Eq. 1

$$\log R = -\alpha \log \eta + \log k \qquad \text{(Eq.2)}$$

may be used to evaluate α, which is the slope, and log k, which is the intercept with the ordinate. For example in Fig. 1 the plot of logarithms of dissolution rates against the logarithms of viscosities measured by a rotational viscometer at 60 rpm in aqueous solutions of methylcellulose, hydroxypropyl cellulose and guar gum at 25° is linear. The slope is -0.51, and k is 67.2.

Since solutions of methylcellulose, hydroxypropyl cellulose and guar gum are pseudoplastic, the viscosity expressed in terms of a rotational viscometer depends on the shear rate (rpm), and the constants vary with changes in rpm. In polymeric solutions the measured viscosity may also be influenced by the mechanical

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[2] USP, Type 1500 cp
[3] Klucel, grade HF, Hercules Inc.
[4] Colony Impt. & Expt. Corp.
[5] Brookfield model LVT Syncho-Lectric

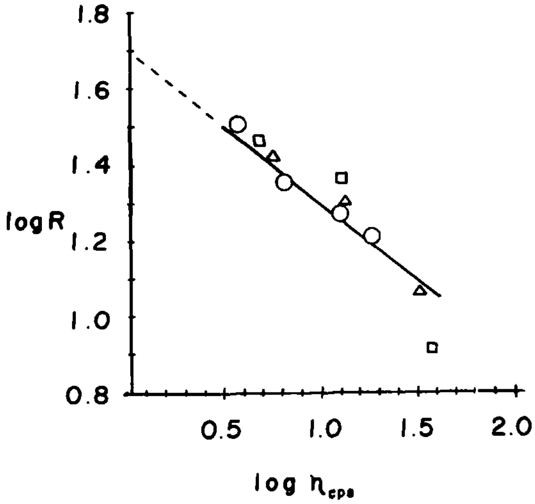

FIGURE 1

Logarithm-logarithm plot of dissolution rate of benzoic acid at 25° and rotational viscosity at 60 rpm of aqueous solutions of various suspending agents. Key: O, methylcellulose; Δ, hydroxypropyl cellulose; and □, guar gum.

design of the viscometer. With these facts under consideration in an attempt to express a viscosity, which is representative of the impendence to movement in the actual environment in which the solute molecule diffuses, the experimental diffusion coefficient (D_{expt}) was measured and by means of the Stokes-Einstein equation

$$\eta_D = \frac{kT}{D} \frac{1}{6\pi r} \qquad \text{(Eq. 3)}$$

a viscosity, η_D, was calculated. The radius (r) of benzoic acid has been reported to be 2.95 A (8). Values of η_D and dissolution rate are given in Table I and II.

In polymeric solutions the obstructive effect is related to the volume fraction of the polymer. Since the solute travels

TABLE I. Dissolution Rate and Diffusion Coefficient of Benzoic Acid at 25° in Aqueous Polymeric Solutions of Various Viscosities

Rate, mg/cm^2/hr	10^5 D_{expt}, cm^2/sec	η_D, cps			
		Stokes-Einstein (Eq. 3)	Wilke-Change (Eq. 6)	Scheibel (Eq. 7)	Davis-Tominaga-Evans (Eq. 12)
		Methylcellulose			
41.17	1.102	0.67	0.88	0.82	1.23
32.41	1.036	0.71	0.94	0.88	1.34
22.79	0.678	1.09	1.43	1.33	2.40
18.82	0.298	2.47	3.24	3.02	7.40
16.36	0.240	3.05	4.01	3.73	9.88
		Hydroxypropyl Cellulose			
26.79	0.650	1.14	1.50	1.39	1.81
20.39	0.372	1.98	2.61	2.43	5.48
11.66	0.186	3.96	5.21	4.85	14.17
		Guar Gum			
29.26	1.055	0.70	0.92	0.86	1.31
23.51	0.446	1.66	2.18	2.03	4.27
8.15	0.167	4.45	5.83	5.43	16.56

TABLE II. Dissolution Rate and Diffusion Coefficient of Benzoic Acid at 25° in Aqueous Polymeric Solutions of Various Viscosities

Rate, mg/cm^2/hr	10^5 D_{expt}, cm^2/sec	Viscosity, cps*	η_D, cps		
			Lusis-Ratcliff (Eq. 10)	Othmer-Thakar (Eq. 9)	Revised Othmer-Thakar (Eq. 11)
			Methylcellulose		
41.17	1.102	0.9	0.87	0.83	0.86
32.41	1.036	3.7	0.93	0.88	0.90
22.79	0.678	6.5	1.42	1.29	1.22
18.82	0.298	12.5	3.21	2.72	2.19
16.36	0.240	19.0	3.96	3.30	2.54
			Hydroxypropyl Cellulose		
26.79	0.650	5.75	1.48	1.35	1.26
20.39	0.372	13.6	2.58	2.24	1.87
11.66	0.186	33.0	5.15	4.19	3.07
			Guar Gum		
29.26	1.055	4.8	0.91	0.87	0.89
23.51	0.446	12.7	2.15	1.90	1.65
8.15	0.167	37.0	5.76	4.64	3.33

*rotational viscometer, 60 rpm

primarily through the fluid phase and collides with the individual polymer segments, the microviscosity and the number of polymer segments present determine the diffusivity. Lauffer (9) showed that

$$D_{expt} = D_{true}\ (1 - 1.5\ \phi) \qquad \text{(Eq.4)}$$

where D_{true} is the true diffusion coefficient of the small solute molecules in a dilute polymer solution containing volume fraction ϕ. In no case of this investigation did the D_{expt} and D_{true} differ by more than 0.3%.

A plot of the logarithms of dissolution rates of benzoic acid at 25° in aqueous solutions of methylcellulose, hydroxypropyl cellulose and guar gum against η_D as calculated by the Stokes-Einstein equation is shown in Fig. 2. The slope is -0.62, and k is 28.02.

From various theoretical approaches to diffusion process, a number of equations were selected to use with the data for a comparison to the Stokes-Einstein equation. When suitably rearranged these expressions are similar and may be written

$$D = \frac{kT}{\eta}\ f \qquad \text{(Eq. 5)}$$

where f varies from model to model. Some equations (see Appendix for symbols), which appear generally useful in dilute polymer solutions, are:

Wilke and Change (10)

$$D = \frac{7.4 \times 10^{-8}\ (xM)^{\frac{1}{2}}T}{\eta\ V_1^{0.6}} \qquad \text{(Eq. 6)}$$

Scheibel (11)

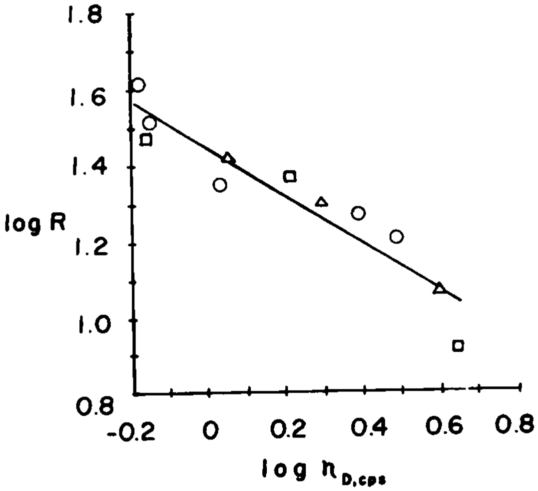

FIGURE 2

Logarithm-logarithm plot of dissolution rate of benzoic acid at 25° and η_D of aqueous solutions of various suspending agents. Key: O, methylcellulose; Δ, hydroxypropyl cellulose; and □, guar gum.

For $V_1 > V_2$

$$D = \frac{8.2 \text{ X } 10^{-8} \; [1 + (3V_2/V_1)^{2/3}]T}{\eta \; V_1^{1/3}} \qquad \text{(Eq. 7)}$$

For $V_1 < V_2$

$$D = \frac{25.2 \text{ x } 10^{-8} \; T}{\eta \; V_1^{1/3}} \qquad \text{(Eq. 8)}$$

Othmer and Thakar (12)

$$D = \frac{14 \text{ x } 10^{-5}}{\eta^{1.1} \; V_1^{0.6}} \qquad \text{(Eq. 9)}$$

Luis and Ratcliff (13)

$$D = \frac{8.52 \times 10^{-8}\, T\, [1.4\, (V_2/V_1)^{1/3} + (V_2/V_1)]}{\eta\, V_2^{1/3}} \qquad \text{(Eq. 10)}$$

Revised Othmer-Thakar (14)

$$D = \frac{13.26 \times 10^{-5}}{\eta^{1.4}\, V_1^{0.589}} \qquad \text{(Eq. 11)}$$

Davis, Tominaga and Evans (15)

$$D_E = \frac{AT}{298.2\, \eta_E^{p}} \qquad \text{(Eq. 12)}$$

The D_{expt} was used in each of the above equations to calculate η_D, which is tabulated in Table I and II with the experimental dissolution rates. A logarithm-logarithm plot of dissolution rates against η_D was linear in each case, and the values of α and k obtained from the individual plots are given in Table III.

The viscosities based on D_{expt} give α of approximately 0.6, while the rotational viscosity gives a value of 0.5. This suggests that the bulk viscosity measured by the rotational viscometer is not the viscosity in the environment through which the solute molecule diffuses. The utilization of the revised Othmer-Thakar equation and the Davis-Tominaga-Evans equation is questionable in aqueous systems as both equations were developed based on diffusion data of solutes in organic solvents.

The values of α and k calculated by Eqs. 6, 7, 9 and 10 are approximately the same as those obtained by use of the Stokes-Einstein equation. Thus, the utilization of the Stokes-Einstein equation as presented seems reasonable. For the non-ionic suspend-

TABLE III. Values of α and k of Eq. 1 Using Viscosities Calculated by Various Diffusion Equations

	k	α	r*
Rotational Viscometer	67.20	0.51	0.943**
Stokes-Einstein (Eq. 3)	28.05	0.62	0.938
Wilke-Change (Eq. 6)	33.27	0.62	0.939
Scheibel (Eq. 7)	31.86	0.62	0.939
Othmer-Thakar (Eq. 9)	31.76	0.69	0.939
LuSis-Ratcliff (Eq. 10)	33.05	0.62	0.939
Revised Othmer-Thakar (Eq. 11)	31.60	0.87	0.939
Davis-Tominaga-Evans (Eq. 12)	38.41	0.44	0.936

*correlation coefficient, regression of 11 points

**regression of 10 points

ing agents studied the empirical relationship between the dissolution rate of benzoic acid at 25° and viscosity is approximately

$$R = 30\ \eta_D^{-0.62} \qquad \text{(Eq.13)}$$

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APPENDIX

Symbols used in the text and in Ref. 10-15 are given below.

D = diffusion coefficient, cm^2/sec

x = "association parameter" of solvent

M = molecular weight of solvent

T = temperature, °K

η = viscosity of solution (solvent), cps

V_1 = molal volume of solute at normal boiling point, cm^3/g mole

V_2 = molal volume of solvent at normal boiling point, cm^3/g mole

r = solute radius, nm

D_E = diffusion coefficient, m^2/sec

η_E = solvent viscosity, kg/m sec

$p = 1.166 - 0.1296/r$

$A = 5.036 \times 10^{-14}\ e^{(1.5124/r)}$