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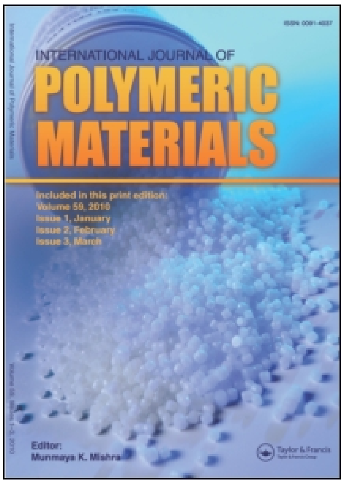

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The Modeling of the Simultaneous Transport of Solvent and Low-Molecular Compounds in Swelling Polymers

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The Modeling of the Simultaneous Transport of Solvent and Low-Molecular Compounds in Swelling Polymers

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Mathematical model has been developed in order to predict the behavior of systems consisting of hydrophylic polymer, water, and low-molecular compound. The model has taken into account the processes of swelling of polymers during water sorption, the existence of embedded form of drug in polymer matrix and some others processes. The dependencies of physico-chemical parameters on concentration of water, drug and on mechanical properties of polymer were justified by corresponding experimental results.

Different ratios of these parameters enable to predict the behavior of matrix systems for controlled release of drugs.

KEY WORDS Mathematical model, hydrophylic polymer, water low molecular compound, swelling, transport

The present modeling was inspired by study of the simultaneous transport of water and drug in swelling glassy polymers which is of great interest for two main reasons. Firstly, the theory of multicomponent transport in filled polymers had so far insufficient discussions.[1,2] And, secondly, the application of the study in question is very essential due to the attempts to develop the matrix polymer system of controlled drug release.

Obviously, the full information concerned with the mechanism of interactions in the system consisting of polymer, solvent and low-molecular compound is required in order to regulate the kinetics of drug transport. Our previous consideration of such system[1] dealt with the dioxidine release out of matrices of different hydrophilic characters was based on the phenomenological equation of the solvent transport

$$\partial C_w/\partial t = D_w \Delta C_w - v \nabla C_w$$

where C_w is the concentration of solvent in polymer, D_w is its diffusion coefficient, and v_w is, so-called velocity of local volume of solvent.

It was shown[1] that v_w was a function of concentration of drug, and this experimental result was justified by differences in the stresses in the polymer resulting from drug loading. At the same time one of the most significant question is still unclear. It is: why the variation of stresses causes namely the change of the velocity of sorption mentioned above? The present work is the theoretical attempt to answer this question by using the model of transport of solvent in swelling glassy polymers which was suggested and successfully confirmed by experiments.[3-5]

Our other aim was to check the possibility to apply this approach for the modeling of simultaneous transport of solvent and low-molecular compound in glassy hydrophilic polymers as a whole.

EXPERIMENTAL JUSTIFICATION OF THE MODEL

Before the discussion of proposed model itself we should briefly remember our previous experimental results which have been obtained under study of triple system of polymer, solvent, and drug.

Figure 1 shows the kinetic curves of water sorption by copolymers of *N*-vinylpyrrolidone (*N*-VP) with butyl- (PPB, Figure 1a) and methylmetacrylate (PPM-1, Figure 1b; PPM-2, Figure 1c). These copolymers are characterized by the different content of hydrophilic (*N*-VP) groups of 0.7 (PPB), 0.4 (PPM-1), 0.2 (PPM-2) following by different equilibrium concentration of water in the swollen polymer (0.46, 0.23, 0.07 g/g, respectively). The main feature of the kinetics of water sorption by copolymers of *N*-VP is the existence of linear part of the kinetic curve, which is well-known to be the Case II of diffusion.[4,6] Noting the increase of the velocity of water sorption to be a function of content of hydrophilic groups in copolymer we are turning our attention in Figure 2 which shows that the load of drug also promotes the increase of the velocity of water uptake. The similar tendencies were observed under study of the process of water transport in polyvinylalkohol (PVA). It was obtained that parameters of the sorption of solvent have been functions of content of sodium acetate in polymer.[7]

On the other hand, the hydrophilic character of the polymer matrix follows by the mechanism of drug release.[1] For instance (Figure 3), kinetic curves of release of dioxidine out of more hydrophilic PPB have a steady-state portion, and the release velocity (for the case of PPB) is equal to the velocity of water sorption. The diffusive mechanism of drug release was observed for moderately hydrophilic copolymer of PPM-2. Finally, the kinetic curve of release for the case of PPM-1 was more complicated and it did not have steady-state or Fickian parts. Investigations have shown that the diffusion coefficient of dioxidine in moderately hy-

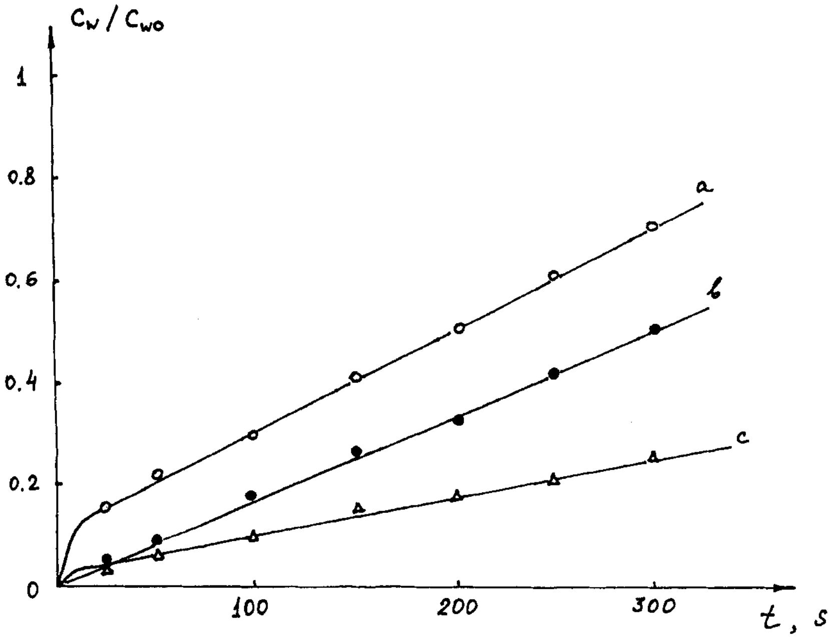

FIGURE 1 Kinetics of water sorption by copolymers of *N*-vinylpyrrolidone-PPB (a), PPM-1 (b) and PPM-2 (c), 1 = 100 μ.

drophilic films of PPM-2 was an increasing function of the initial content of drug in matrix. This copolymer was also characterized by the existence of embedded form of drug which did not release during interaction of matrix with water. We explained this fact[1] by particular inaccessibility of polymer for molecules of solvent which is the general feature of interaction between water and moderately hydrophilic polymers.[8,9] Another explanation could be as follows. Initial content of drug in PPM-2 usually was much more than its solubility in polymer as well as its solubility in water being in polymer. As drug released its unsoluble part dissolved and became mobile. At present we have sufficient data (Figure 3, curve c) in order to propose that this explanation is more appropriate than made in Reference 1.

Experimental results indicated above were interpreted by mathematical modeling.

The Model of Simultaneous Transport of Solvent and Low-Molecular Compound in Swollen Copolymers

The main parameters being used are as follows: C_w is solvent (water) concentration in polymer; C_s is the concentration of low-molecular compound (salt) in polymer; C_{ss} is the concentration of its soluble form in polymer; a_s is the activity of salt in polymer; C_s^0 is the concentration of saturated solution of salt in water ($a_w = 1$); S is the salt solubility in polymer; D_w is the Fickian diffusion coefficient of water in polymer; D_{Ts} is the thermodynamic diffusion coefficient of salt in polymer; l is the thickness of polymer film; f is the mechanical stress; s is the swelling strain;

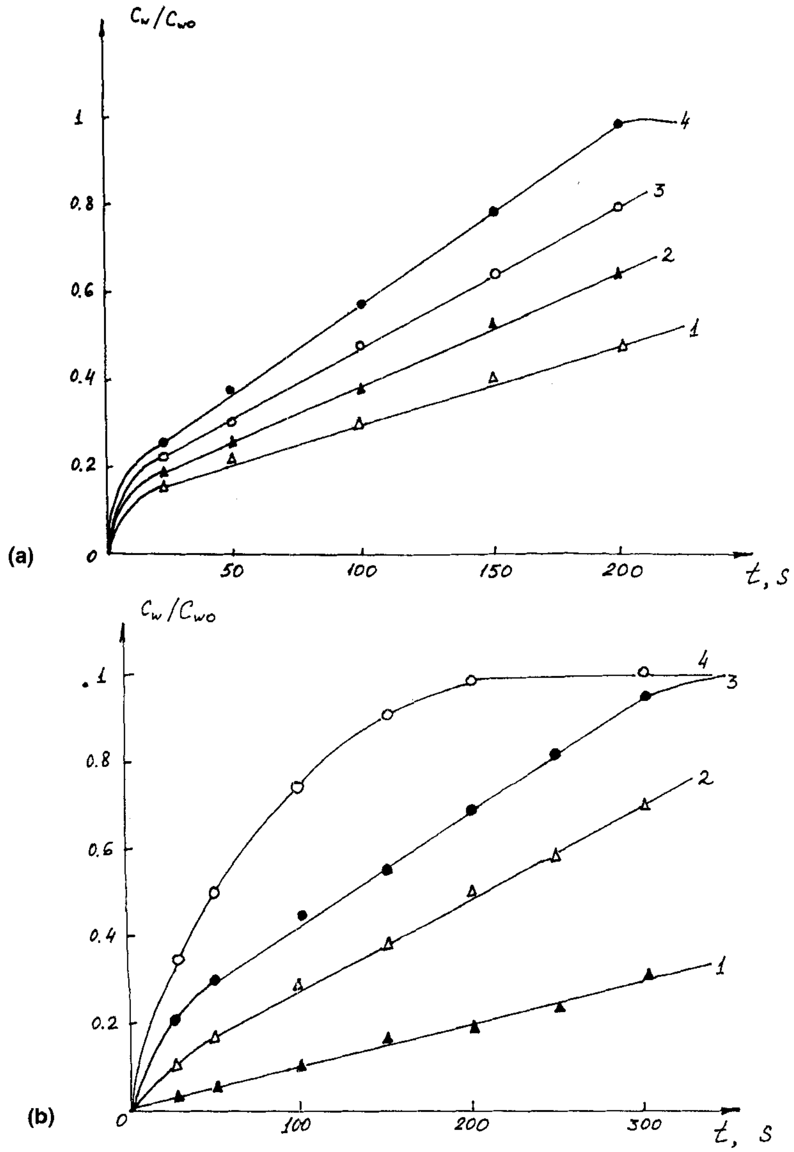

FIGURE 2 Kinetics of water sorption by hydrophilic polymers containing different amount of low-molecular compound. PPB-dioxidine (a) –0 (1), 0.05 (2), 0.1 (3), 0.2 (4) g/g; PVA – NaAc (b) –0 (1), $7.5 \cdot 10^{-3}$ (2), 0.02 (3), 0.04 (4) g/g. 1 = 100 μ.

G_0, G_∞ are the initial and final elastic moduli and β is the frequency of stress relaxation.

Other parameters will be involved to the text.

The so-called Maxwell model of stress relaxation taking into account interrelations between the viscosity (η), elastic modulus, and the frequency of relaxation have been used to be the basis of present modeling. Apparently J. Petropoulos[4]

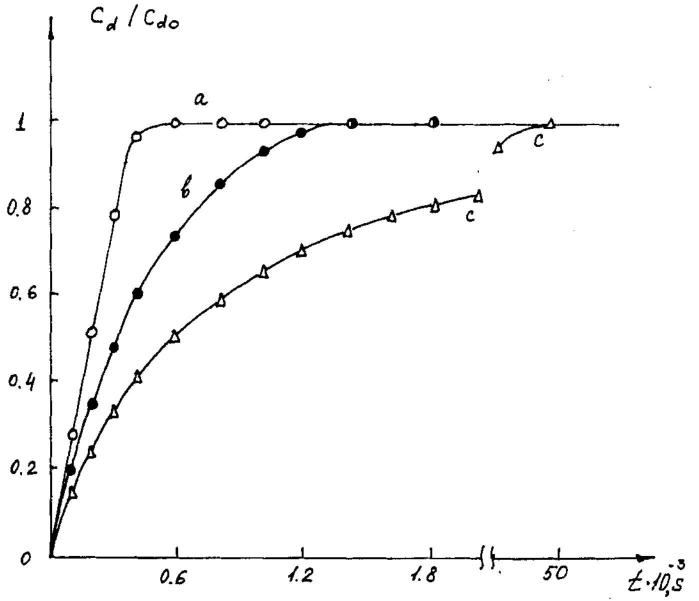

FIGURE 3 Kinetics of drug release out of copolymers of NVP. PPB (a), PPM-1 (b), PPM-2 (c). C_d is the mean concentration of drug desorbed to aqueous solution, C_{d0} is the initial concentration of drug in polymer.

was one of the first who applied Maxwell model namely for swelling processes in glassy polymers when he suggested to describe the transport of solvent by Equation

$$\partial C_w/\partial t = \partial/\partial x(D_w)\partial C_w/\partial x \qquad 0 < x < l \tag{1}$$

where

$$D_w = D^*_{w0} \exp(k_{w1}C_w + k_{w2}f) \tag{2}$$

$$\begin{aligned} \partial f/\partial t &= (G_0 - G_\infty)\partial s/\partial t + \partial(sG_\infty)/\partial t \\ &\quad + ((G_0 - G_\infty)^{-1}\partial(G_0 - G_\infty)/\partial t - \beta)(f - sG_\infty) \end{aligned} \tag{3}$$

$$s = (1 + k_s C_w)^{-1} - 1$$

Expressions (2) and (3) are written in form which is more convenient for calculation procedure we used. For this reason the record of Expressions (2 and 3) is slightly differed from original record.[4]

The most significant point of present study is the selection of dependencies of parameters involved to the Equation (1) and Expressions (2 and 3) on concentrations of solvent and low-molecular compound. Therefore, we should discuss in details the justification of dependencies selected.

First of all, proposed dependencies of diffusion coefficients of solvent and low-molecular component are in agreement with the theory of free volume. For this reason the concentration of salt does not appear in Expression (2) in evident form. Nevertheless it is obvious that diffusion coefficient of water depends on C_s due to the existence of dependence $f(C_s)$. We also accept the justification of authors of paper[4] for the same Expressions for initial and final elastic moduli.

$$G_0 = G_\infty g(C_w, C_s)$$

$$G_\infty = G_{\infty 0} g(C_w, C_s)$$

The proposal about the decrease of elastic modulus as concentration of solvent in polymer increases have been confirmed by experimental comparison of mechanical properties of the films containing water in equilibrium with vapours and those which were dried at lower pressure. The considerable difference between elastic moduli of highly hydrophilic PPB and moderately hydrophilic PPM-2 should be mentioned. Corresponding properties of PPM-1 were intermediate as well as those we indicated in our previous study.[1] On the other hand the load of drug to polymer matrix leaded to the increase of elastic modulus. This enable to draw conclusion that the influence of solvent and lower molecular compound are opposite for this set of polymers. In fact, empirical polynomial dependencies of mechanical parameters of polymer on concentrations of solvent, additives, fillers, etc.[10,11] except their further theoretical justification. For this reason from our point of view the exponential expressions for dependencies in question could be more logical.

$$G_0 = G_{00} \exp(-k_{g1} C_w + k_{g2} C_s)$$

$$G_\infty = G_{\infty 0} \exp(-k_{g1} C_w + k_{g2} C_s)$$

Here and further we propose that all kinetic constants are positive.

Rather unexpected results have been obtained during study of the dependence of frequency of stress relaxation on C_w and C_s. It has been shown that increase of content either of water and drug followed by acceleration of the transition of overmolecular structure for all polymers under study. This means that both components cause change of relaxation properties of polymer on the same direction. Usually, the increase of the frequency of relaxation follows such phenomena as plastification, for which the fall of viscosity (η) is more essential than the decrease of elastic modulus. This is in accordance with Equation

$$\beta = G/\eta$$

For our system this was observed only for the process of water sorption. On the other hand, direct dependence of G, η (and β, respectively) on concentration of additives does not exist. For example, copolymers PPB, PPM-1, PPM-2 have the same viscosity and moduli which are differed by orders. However, further study in details of unusual dependencies $\beta(C_s)$, $G(C_s)$ is required for their explanation.

As far as present investigation is concerned we should write in accordance with results obtained

$$\beta = \beta_0 \exp(k_{d1} C_w + k_{d2} C_s)$$

The Equation proposed in Reference 2 and took into account that the solubility of salt in water and in polymer could be lower its content in a matrix have been used for description of transport of low-molecular compound in the system in question.

$$\begin{aligned} \partial C_s/\partial t &= \partial/\partial x(D_{Ts}\cdot S)\partial a_s/\partial x && \text{for } C_s \leq S \\ & && 0 < x < l \qquad (4) \\ C_s &= C_{s0} && \text{for } C_s > S \end{aligned}$$

where

$$D_{Ts} = D_{Ts0} \exp(-k_{w3}/C_w)$$

is in agreement with the free volume theory.

Boundary and initial conditions were selected for present study as follows.

$$C_w(0, t) = C_w(l, t) = C_{w0}$$

$$C_s(0, t) = C_s(l, t) = 0$$

$$C_w(x, 0) = 0$$

$$C_s(x, 0) = C_{s0}$$

where C_{w0} is the equilibrium concentration of water in polymer, and C_{s0} is the initial content of low-molecular compound in polymer.

We should mentioned again that present theoretical study was based on experimental results discussed above. At the same time, we suppose that our approach could be applied for other systems by use of different Expressions for dependencies of diffusion coefficients as well as by wide variation of boundary and initial conditions.

Calculation Procedure

The dimensionless parameters were selected as follows:

$$\begin{array}{rclrclrcl}
\bar{x} & = & x/l & \bar{D}_w & = & D_w/D_{w0} & \bar{k}_{w1} & = & k_{w1}C_{w0} \\
\bar{t} & = & D_{w0}t/l^2 & \bar{D}_{Ts} & = & D_{Ts}/D_{w0} & \bar{k}_{w2} & = & k_{w2}G_{\infty 0} \\
\bar{C}_w & = & C_w/C_{w0} & \bar{f} & = & f/G_{\infty 0} & \bar{k}_s & = & k_sC_{w0} \\
\bar{C}_s & = & C_s/C_{s0} & \bar{G}_0 & = & G_0/G_{\infty 0} & \bar{k}_{d1} & = & k_{d1}C_{w0} \\
\bar{C}_{ss} & = & C_{ss}/C_{s0} & \bar{G}_\infty & = & G_\infty/G_{\infty 0} & \bar{k}_{d2} & = & k_{d2}C_{s0} \\
\bar{C}_s^0 & = & C_s^0/C_{s0} & \beta & = & \beta l^2/D_{w0} & \bar{k}_{g1} & = & k_{g1}C_{w0} \\
\bar{S} & = & S/C_{s0} & \beta_0 & = & \beta_0 l^2/D_{w0} & \bar{k}_{g2} & = & k_{g2}C_{s0} \\
 & & & & & & \bar{k}_{w3} & = & k_{w3}C_{w0}
\end{array}$$

Using parameters $\bar{G}_1 = \bar{G}_0 - \bar{G}_\infty$ and $\bar{f}_1 = \bar{f} - s\bar{G}_\infty$, as well as the Expressions for S and $C_{ss}{}^2$:

$$S = k\bar{V}C_wC_s^0$$

$$C_{ss} = k\bar{V}C_wa_sC_s^0$$

we obtain the system of Equations

$$\partial\bar{C}_w/\partial\bar{t} = \partial/\partial\bar{x}(\bar{D}_w)\partial\bar{C}_w/\partial\bar{x} \qquad 0 < \bar{x} < 1 \tag{1'}$$

$$\bar{C}_s = \begin{cases} 1 & \text{for } \bar{C}_s > \bar{S} \\ \bar{C}_{ss} : \partial\bar{C}_{ss}/\partial\bar{t} = \partial/\partial\bar{x}(\bar{D}_{Ts})\partial/\partial\bar{x}(\bar{C}_{ss}/\bar{C}_w) & \text{for } \bar{C}_s \le \bar{S} \end{cases} \tag{4'}$$

with boundary and initial conditions

$$\bar{C}_w(0, \bar{t}) = \bar{C}_w(1, \bar{t}) = 1$$

$$\bar{C}_s(0, \bar{t}) = \bar{C}_s(1, \bar{t}) = 0$$

$$\bar{C}_w(\bar{x}, 0) = 0$$

$$\bar{C}_s(\bar{x}, 0) = 1$$

where $\bar{D}_w = \exp(\bar{k}_{w1}\bar{C}_w + \bar{k}_{w2}(\bar{f}_1 + s\bar{G}_\infty))$; $\bar{D}_{Ts} = D_{Ts0}\cdot\exp(-(1 + \bar{k}_{ws}\bar{C}_w)^{-1})/D_{w0}$; $\partial\bar{f}_1/\partial\bar{t} = \bar{G}_1(\bar{k}_s/(1 + \bar{k}_s\bar{C}_w)^2)\partial\bar{C}_w/\partial\bar{t} + ((k_{g2}\partial\bar{C}_s/\partial\bar{t} - \bar{k}_{g1}\partial\bar{C}_w/\partial\bar{t})/\bar{G}_1 - \bar{\beta}))\bar{f}_1$; $\beta = \beta_0 \exp(k_{d1}C_w + k_{d2}C_s)$; $\bar{f}_1(0) = 0$; $s(0) = 0$.

Let us suppose that h is the step for $\bar{x} : j = 0, 1, \ldots, j1$; $j1 \cdot h = 1$. For present calculations we usually took h to be equal to 0.01, but it is not necessary generally.

Let, further, all functions $C_{wj}(\tau)$, $C_{sj}(\tau)$, $f_{1j}(\tau)$ are defined, continuous, and have continuous derivative at all intervals $(idt, (i + 1)dt)$, where dt is the step t, and $i = 0, 1, \ldots, \infty$.

Then we obtain the system of ordinary linear differential Equations of the first order which is consequences of system (1′) and (4′).

$$dC_{wj}/d\tau = q_w - p_w C_{wj}$$

$$dC_{sj}/d\tau = \begin{cases} 0 & \text{for } C_{sj+1} \geq S \\ q_s - p_s C & \text{for } C_{sj+1} < \bar{S} \end{cases}$$

$$df_{1j}/d\tau = q_f - p_f f_{1j}$$

with initial conditions

$$C_{wj}(idt) = C_{wij}$$

$$C_{sj}(idt) = C_{sij}$$

$$f_{1j}(idt) = f_{1ij}$$

where

$$q_w = (D_{i+1,j+1} C_{i+1,j+1} + D_{i,j-1} C_{wi,j-1} + D_{ij}(C_{wi+1,j+1} + C_{wi,j-1}))/2h^2$$

$$p_w = (D_{i+1,j+1} - 2D_{ij} + D_{ij-1})$$

$$q_s = (D_{ij}^{Ts}(C_{si+1,j+1} + C_{si,j-1}) + (D_{i+1,j+1}^{Ts} C_{si+1,j+1}/C_{wi+1,j+1}$$
$$+ D_{i,j-1}^{Ts} C_{si,j-1}/C_{wi,j-1})C_{wij})/2h^2$$

$$p_s = (D_{i+1,j+1}^{Ts} + D_{i,j-1}^{Ts} + D_{ij}^{Ts}(C_{wi+1,j+1} + C_{wi,j-1})/C_{wij})$$

$$q_f = (-\bar{k}_s(G_\infty/G_{\infty 0} - 1)\exp(-\bar{k}_{g1} C_{wij} + \bar{k}_{g2} C_{sij})/(1 + \bar{k}_s C_{wij})^2)(dC_{wj}/d\tau)_{\tau = idt}$$

$$p_f = \bar{\beta}_0 \exp(\bar{k}_{d1} C_{wij} + \bar{k}_{d2} C_{sij}) - (C_{\infty 0} \exp(\bar{k}_{g1} C_{wij} - \bar{k}_{g2} C_{sij})/(G_\infty - G_{\infty 0}))$$
$$\cdot (\bar{k}_{g2}(dC_{sj}/dt)_{\tau = idt} - \bar{k}_{g1}(dC_{wj}/d\tau)_{\tau = idt})$$

$$(dC_{wj}/d\tau)_{\tau = idt} = q_w - p_w C_{wj}$$

$$(dC_{sj}/d\tau)_{\tau = idt} = \begin{cases} 0 & \text{for } C_{sj+1} \geq \bar{S} \\ q_s - p_s \bar{C}_{sij} & \text{for } C_{sj+1} < \bar{S} \end{cases}$$

The whole computations was initiated by using boundary and initial conditions

$$C_{wi0} = C_{wij1} = 1$$

$$C_{si0} = C_{sij1} = 0$$

$$C_{w0j} = 0 \quad C_{sij} = 1 \quad f_{10j} = 0 \quad s_{0j} = 0$$

The iterations were started by the estimation of

$$D_{wij} = \exp(\bar{k}_{w2})$$

$$\bar{D}^{Ts}_{ij} = D_{Ts0}\exp(-1)/D_{w0}$$

and were continued by calculation of

$$C_{w1j} = C_{w0j}\cdot\exp(-p_w\,dt) + (q_w/p_w)(1 - \exp(-p_w\,dt))$$

$$C_{s1j} = \begin{cases} C_{s1,j+1} & \text{for } C_{s1,j+1} \geq \bar{S} \\ C_{s0j}\cdot\exp(-p_s\,dt) + (q_s/p_s)(1 - \exp(-p_s\,dt)) & \text{for } C_{s1,j+1} < \bar{S} \end{cases}$$

$$f_{11j} = f_{10j}\cdot\exp(-p_f\,dt) + (q_f/p_f)(1 - \exp(-p_f\,dt))$$

Then iterations were repeated until equilibrium water and drug distribution would be obtained.

RESULTS AND DISCUSSION

In order to check the reliability of calculation procedure we made test calculations of water uptake for different values of D_w, β, G_0 and of other parameters for which similar calculations were made in Reference 4. The results obtained were the same, and for present study we took the main intention to the dependencies of kinetics of water sorption and release of low-molecular compound on constants $\bar{k}_{w1}$, $\bar{k}_{w2}$, $\bar{k}_{d1}$, $\bar{k}_{g1}$ and $\bar{k}_{g2}$, which are characterized by the properties of polymer, water solubility, and salt content. Values of other parameters were selected in agreement with experimental results and data described in literature. They were: $k_s = 0.1$ (this means that the strain under swelling was equal to 10% or less); $\bar{D}_{Ts0} = 100$ (diffusion coefficient of low molecular component is of two orders higher than diffusion coefficient of water in polymer); $\bar{k}_{w3} = 4.6$; ($\bar{D}_{Ts}(\bar{C}_w = 1)/\bar{D}_{Ts0} = 10^{-2}$—diffusion coefficients of water and low molecular components were values of the same order) and, finally, $\bar{G}_{10}$ and $\bar{\beta}_0$ were selected to be equal to 1.

It was shown (Figure 4) that the increase of k_{w1} (as well as decrease of k_{w2}) leaded to the acceleration of water uptake accompany with slightly increase of the velocity of drug release. Usually we did not observe the change of the mechanism

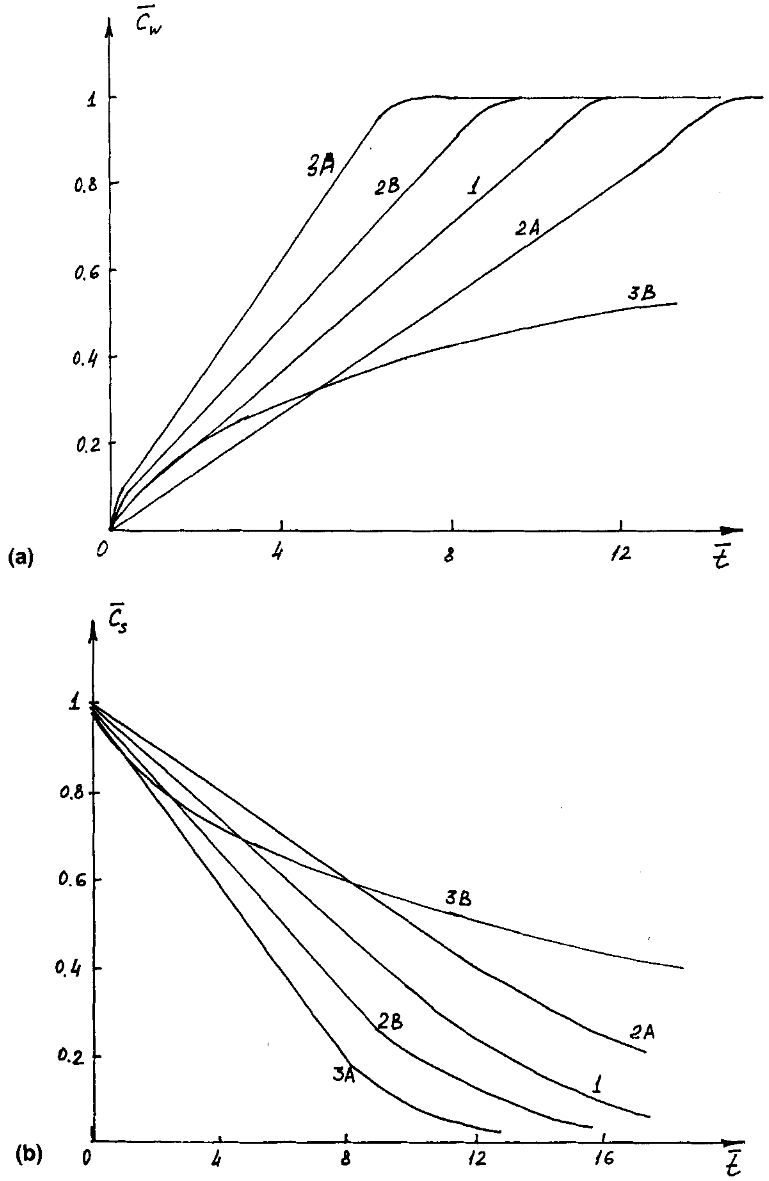

FIGURE 4 Calculated kinetics curves of water sorption (a) and release of low-molecular compound (b) at different values of constants which characterize transport properties of solvent. $\bar{k}_{w2} = 1$ ($\bar{k}_{w1} = 1$ (1), 0.1 (2A), 10 (3A)); $\bar{k}_{w1} = 1$ ($\bar{k}_{w2} = 0.1$ (2B), 10 (3B)), $D_{Ts0} = 100$, $\bar{k}_{g1} = \bar{k}_{g2} = \bar{k}_{d1} = \bar{k}_{d2} = 1$.

of transport processes except the case of high values of $\bar{k}_{w2}$ ($\bar{k}_{w2} \geqslant 10$), when Fickian diffusion of water simultaneously with its deceleration has been obtained. Apparently this result could be explained by the increase of modulus $G_{\infty 0}$ following corresponding changes of mechanical properties of polymer.

We were mostly interested in comparison of the results of computation with

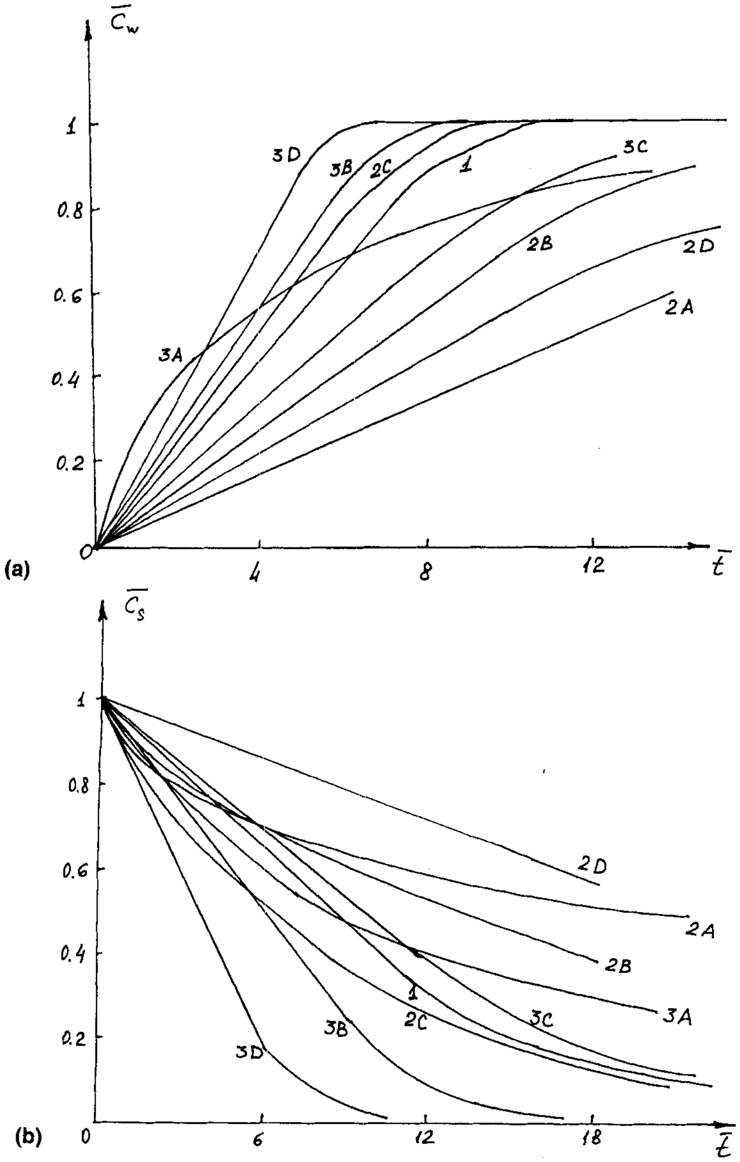

FIGURE 5 Calculated kinetics curves of water sorption (a) release of low-molecular compound (b) at different values of constants which characterize the influence of hydrophilic character of polymer and solubility of low-molecular compound on mechanical properties of matrix. $\bar{k}_{g1} = 1$, $\bar{k}_{g2} = 1$, $\bar{k}_{d1} = 1$, ($\bar{k}_{d2} = 1$ (1), 0.1 (2A), 10 (3A)); $\bar{k}_{g1} = 1$, $\bar{k}_{g2} = 1$, $\bar{k}_{d2} = 1$, ($\bar{k}_{d1} = 0.1$ (2B), 10 (3B)); $\bar{k}_{g1} = 1$, $\bar{k}_{d1} = 1$, $\bar{k}_{d2} = 1$, ($\bar{k}_{g2} = 0.1$ (2C), 10 (3C)); $\bar{k}_{g2} = 1$, $\bar{k}_{d1} = 1$, $\bar{k}_{d2} = 1$, ($\bar{k}_{g2} = 0.1$ (2D), 10 (3D)), $D_{Ts0} = 100\ \bar{k}_{w1} = \bar{k}_{w2} = 1$.

experimental data concerned with the kinetic of water sorption and drug release which were discussed above. Theoretically the dependence of these processes on water solubility and initial concentration of drug was studied by the variation of constants $\bar{k}_{d1}$, $\bar{k}_{d2}$, $\bar{k}_{g1}$ and $\bar{k}_{g2}$.

Different ratios of these parameters enable to describe all kinds of experimental curves obtained as it could be seen in Figure 5. The effects we mostly mean are as follows: a) acceleration of water sorption in the area of Case II diffusion as water solubility in polymer is increasing; b) similar behaviour of water sorption following the increase of the content of drug in polymer; c) transition from Case II to Fickian diffusion of water at high values of $\bar{k}_{d2}$, which corresponds to higher concentrations of drug and characterizes its influence on the time of relaxation.

It was mentioned above that the last effect was observed earlier[7] under experimental study of water sorption by PVA containing different amount of sodium acetate (Figure 2b), and at that time it was not explained.

The modeling of desorption of the low-molecular compounds by Equation (4) accompany with the equation of transport of Solvent (1) has shown that three cases which were observed experimentally for the kinetics of drug release could be explained as follows: i) Fickian diffusion corresponds to the moderately swelling polymers ($C_{s0} > S$) and lower velocities of water sorption; ii) highly swelling polymers ($C_{s0} > S$) are characterized by either Case II release and higher velocity of water sorption; iii) the case which is intermediate between Fickian and Case II diffusion follows moderate velocity of water sorption described by Case II and values of C_{s0} closed to S.

We should also emphasize that the processes of drug release out of highly hydrophilic polymers can be described by Fick's law, but this case must correspond only to Fickian diffusion of water in such polymers. That is why we can draw the general conclusion that water sorption by highly hydrophilic polymers is the limiting stage of release of low-molecular compounds involved in this polymers, particularly it is limiting stage of drug release.

Of course the results we discussed in present paper do not cover all consequences from the model suggested. The reason is the system in question is rather complicated. Therefore we look forward to developing of proposed theoretical approach and its applying to other systems to be the aim of our further research.

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