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Application of Shrinking-Core Model for Ionization of Hydrophobic Ionic Beads

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ABSTRACT

A model based on the pseudo-steady-state shrinking core for the ionization of PMMA/MAA beads is presented. This accounts for the film mass transfer, intraparticle diffusion, and chemical reaction resistances in series. The film mass transfer resistance plays a minor role in the overall ionization process for the range of experiments studied herein. The specific reaction rate constants and diffusion coefficients increase as the pH of phosphate buffer increases, due to the increased accessibility of hydroxide ion and increased swelling of the gel layer, respectively; the specific reaction rate constants and diffusion coefficients are little influenced by the change of ionic strength of the phosphate buffer. The model shows that the rate of ionization depends upon the concentration of the buffer solution.

INTRODUCTION

Cross-linked ionic polymers have been recognized as useful matrices for controlled-release drug delivery (1) and the separation of solutes by gel extraction (2). These polyelectrolytes are sensitive to the physicochemical environment of the swelling medium such as pH, ionic strength, and ionic composition. The extent of swelling of the ionic gel is further affected by the physicochemical properties of the ionic polymer such as the charge density, degree of cross-linking, and chemical composition. Although attempts have been made to utilize ion-exchange resins in extended-release dosage forms (3), a new interest in using gel-type ionic polymers has been reported for controlled drug delivery by manipulating the swelling kinetics. Siegal et al. (4) reported that the linear release of caffeine from poly(methyl methacrylate-*co*-dimethylaminoethyl methacrylate) (PMMA/DMAEMA) at pH 3 and 5 is dependent on linear water absorption (weight gain). It also has been shown that the release of theophylline from poly(2-hydroxyethyl methacrylate-*co*-methacrylic acid) (PHEMA/MAA) retains a quasi-linear profile (5). This indicates that drug release from the ionic polymer matrix is governed by protonation or ionization of pendant groups in the polymer matrix.

The swelling of these dehydrated ionic polymers, which are hydrophobic until the pendant group is ionized, is generally controlled by a diffusion-reaction process which governs the rate of ion exchange, and a deformation process. For the mathematical description of such an ion-exchange process, many researchers have used a pseudo-steady-state shrinking-core model (PSSCM) (moving-boundary model) (6–8) and an unsteady-state ion-exchange model (9). This moving-boundary concept has been used by several investigators for noncatalytic gas–solid reactions (10,11). Such a moving-boundary process in ion exchange, as suggested by Helfferich (12), would result when a solution containing the counterion comes into contact with the fixed ion in the ion-exchange resin; a sharp concentration gradient is established by the immediate removal of ions from solution by the resin. This sharp moving front advances from the outer shell of the beads toward the center of the resin beads. Moving boundaries in ion-exchange processes have been observed by photographic investigation of resin beads to record the position of the color change during the protonation process (7,9). Most of these existing ion-exchange resins are highly cross-linked and macroreticular, with a microporous structure. As a result, the fast ion-exchange process takes place in the porous structure in the resins. For the ion-exchange process, several investigators adopted the PSSCM for the extreme cases of film diffusion, intraparticle diffusion, or a combination of both (6,7). The latter does not include situations where chemical reaction with both film diffusion and intraparticle diffusion is important, which is the case with gel-type nonporous hydrophobic polymer beads as well as noncatalytic gas–solid reactions and liquid–solid leaching processes (10,13). Recently it has been shown that lightly cross-linked gel-type poly(methyl methacrylate-*co*-methacrylic acid) (PMMA/MAA) beads exhibit a sharp moving boundary between the ionized and nonioinized portion of the polymer (14). In this process, as the reaction proceeds, a porous ionized rubbery gel layer forms around the glassy nonionized shrinking core of the polymer. Further conversion of carboxylic acid to carboxylate ion occurs by diffusion of counter ions (Na^+ or K^+) through the rubbery gel layer to the core of the polymer.

The purpose of this work described herein is to investigate the kinetics of the overall process of ionization of the hydrophobic PMMA/MAA beads in which intraparticle diffusion, chemical reaction, and film diffusion are important.

SHRINKING-CORE MODEL

The kinetic concept of a moving boundary can be illustrated in a manner similar to that developed by Shen and Smith (11) for the noncatalytic gas–solid reaction within nonporous particles. Figure 1 depicts the concentration profile of the inward-moving counterion. The kinetics depend upon the film diffusion resistance at the outer boundary, upon diffusion resistance in the rubbery gel layer, and upon the reaction resistance at the interface. Volume swelling of the polymer beads is neglected in this treatment, for the sake of simplicity. As the reaction proceeds, product **P** forms as a rubbery gel around the shrinking core of **B**, according to the following general reaction:

$$\underset{\mathbf{B}}{-\mathrm{COOH}} + \underset{\mathbf{A}}{\mathrm{Na}^+ (\text{or } \mathrm{K}^+)} \Leftrightarrow \underset{\mathbf{P}}{-\mathrm{COO}^-\mathrm{Na}^+ (\text{or } \mathrm{K}^+)} + \underset{\mathbf{C}}{\mathrm{H}^+} \qquad (1)$$

The moving boundary may be assumed to be stationary, implying that the displacement of the reaction surface is slow with respect to the diffusion of counterion through the rubbery gel layer for the establishment of a steady-state concentration profile, as follows:

$$\frac{d}{dr}\left(r^2 \frac{dC_A}{dr}\right) = 0 \qquad (2)$$

where r and C_A are the radius of sphere and the counterion concentration, respectively. The rate of consumn-

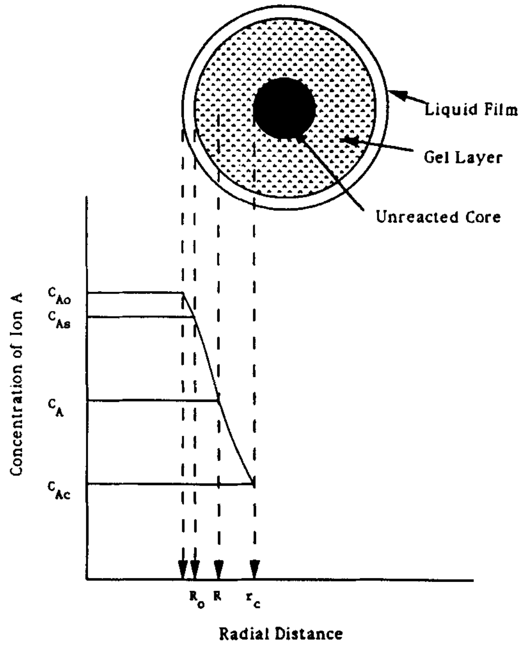

Figure 1. Idealized concentration profiles in the reacting bead.

tion of the counter ion can be expressed in terms of: the mass transfer of counterion **A** from the bulk solution to the bead's surface, or the diffusion through the rubbery gel layer, or the rate of reaction at the moving front. All processes are considered to occur in series. The reaction at the moving front is assumed to be first-order and irreversible with respect to the counterion concentration. The concentration of counterions in the bulk fluid phase is constant during the entire ionization process. The solution of the shrinking-core model for Eq. (2) is given by Ref. (11):

$$t = \left(\frac{R_0 C_{s0}}{C_{A0}}\right)\left\{\left(1 - \frac{r_c}{R_0}\right)/k_s + \left[1 - 3\left(\frac{r_c}{R_0}\right)^2 + 2\left(\frac{r_c}{R_0}\right)^3\right] / 6D + \left[1 - \left(\frac{r_c}{R_0}\right)^3\right] / 3k_f\right\} \quad (3)$$

where R_0 is the radius of the sphere, C_{s0} the concentration of the unreacted polymer, C_{A0} the initial counterion concentration in the bulk phase, r_c the radius of the moving boundary, k_s the specific reaction rate constant, D the diffusion coefficient of the counterion species, and k_f the film diffusion coefficient. The time required to complete the reaction of the polymer bead is determined by setting Eq. (3) $r_c/R_0 = 0$ or

$$T = t_{r_c=0} = \left(\frac{R_0 C_{s0}}{C_{A0}}\right)\left(\frac{1}{k_s} + \frac{1}{6D} + \frac{1}{3k_f}\right) \quad (4)$$

Dividing Eq. (3) by Eq. (4) in the dimensionless relationship between the position of the moving boundary and time yields

$$\Phi = \frac{t}{T} = \left(1 - \frac{r_c}{R_0}\right)\left\{1 + \left(\frac{Y_2}{6}\right)\left[1 + \frac{r_c}{R_0} - 2\left(\frac{r_c}{R_0}\right)^2\right] + \left(\frac{Y_1 Y_2}{3}\right)\left[1 + \frac{r_c}{R_0} + \left(\frac{r_c}{R_0}\right)^2\right]\right\} \Big/ \left[1 + \frac{Y_2}{6} + \frac{Y_1 Y_2}{3}\right] \quad (5)$$

where $Y_1 = D/k_f R_0$ and $Y_2 = k_s R_0/D$. When the rate is controlled by a combination of film diffusion and intraparticle diffusion, Eq. (3) reduces to the expression derived by Dana and Wheelock (7); whereas when the rate is dominated by the extreme cases of intraparticle diffusion, film mass transfer, or chemical reaction, Eq. (3) becomes identical to that derived by Levenspiel (15).

RESULTS AND DISCUSSION

Bischoff (16) has examined the validity of the pseudo-steady-state assumption for the case of gas–solid reactions. Taylor et al. (17) extended it further for liquid–solid reactions and has shown that for all practical purposes, the pseudo-steady-state solution is valid for $\gamma < 0.1$ for the liquid–solid reactions. γ is the measure of the fraction of the incoming flux of the counterion solution which crosses the outer surface and is used to bring about concentration changes within the reacted region. For a 0.2 M phosphate buffer solution, $\gamma = 0.02$.

Recently experimental data have been reported on the ionization of PMMA/MAA beads in phosphate buffers of pH 6.9, 7.4, and 9.0 with the same ionic strength $I = 0.6$ M; and $I = 0.13$ M, 0.26 M, and 0.6 M at pH 7.4 (14). An interesting feature of this PMMA/MAA bead system is that the associated dimensional changes appear to end when the penetrating ionization fronts meet at the core, suggesting that there is a negligible counterion concentration gradient behind the sharp ionization front. This phenomenon is similar to the swelling behavior of PMMA during methanol penetration (18).

Figure 2 shows a plot of Eq. (5) along with the plots on other mechanisms. Y_1 is the ratio of the relative rates of boundary layer mass transfer and intraparticle diffu-

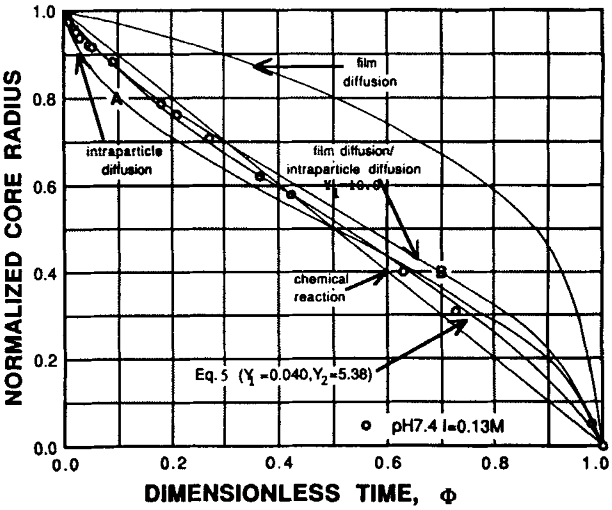

Figure 2. Position of the ionization front boundary based on different mechanisms with experimental data (pH 7.4, $I = 0.13$).

sion within the system. On the other hand, Y_2 is the ratio of the relative rates of chemical reaction and intraparticle diffusion. These plots can be utilized for pinpointing the controlling ionization mechanism. Curve A in Fig. 2 corresponds to the case where intraparticle diffusion alone controls the process, whereas curve B represents a system controlled by a combination of film and intraparticle diffusion processes. In this study, the nonlinear least square minimization (Marquate's compromise method) subroutine called UWHAUS was supplied by McMaster University to estimate k_s, k_f, and D. Figure 2 also shows the calculated curves based on the film diffusion/intraparticle diffusion mechanism and the reaction mechanism alone. The mechanisms mentioned above cannot describe the ionization mechanism of PMMA/MAA beads in the phosphate buffer. The film mass transfer/intraparticle diffusion can only describe the extreme of the experimental data, but it deviates appreciably when attempting to describe all of the data.

Other mechanisms should be considered to describe the experimental data. A combination of chemical reaction and film mass transfer was ruled out because the predicted curve never passes the lower section of the diagonal line. A three-resistance model, Eq. (3), was engaged to simulate the data. At first, Eq. (5) was applied to obtain the estimates of parameters, Y_1 and Y_2, and then Eq. (3) was used to obtain the parameters, k_s, k_f, and D. In general, the model describes the experimental data (pH 7.4, $I = 0.13$) with the estimated values of $Y_1 = 0.040$ and $Y_2 = 5.38$. The relative magnitude of film diffusion resistance to intraparticle diffusion resistance is minimal (4%), indicating that the film mass transfer resistance does not contribute much to the overall kinetics of ionization of PMMA/MAA beads. This result shows that the ionization of PMMA/MAA beads by phosphate buffer solution, in the range of experimental conditions studied, can be expressed by a combination of chemical reaction and intraparticle diffusion processes. An equation based on a combination of chemical reactions and intraparticle diffusion was applied to obtain the parameters k_s and D. As the values of Y_2 in Table 1 indicate, the ionization of PMMA/MAA beads is strongly dependent upon the intraparticle diffusion and chemical reaction processes.

Figure 3 presents the experimental and calculated results given in terms of the normalized shrinking-core radius versus time. Figure 3 shows the use of the pseudo-steady-state shrinking-core model to predict the experimental results. As shown in Table 1, the values of the diffusion coefficients obtained by the PSSCM are of the order of 10^{-6} cm^2/sec for pH 9, which is the same order of magnitude reported by Holl and Sontheimer (9), using an unsteady-state diffusion model for the protonation of weak acid ion-exchange resins of polymethacrylic acid beads cross-linked with divinylbenzene. As shown in Table 1, the simulation gives consistently increasing values of intraparticle diffusion coefficients and specific chemical reaction rate constants as the pH of the phosphate buffer solution increases. The faster reaction rate of ionization at high pH is directly attributable to the increasing availability of mobile hydoxide ions, which can result in a faster ionization of pendant carboxylic acid groups in PMMA/MAA chains with a higher specific reaction rate constant. The ionized pendant group expands more at a higher pH, resulting in a more porous, rubbery gel layer with a higher diffusion rate of ionic species. On the other hand, the specific rate constants and intraparticle diffusion coefficients do not vary much with variation of the ionic strength. This implies that the increase of phosphate buffer concentration increases the reaction rate proportionately

Table 1

Diffusion and Reaction Characteristics of Ionization of PMMA/MAA Beads

pH	I (mol/L)	D (cm^2/sec)	k_s (cm/sec)	Y_2
7.4	0.13	5.40	3.58	3.66
7.4	0.26	5.45	4.03	4.12
7.4	0.60	6.59	3.80	3.04
9.0	0.60	10.1	4.31	2.26
6.9	0.60	6.07	2.04	1.80

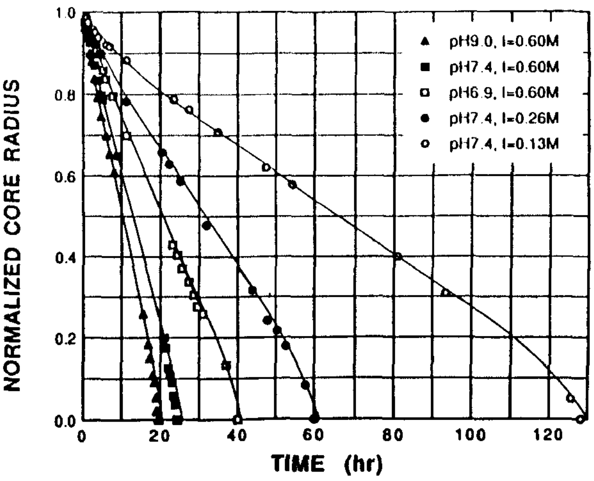

Figure 3. Normalized ionization core radius versus ionization time.

while maintaining the same diffusion rate. This is a result of the faster ionization occurring at an increased electrolyte uptake due to a more effective reduction of Donnan potential (14). However, this faster ionization should not increase or affect the diffusion of counterion species through the rubber gel layer. Theoretically, the diffusion coefficient of ionic species in the gel layer should not be changed even though the total reaction time changes drastically with a change of buffer concentration, because the diffusion coefficient is intrinsic to gel layer/ion species. This has been observed in the present study.

CONCLUSIONS

In order to describe the ionization of PMMA/MAA beads with phosphate buffers, a pseudo-steady-state shrinking-core model of the exchange kinetics has been applied. The reaction-coupled ionization is regarded as a diffusion process which is accompanied by a slow chemical reaction. The film mass transfer resistance plays a small role compared to the overall ionization process of PMMA/MAA beads. In general, chemical reaction resistance may contribute about 24–56% to the ionization process in comparison with the intraparticle diffusion resistance. As expected, the diffusion coefficients increase as the pH of phosphate buffer increases due to increased *accessibility of hydoxide ions*. The specific reaction rate constants are not influenced by the ionic strength of buffer solutions but by the pH of buffers. The model shows that the rate of ionization depends on the concentration of the buffer solution. Experimental results have been shown to be consistent with the proposed PSSCM.

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