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RELATIONSHIP OF DISSOLUTION RATE IN ANIONIC POLYMERIC SOLUTIONS TO VISCOSITY

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ABSTRACT

The influence of viscosity on the dissolution rate of m-acetotoluidide in aqueous solutions of acacia, gelatin type B, sodium carboxymethylcellulose, sodium alginate and xanthan gum was investigated. The viscosity was measured by a rotational viscometer. The dissolution rates decreased as the viscosities of solutions of anionic polymers increased. The curves representing the relationship of dissolution rate and viscosity varied for each polymeric solution depending on the structural characteristics of the polymer.

INTRODUCTION

Diffusion-controlled dissolution would be expected to decrease in rate with an increase in viscosity (1-4). Empirical equations have been suggested that show the dissolution rate to be a function of the viscosity raised to a power ranging from -0.25 to -0.8 (5-7). In a study of the dissolution rate of benzoic acid in aqueous solutions of three nonionic polymers (methylcellulose, hydroxypropyl cellulose and guar gum) a single curve could be constructed to represent the relation of dissolution rate to the microviscosity as calculated by the Stokes-Einstein equation (8). The purpose of this investigation was to study the relationship of dissolution rate of a neutral, nonionic compound and viscosity in solutions of anionic polymers which are chemically similar but have different molecular weights and configurations.

EXPERIMENTAL

The methodology and procedures have been reported (8). The bulk viscosity was measured at 25°C by a Brookfield model LVT Syncho-Lectric viscometer fitted with a #1 spindle operating from 0.3 to 60 rpm. Under sink conditions dissolution rates of m-acetotoluidide (Alfa Products, Lot No. 060485) from spherical 1.273 ± 0.005 cm tablets compressed at 2270 kg of force were determined in various concentrations of aqueous solutions of acacia (Fisher Scientific, Lot No. 872570), gelatin type B (Fisher Scientific, Lot No. 861103), sodium carboxymethylcelluose, medium viscosity (Sigma Chemical Company, Lot No. 116F-0231), sodium alginate (Aldrich Chemical Company, Lot No. 022225 KP) and xanthan gum (Kelzan, Kelco Division of Merck & Co., Inc., Lot No. 39035K).

RESULTS AND DISCUSSION

Viscosity. As the anionic polymers studied formed pseudoplastic solutions, it was essential to use a viscometer that is able to relate shearing stress and rate of shear. A semilogarithmic plot of the viscosities of various concentrations of sodium carboxylcellulose solutions as a function of rpm is shown in Figure 1. At speeds exceeding 10 rpm the upper Newtonian viscosity for

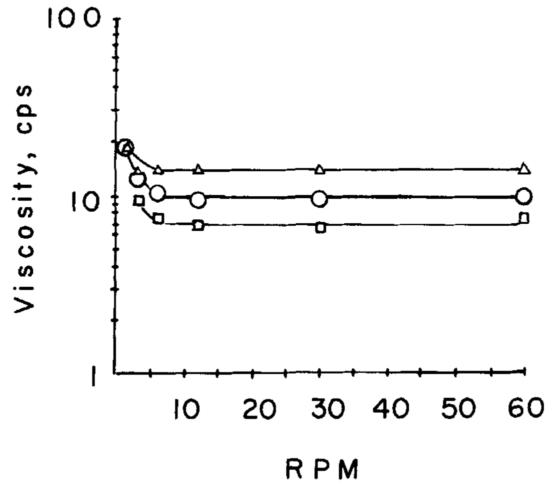

FIGURE 1

Influence of rotations per minute on viscosities of aqueous solutions of various concentrations of sodium carboxymethylcellulose. Key: □ , 0.1%; ○ , 0.2%; and △ , 0.3% w/v.

dilute solutions was attained, and the viscosity did not decrease as the shear rate was further increased (9). A similar relationship was found for solutions of acacia, gelatin type B and sodium alginate. The Brookfield LVT viscometer fitted with spindle #1 provides a shear rate of 13.2 sec-1 at 60 rpm (10). The viscosity determined in the upper Newtonian region should represent the bulk viscosity in the dissolution apparatus in which the speed was 324 rpm.

For aqueous solutions of xanthan gum within the range of the Brookfield viscometer the upper Newtonian viscosity was not reached. Rocks (11) and others (12-16) used the empirical power law (Ostwald-de Waele equation) to characterize the flow behavior

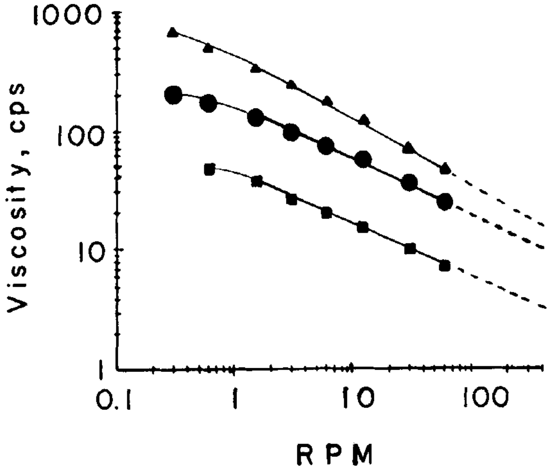

FIGURE 2

Log-log relationship of viscosity and rotations per minute for solutions of xanthan gum. Key: ■ , 0.01%; ●, 0.05%, and ▲ , 0.10% w/v.

of solutions of xanthan gum. Plots of the logarithm of viscosity against the logarithm of rpm are shown in Figure 2. The linear portions of the curves were extrapolated to evaluate the viscosities at 324 rpm, which was the rate of shear in the dissolution apparatus. The values are given in Table 1.

The variation of viscosity as a function of concentration of polymer is shown in Figure 3. The viscosity is increased as the concentration of the polymers is increased but to different degrees for the polymers that have different molecular weights and configurations in solution. A polymer having a high molecular weight produces a mucilage of a high viscosity. Branched polymeric molecules in solution induce a lower viscosity than linear polymeric molecules of the same molecular weight if the side chains are

TABLE 1. Solubility and Dissolution Rate of m-Acetotoluidide in Various Concentrations and Viscosities of Polymeric Solutions at 25°C

Dissolution Medium	Percent w/v	Solubility, mg/mL	Viscosity[a], cps	Rate[b] mg/cm^2/hr
Distilled water	-	5.82	0.895	54.77
Sodium carboxymethyl-cellulose	0.1	5.82	7.05	29.70
	0.2	5.86	9.81	25.34
	0.3	5.71	13.89	22.15
Sodium alginate	0.1	5.75	4.90	33.82
	0.3	5.68	8.56	25.98
	0.5	5.75	13.62	21.60
Gelatin type B	1.0	5.72	2.95	46.78
	3.0	6.02	5.05	34.35
	5.0	6.11	8.00	26.49
Acacia	2.0	5.68	3.74	38.04
	3.0	5.65	3.98	33.48
	5.0	5.69	5.46	27.80
	7.0	5.64	6.24	23.15
Xanthan gum	0.01	5.71	3.49[c]	34.65
	0.05	5.71	11.34	8.82
	0.10	5.70	18.20	4.49

[a] measured in upper Newtonian region (60 rpm); [b] triplicate determination;

[c] extrapolated from Figure 2 at 324 rpm

not long enough to participate in entanglement. Branched molecules are more compact than linear ones and offer less resistance to flow (lower viscosity).

Xanthan gum has a molecular weight approximately ten times as great as the other viscosity-inducing agents studied; therefore, at a given concentration xanthan gum produces a solution of much

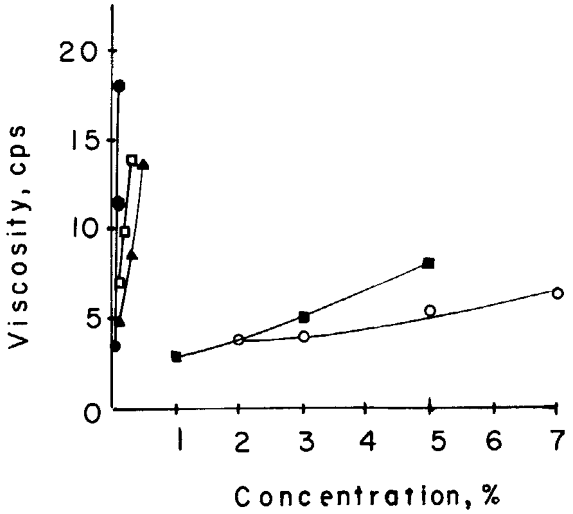

FIGURE 3

Viscosity as a function of concentration in water at 25°C. Key: □ , sodium carboxymethylcellulose; ▲ , sodium alginate; ■ , gelatin type B; ○ , acacia; and ● , xanthan gum.

greater viscosity. Solutions of sodium carboxymethylcellulose and sodium alginate have a high viscosity as the molecules are linear and offer considerable resistance to flow. Acacia and gelatin are branched molecules; thus, they offered less resistance to flow and have a lower viscosity.

Relation of Dissolution Rate and Viscosity. As shown in Figure 4 at sink conditions the dissolution rates of m-acetotoluidide is reduced by the addition of these polymeric molecules in solution. The order of effectiveness in reducing the dissolution rate is in accord with that in enhancing the viscosity of the dissolution medium as shown in Figure 5. This indicates that the dissolution rate may be correlated to the viscosity.

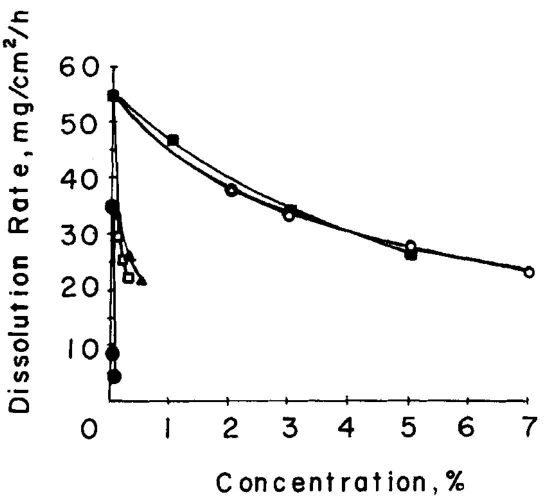

FIGURE 4

Dissolution rates of m-acetotoluidide in various concentrations of aqueous solutions. Key: same as Figure 3.

It has been reported that the dependence of dissolution rate of benzoic acid on viscosity can be represented by a single curve when non-ionic polymers are used as the viscosity-enhancing agents (8). In Figure 5 it appears that in aqueous solutions of sodium carboxymethylcellulose, sodium alginate and gelatin there is a similar relationship of dissolution rate to viscosity, but the behavior is different for the dissolution of m-acetotoluidide in solutions of acacia and xanthan gum.

If dissolution of a one-component, non-disintegrating sphere occurring in a non-reactive medium at sink condition is diffusion controlled, the dissolution rate (R) may be expressed (17)

$$R = \frac{DC_s}{h} \qquad \text{(Eq. 1)}$$

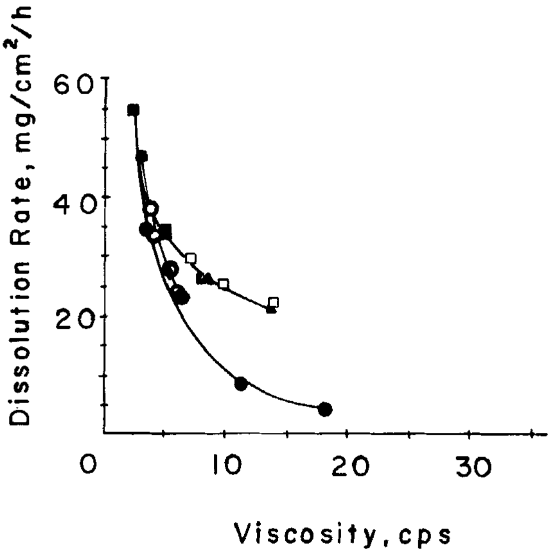

FIGURE 5

Influence of viscosities of various polymeric solutions on dissolution rates of m-acetotoluidide. Key: same as Figure 3.

where D is the diffusion coefficient of the solute molecule in the dissolution medium, C_s is the solubility, and h is the effective diffusion layer thickness. Taking convective transport into account, the effective diffusion layer thickness may be expressed (18, 19)

$$h = k_1 D^p \upsilon^q U^r X^s \qquad \text{(Eq. 2)}$$

where υ is kinematic viscosity, U is the free stream velocity or rotational speed, and X is characteristic length in the system. The empirical coefficients (k_1, p, q, r and s) depend on the experimental conditions. If the velocity of the moving fluid and the characteristic length remain constant, Eq. 2 reduces to

$$h = k_2 D^p \eta^q \qquad \text{(Eq. 3)}$$

Substitution of Eq. 3 into Eq. 1 yields

$$R = k_3 D^{1-p} \eta^{-q} C \qquad \text{(Eq. 4)}$$

The diffusivity of a substance in a particular medium depends on the properties and the degree of interaction between the diffusant and the diffusion medium (20). In general there is an inverse relationship of diffusion coefficient and viscosity (21). Many empirical diffusion coefficient equations applicable to dilute solutions have been developed and can be generalized as (22-25)

$$D = a\eta^{-b} \qquad \text{(Eq. 5)}$$

where a and b are empirical coefficients dependent on the system. Substituting Eq. 5 into Eq. 4 yields

$$R = m\eta^{-n} C \qquad \text{(Eq. 6)}$$

where m and n are coefficients depending on the molecular weight and configuration of the polymer in solution. The solubilities are given in Table 1. Equation 6 may be written in its logarithmic form

$$\log R = \log m - n \log\eta + \log C_s \qquad \text{(Eq. 7)}$$

Utilizing the data in Table 1 plots of logarithms of dissolution rates against the logarithms of viscosities of the solutions of the polymers are shown in Figure 6. The values of the coefficients of Eq. 6 evaluated from the experimental dissolution rate, viscosity and solubility are given in Table 2.

The plots of logarithm of dissolution rate for m-acetotoluidide against the logarithm of viscosity appear superimposable for sodium carboxymethylcellulose and sodium

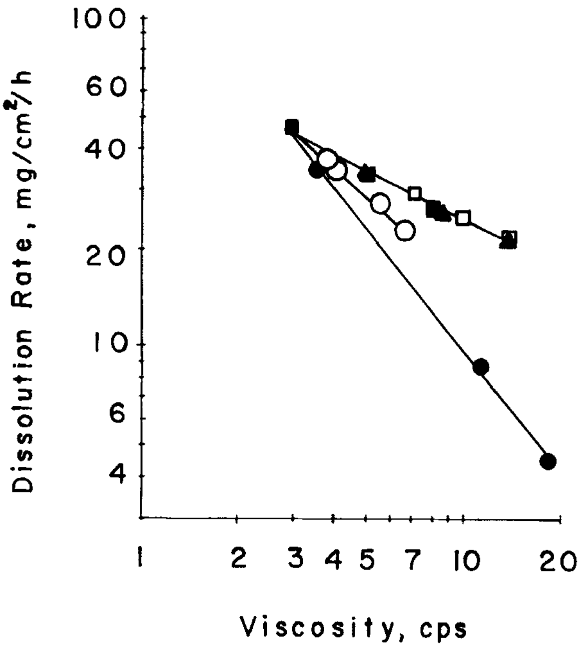

FIGURE 6

Log-log relationship of dissolution rate and viscosity for various polymeric solutions. Key: same as Figure 3.

TABLE 2. Values of m and n from Eq. 7 Based on Observed Dissolution Rate, Solubility and Viscosity

Polymer	m	n
Sodium carboxymethyl-cellulose	10.60	0.37
Sodium alginate	10.23	0.37
Gelatin type B	15.44	0.61
Acacia	18.28	0.80
Xanthan gum[a]	25.90	1.16

[a] 324 rpm

alginate. Sodium carboxymethylcellulose and sodium alginate are linear polysaccharides of approximately the same molecular weight and are highly ionized in solution. The distribution of negative charges along the molecules and the mutual repulsion maintain linear but coiled polymeric chains that are disentangled and aligned in the direction of flow. Hence a common relationship (same values of m and n) between dissolution rate and viscosity is observed for sodium alginate and sodium carboxymethylcellulose.

The relation of dissolution rate of m-acetotoluidide to viscosity of the dissolution medium may be interpreted in terms of the structural characteristics of the polymeric molecules. The molecular structures of acacia and xanthan gum are branched. Thus, steric hindrance of the branching negates coiling of the polymeric chain. When compared with linear polymeric chains of the same molecular weight, branched polymeric chains are more apt to retard mass transport when their long axes are oriented in the direction of flow. At a given bulk viscosity this may result in more frictional resistance (smaller diffusion coefficient) and a slower dissolution rate in the solutions of branched polymers.

With a linear polymer when a certain shear rate is applied, some of the solvent associated with the molecule may be released to a greater extent than from a branched molecule. Consequently, different viscosity characteristics due to configuration are anticipated. Since gelatin molecules are only slightly branched, the dissolution rate of m-acetotoluidide in gelatin solution is similar to that in linear, anionic polymerics solutions. Acacia being more branched still further decreased the dissolution rate.

In the dissolution apparatus the solutions of xanthan gum exhibited pseudoplastic behavior as the molecular chains were not completely uncoiled. The slowest dissolution rate in solutions of xanthan gum of m-acetotoluidide of the solutions studied was attributed to the coiled chains and the greater molecular weight of the xanthan gum.

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