Starch Urea Formaldehyde Matrix Encapsulation of Solid Agrochemicals. II. Release Mechanism and Release Modeling

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SYNOPSIS

Based on experimental observation, a mechanism is proposed to describe the release of carbofuran from a starch-UF matrix. A simple mathematical model is developed to describe the diffusion-controlled release of a solid insecticide from a porous starch-UF matrix undergoing both volume and surface erosions. The model is tested with the release data collected for different matrices and with different pH values of the environmental liquid. The comparison between the model predictions and data is found to be reasonably good. The model describes the release process at different pH values by accounting for the influence of pH on the erosion rates.

INTRODUCTION

The release of solid active agent such as carbofuran from a porous starch-UF matrix can be described by Higuchi kinetics for a highly crosslinked matrix such as that obtained at a urea to starch weight ratio of 0.6.[1] For matrices with a lower extent of crosslinking as well as those in contact with alkaline and acidic environmental liquids, the erosion of the matrix substantially influences the release process. Although in these cases a power law type release equation $M_t/M_\infty = kt^n$ can be used, the parameters k and n vary with all system variables thereby virtually eliminating any a priori prediction. In these cases it may be necessary to compensate for the effects of erosion which may alter the release rates, by making the matrix more porous and smaller in size. Both surface and volume erosions are likely to occur; a model describing the release process of such a system has not yet been reported in the literature. In this paper, a simple mathematical model is presented to describe the release of a solid active agent from starch-UF erodible matrix. This model is developed

by incorporating the effects of decrease in matrix size and increase in matrix porosity into Higuchi's model.[2,3] The model predictions are consistent with release measurements taken for matrices with different extents of crosslinking (U/S) and with different pH values for the environmental liquid.

The release of an active agent entrapped in a solid polymer matrix has been modeled by several investigators.[3-10] The models reported in literature can be broadly categorized as those that assume diffusion to be the controlling step and those that assume swelling to be the controlling step. One of the earlier models based on a diffusion controlling step is that of Higuchi, which is developed for a nonerodible matrix containing an active agent at a concentration much higher than its solubility. A pseudo–steady state approach and perfect sink condition have been used.[2,3] Using a refined integral method, Lee has solved the problem of diffusional release from an erodible matrix with constant finite external volume.[6] When the loading of active agent is much higher than the solubility, Lee's approximate analytical solution agrees with Higuchi's model prediction with pseudo–steady state assumptions. Lee's formulation however does not account for the variations in effective diffusivity due to bulk erosion. Effective diffusivity variations were incorporated in the model developed by Thombre and Himmelstein,

who considered the release of a bioactive agent from a matrix undergoing catalyzed erosions.[7] They solved the model equations numerically to obtain predictions on release and erosion processes.

Modeling of the controlled release process for swellable matrix systems, where swelling has considerable influence, has been addressed by a number of investigators.[5,8,9,10] These studies, however will not be discussed here. The swelling phenomenon in this matrix system is a relatively rapid process as compared to the release of active agent through leaching and subsequent diffusion. The swelling process is likely to influence the rate of release only during the early period of release, if at all. The effective diffusivity used in the model will correspond to that of a completely swelled state.

MODEL FORMULATION

The basic processes occurring when a matrix particle containing active agent is immersed in the environmental liquid are:

1. Imbibition of environmental liquid into the matrix pore space
2. Swelling of the hydrophilic portions of the matrix
3. Volume erosion of the matrix which leads to an increase in the porosity and surface erosion of the matrix with a resulting decrease in the size of the particles.
4. Diffusion of the active agent in the polymeric material.
5. Leaching of the active agent into the environmental liquid filling the pore space, and subsequent diffusion of active agent in the pore liquid
6. Diffusion of degraded polymeric species in the pore liquid.

The imbibition of environmental fluid and the resultant swelling of the starch-UF matrix and filling of the pore space are observed to be much faster processes than the release process. In addition, the rate of erosion of the starch-UF matrix is found to be slower than the diffusional processes. Consequently, one can assume that the diffusion occurs independent of the erosion, and that the effect of erosion is to increase the effective diffusivity and decrease the effective length of diffusion within the matrix over the time that release occurs. With these considerations, the release process can be assumed to be described by the process of leaching of the active agent into the pore liquid, followed by diffusion in the pore liquid. Furthermore it is assumed that the rate of diffusion is slower than the rate of leaching, and that, therefore, the diffusion of active agent through the swelled matrix controls the rate of release. It may be added that under leaching-controlled conditions the fractional release (FR) would be linear with time, which is not in agreement with experimental measurements.[11]

When the matrix is loaded with an active agent at concentrations much higher than the solubility, the matrix has two regions separated by a front at any time during the release.[2,3] The diffusion region lies in the outer portion in which there is a concentration gradient, and the undepleted region lies in the inner core where the concentration is uniform. The front separating these regions moves inward at a rate depending on the diffusion rate in the outer region.

Let us consider the erosion of the matrix. The total rate of dissolution of matrix material (r_t) is equal to the sum of surface and volume erosions and is given as

$$r_t = -(1 - \phi)\tfrac{4}{3}\pi R^3 r_b - (1 - \phi)4\pi R^2 r_s \quad (1)$$

where r_b is the rate of volume erosion $(kg/m^3 \cdot s)$, r_s is the rate of surface erosion, $(kg/m^2 \cdot s)$ and R and ϕ are the values of radius and porosity at any time (t) respectively.

From the material balance on the matrix material, following equation can be written

$$\frac{d}{dt}[(1 - \phi)\tfrac{4}{3}\pi R^3 \rho_p]$$
$$= -(1 - \phi)\tfrac{4}{3}\pi R^3 r_b - (1 - \phi)4\pi R^2 r_s \quad (2)$$

where ρ_p is the density of the matrix material.

As the matrix erodes at the surface, the radius decreases; it can be found from the equation given below which equates the rate of volume change by surface erosion to that due to the decrease in size

$$\frac{d}{dt}[\tfrac{4}{3}\pi R^3] = \frac{-(1 - \phi)4\pi R^2 r_s}{(1 - \phi)\rho_p} \quad (3)$$

Equation (4) can be integrated using initial condition $R = R_0$ at $t = 0$ to yield

$$R = R_0 - \left(\frac{r_s}{\rho_p}\right)t \quad (4)$$

We define following dimensionless variables:

$$\eta = \frac{R}{R_0}, \qquad \theta = \frac{t}{\tau}, \qquad \beta = \frac{r_b R_0}{r_s} \qquad (5)$$

where $\tau = \dfrac{\rho_p R_0}{r_s}$ and τ represents time required for the matrix to erode completely. With these dimensionless variables, eq. (5) and (3) can be written as

$$\eta = 1 - \theta \qquad (6)$$

$$\frac{d\phi}{d\theta} = (1 - \phi)\beta \qquad (7)$$

Equation (7) can be solved with eq. (2) to yield

$$\phi = 1 - (1 - \phi_0)\exp(-\beta\theta) \qquad (8)$$

Assuming a pseudo-steady state condition and that diffusivity is dependent on radial distance at given time t, the diffusion of species in the diffusion region (between R^* and R) and in the boundary layer region (between R and $R + \delta$) is governed by the following equations,

$$\frac{d}{dr}\left(r^2 \frac{dC_1}{dr}\right) = 0 \qquad (9)$$

$$\frac{d}{dr}\left(r^2 \frac{dC_2}{dr}\right) = 0 \qquad (9a)$$

where C_1 and C_2 are the concentration of active agent in the diffusion and boundary layer region respectively.

The four boundary conditions are

$$C_1 = C_s \quad \text{at} \quad r = R^* \qquad (9b)$$

$$C_2 = 0 \quad \text{at} \quad r = R + \delta \qquad (9c)$$

$$C_1 = C_2 \quad \text{at} \quad r = R \qquad (9d)$$

$$D_e \frac{dC_1}{dr} = D_L \frac{dC_2}{dr} \quad \text{at} \quad r = R \qquad (9e)$$

where D_e and D_L are the effective diffusivity in the completely swelled matrix and diffusivity in the boundary layer respectively, and δ is the thickness of the boundary layer.

Equations (9)–(9e) can be solved simultaneously to obtain

$$C_1 = \frac{C_s}{1 - \gamma}\left[\frac{R^*}{r} - \gamma\right] \qquad (10)$$

where

$$\gamma = R^*/R + \epsilon \qquad (10a)$$

$$\epsilon = \frac{R}{R + \delta} - \frac{R^* \alpha}{R} \qquad (10b)$$

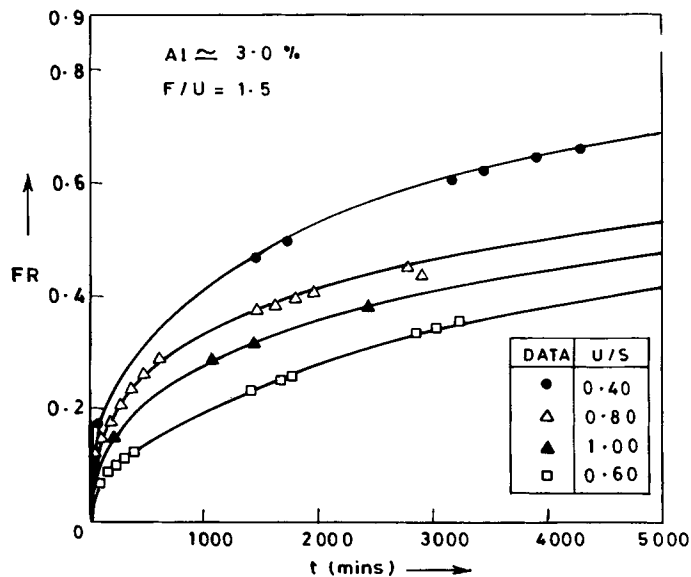$$\alpha = \frac{D_e}{D_L} \qquad (10c)$$

Figure 1   Fractional release of carbofuran from starch-UF matrix prepared at different U/S ratios.

The rate of inward movement of the diffusion front (the rate of decrease of R^*) is found by equating the rate of diffusion with the rate of release of species from the unextracted region due to the movement of diffusion front.

The rate of diffusion is given as

$$-4\pi R^2 D_e \frac{dC_1}{dr}\bigg|_{r=R} = \frac{4\pi D_e R^* C_s}{1-\gamma}$$

The rate of release of species due to inward movement of R^* is given as

$$\frac{d}{dt}\left(\tfrac{4}{3}\pi R^{*3} C_a(1-\phi)\right)$$

where C_a is the concentration of the active agent in the undepleted central core of the matrix. By equating, one obtains,

$$\frac{d}{dt}\left[(1-\phi)C_a\tfrac{4}{3}\pi R^{*3}\right] = \frac{-4\pi D_e R^* C_s}{1-\gamma} \quad (11)$$

Let M be the total amount of active agent remaining at time (t)

$$M = \tfrac{4}{3}\pi R^{*3}(1-\phi)C_a \quad (12a)$$

Note that the amount in the diffusion layer is neglected as compared to that in the undepleted core.

The initial amount (M_∞) is given as

$$M_\infty = \tfrac{4}{3}\pi R_0^3(1-\phi_0)C_a \quad (12b)$$

Let us define

$$\chi = \frac{M_\infty - M}{M_\infty} = \frac{M_t}{M_\infty} = \text{fractional release (FR)}$$

$$\chi = 1 - \frac{\eta^{*3}}{1-\phi_0}(1-\phi) \quad (13)$$

Equation (11) can be demensionalized and rearranged to obtain,

$$\frac{d\eta^*}{d\theta} = \frac{-D_e C_s \tau}{\eta^*(1-\gamma)} \frac{1}{(1-\phi)C_a R_0^2} + \frac{\eta^* \beta}{3} \quad (14)$$

and $\eta^* = 1$ at $\theta = 0$.

We can calculate χ as a function of time in the following manner. First, eqs. (14), (7), and (5) are solved to obtain an η^* versus time relationship and then eq. (13) is used to obtain χ from known values of η^*. Assuming that the release of a particle is independent of other particles present, the fractional release values calculated using the model can be compared with the data taken for a small amount of matrix material.
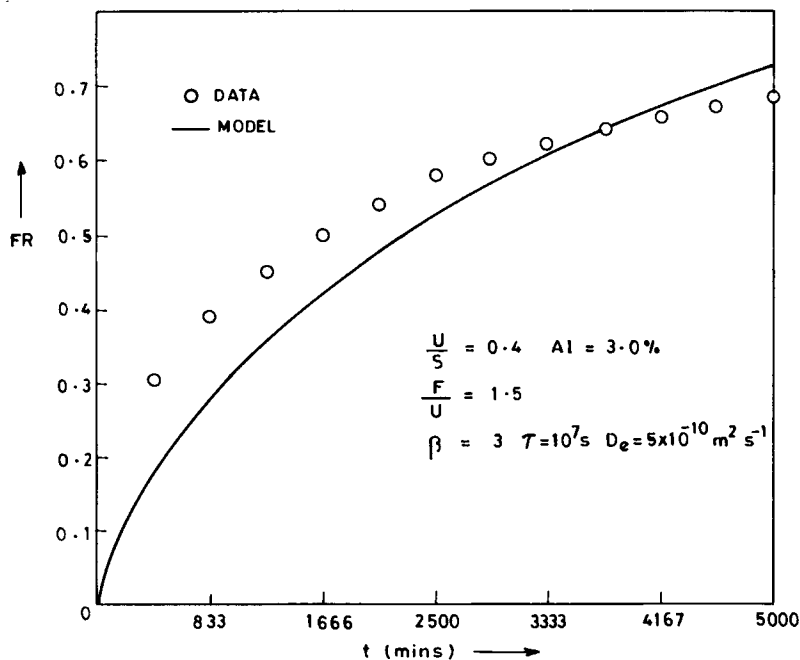

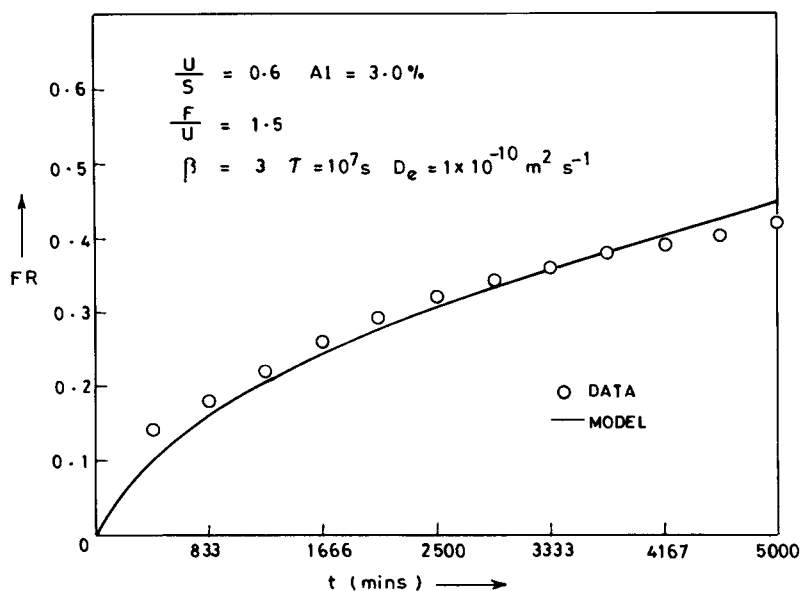**Figure 2** Comparison between data and model predictions.

Figure 3 Comparison between data and model predictions.

COMPARISON BETWEEN MODEL CALCULATIONS AND DATA

The model is first used to calculate the fractional release (FR) at different times (t) for starch-UF matrices containing carbofuran having different U/S weight ratios (0.4, 0.6, 0.8, and 1.0) and is then used to calculate the fractional release for a matrix (U/S weight ratio = 0.6) in the environmental liquid with pH values 5, 6, 7, and 8. The details of the release measurements are presented in the preceding paper.[1] The data are presented in Figure 1. The range in values of parameters adopted for model calculations are given below:

$$R_0 = 10^{-3} \text{ m} \qquad D_L = 10^{-9} \text{ m}^2 \cdot \text{s}^{-1}$$

$$\beta = 3\text{--}10 \qquad \tau = 10^7\text{--}10^9 \text{ s}$$

$$D_e = 10^{-9}\text{--}10^{-11} \text{ m}^2 \cdot \text{s}^{-1} \qquad \phi_0 = 0.5$$
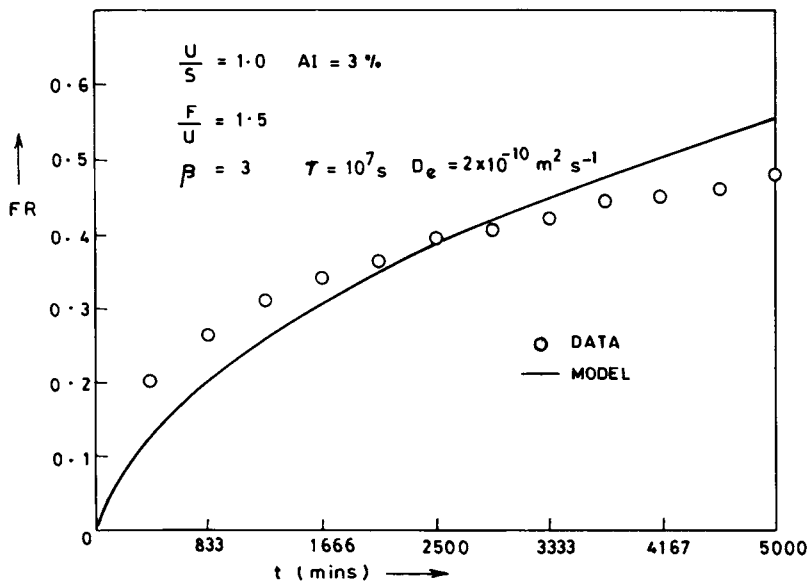

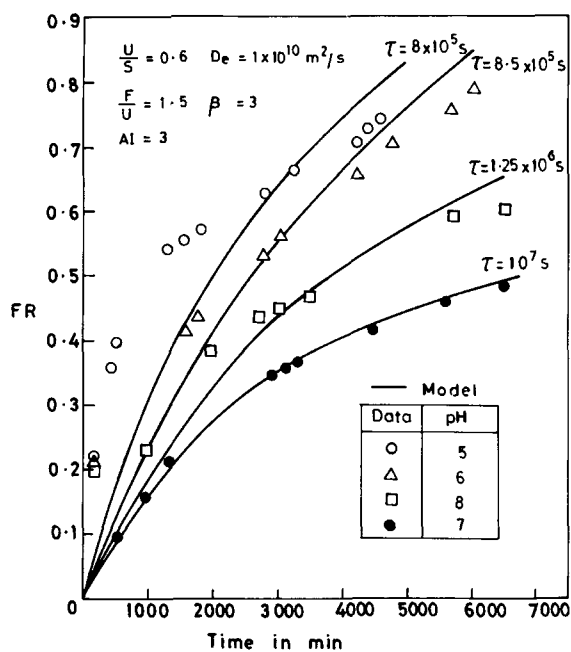**Figure 4** Comparison between data and model predictions.

Figure 5 Comparison between data and model predictions at different pH values.

The matrix granules used are of irregular shape and of size −10 + 14 mesh. These are approximated by a spherical matrix of 10^{-3} m of radius. The value of diffusivity of carbofuran in water is not available and hence a reasonable value of 10^{-9} $m^2 \cdot s^{-1}$ is taken for all calculations. The value of β can be obtained in the following manner.

$$\beta = \frac{r_b R_0}{r_s} = \left(\frac{kg \cdot m^{-3} \cdot s^{-1}}{kg \cdot m^{-2} \cdot s^{-1}} \right)$$

$$= \left(\frac{m^2}{m^3} \right) m = \left(\frac{surface\ area}{volume} \right) m$$

The implicit assumption is that the reaction mechanism for volume and surface erosion is the same. Considering a sphere of R_0

$$\beta = \left(\frac{4\pi R_0^2}{4/3\pi R_0^3} \right) R_0 = 3.0$$

Where the particles are not of spherical shape, the ratio of surface area to volume will be greater
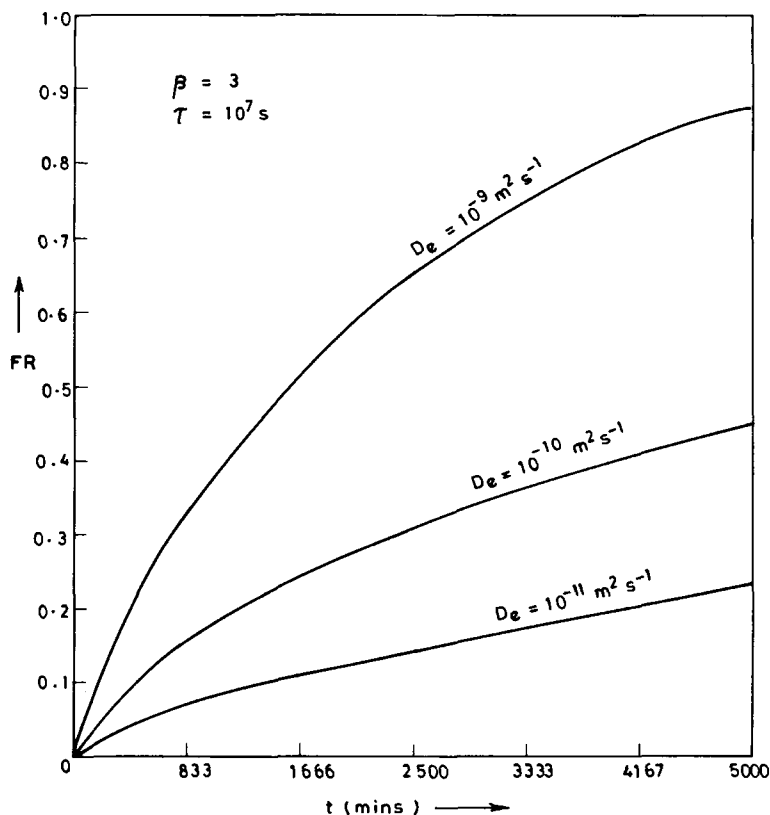

Figure 6 Fractional release vs. time at different values of effective diffusivity.

than 3 and therefore a range of 3–10 is used for β. The life of the capsule, τ, is taken as 10^7–10^9 s. It should be mentioned here that the value of τ will depend on the pH of the environmental liquid since pH significantly affects the erosion process. The effective diffusivity of carbofuran (D_e) in the liquid-filled pores is, in general, one to two orders of magnitude less than that in the bulk liquid. The range of values selected is 10^{-9}–10^{-11} m^2·s^{-1}. A reasonable value for boundary layer thickness δ is taken (10^{-4} m). It is found that the calculated fractional release values are not sensitive to the value of δ. As the U/ S weight ratio increases, the level of crosslinking, in general, increases and therefore one would expect a decrease in effective diffusivity (D_e) and an increase in τ. The comparisons between experimental data and the best fit from the model calculations are shown in Figures 2, 3, and 4.

One observes from Figures 2–4 that agreement between calculated fractional release, using the model presented, and the experimental data is good, indicating that the release process can be described by the model. The value of effective diffusivity obtained by fitting the data are 5.0×10^{-10}, 2.8×10^{-10}, 2.0×10^{-10}, and 1.0×10^{-10} m^2·s^{-1} for the matrices of U/S weight ratio 0.40, 0.80, 1.0, and 0.60 respectively. It should be noted that at a U/S ratio of 0.60, the release rate was found to be the slowest and therefore the value of diffusivity is the smallest. The value of the effective diffusivity (D_e) decreases, in general, with increase in the U/S ratio due to an increase in the extent of crosslinking and a decrease

in number of microvoids. Figure 5 shows the comparison between model calculations and data taken at different pH values for the environmental liquid. In these calculations only the life of the capsule, τ, was varied. The other model parameters such as D_e, β, and C_s are likely to remain unaltered due to change in pH. The parameter, β, being the ratio of two erosion rates will not change due to change in pH. Measurements showed that the solubility, C_s, does not change with pH. Carbofuran being a neutral molecule, its diffusivity is not likely to depend on the pH. Therefore, only τ was varied in the model calculations.

One observes from Figure 5 that by varying only τ the release data can be fitted reasonably well. At alkaline and acidic pH, the values of τ are lower since the rates of erosions are likely to be higher.

Figures 6–8 show the calculated values of fractional release at different values of the parameters. Figure 6 shows the variation in FR versus time plots at three different effective diffusivities $D_e = 10^{-9}$, 10^{-10}, and 10^{-11} m^2·s^{-1}). One observes that the release process is strongly influenced by diffusivity, and, as expected, a higher rate of release is obtained at higher diffusivity. Figure 7 shows the effect of parameter β on fractional release. One observes from this figure that as β increases, the release rate also increases, due to the increase in surface area to volume ratio. Effect of τ on fractional release are shown in Figure 8. For higher values of τ (very slow surface erosion), the influence of τ on the release is insignificant.
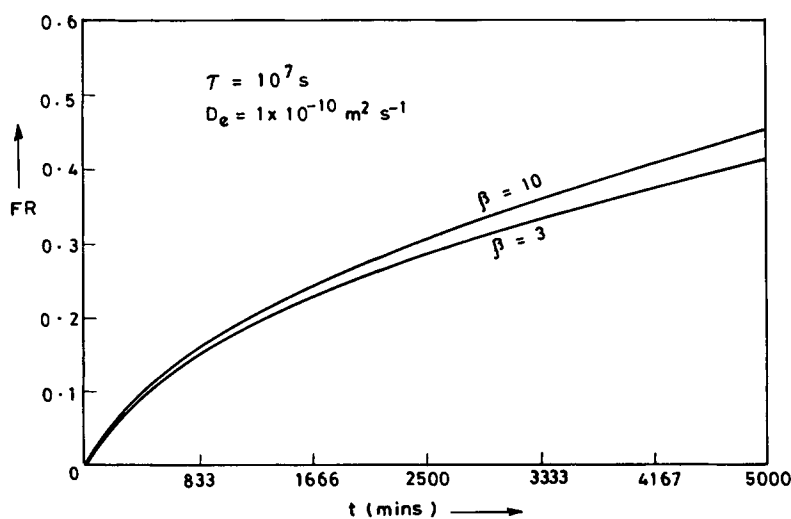

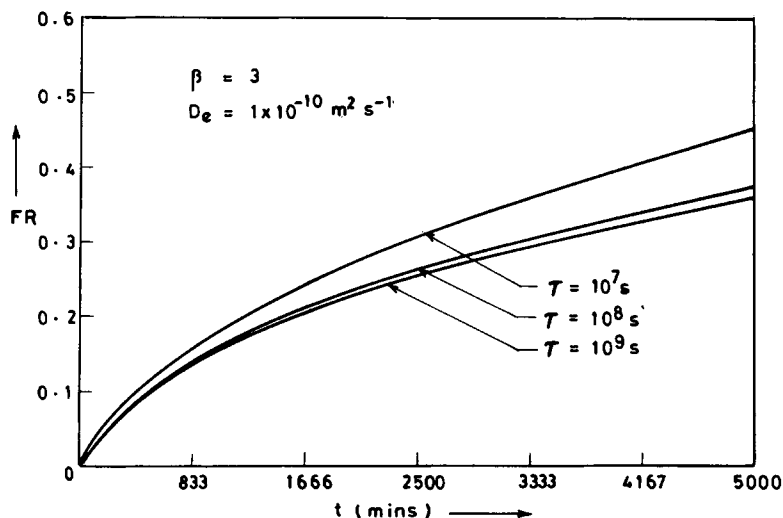**Figure 7**   Fractional release vs. time plots at different values of β.

Figure 8 Fractional release vs. time plots at different values of τ.

CONCLUSIONS

The mechanism of release of carbofuran from starch-UF matrices has been delineated. Based on a pseudo–steady state approach, a simple mathematical model was developed to describe the release of a solid agrochemical from erodible polymer matrix. The model accounts for both surface and volume erosions and was developed for a diffusion-controlled case. The data on release of carbofuran from starch-UF matrices at different levels of crosslinking and with different pH values for the environmental liquid are consistent with model calculations.

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