Mathematical Modeling of Insulin Sorption by Ion-Exchange Fiber

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ABSTRACT: The objective of this study was to investigate the phenomenon and kinetics of insulin chemisorption by cation-exchange acrylic fibers, as well as the development of theoretical modeling of the chemisorption process. Change of the insulin concentration in solution was determined by UV spectrophotometric method. The profile of insulin concentration in the fiber was determined by application of mathematical model. The developed mathematical model describes the chemisorption process using fractional kinetics equations of diffusion. Taking all the relevant conditions, regarding this experiment, into consideration, the coefficient of insulin diffusion into the fiber, overdamped effect parameter, as well as the concentration ratio parameter were determined by the mathematical model. Proposed modeling approach is useful for the description of transport dynamics in complex systems as polymer transport through the porous matrices, which are governed by anomalous diffusion. © 2007 Wiley Periodicals, Inc. J Appl Polym Sci 104: 253–260, 2007

Key words: modeling; chemisorption; insulin; cation-exchange fibers; diffusion coefficient

INTRODUCTION

Artificial fibrous drug depots with a programmed and controlled drug release, present novel fibrous materials, are applied in medical and other fields. Polymer-based drug delivery systems have been considered for many applications to supplement standard means of medical therapeutics.[1–3]

An appropriate selection of the polymer matrix is necessary to develop a successful drug delivery system. The polymer could be nondegradable or degradable. A major disadvantage of nondegradable polymers is that a surgery is required to remove these polymers from the body once they are depleted of the drug. Hence, nondegradable polymers can be used only if removal of the implant is easy.[2]

Morphology of the polymer matrix plays an important role in governing the release characteristics of the encapsulated drug. The polymer matrix could be formulated as either microspheres or nanospheres, in gel, film, or an extruded shape (such as cylinder, rod, etc). The shape of the extruded polymer can be important for the drug release kinetics. Recently, it has also been proposed to use ion-exchange fibers in medical and pharmaceutical applications, e.g., as a drug reservoir in an ionophoretic patch for transdermal drug delivery.[1–3]

Fibrous ion-exchange materials are suggested to have a larger surface area to unit volume ratio, which leads to a higher absorption rate and absorption capacity as compared with the resin. Information about the research on ion-exchange fibers has been published mostly in China, Japan, and in Eastern European countries.[4–7]

Our research, in recent years, is directed toward obtaining biologically activate fibers in the form of complex ion-exchange fibers—insulin as an artificial store of insulin. The fibrous ion exchangers are relatively new materials. The fibrous insulin delivery system was prepared by chemisorption of insulin with ion-exchanged polyacrylonitrle (PAN) fibers. Cation-exchange polyacrylonitrile fibers were chosen for this purpose, above all, because of their good chemical stability and their high degree of porosity.[8] Our previous results showed that it is possible to obtain the insulin fibrous depot with a significant amount of insulin, even reaching the amount of 800 mg per gram of fiber.[8–12] These insulin artificial stores provide controlled release of insulin in blood, with constant rate for long period. In addition, it increases patient comfort as well as offers a number of potential advantages in regard to conventional diabetes treatment. Based on our artificial depot, it is possible to achieve the activity of the system for the period of 3 months. Depending on the amount of insulin bonded within

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the fiber, it is possible to prolong or reduce the time of its action. When insulin is exhausted, it is necessary to remove the fibrous carrier from the living organism and to implant a new artificial store.

Mechanism of insulin chemisorption could be described like a mechanism of binding amino to acid groups. Insulin is one of the smallest proteins, having molecular weight 5733. The amino acid residues are joined together in protein by the formation of amide or peptide bonds between the α-carboxyl group and the α-amino group of the residues. The insulin protein has isoelectric point at pH 5.4 when existing in the form of zwitterion. The hydrogen from carboxyl group of sorbent moved to carboxyl group of zwitterion ($^{+}NH_3—R—COO^{-}$). In acid and neutral solutions, in concentrations relevant for pharmaceutical formulation, the insulin monomer assembles to dimers and at neutral pH, in the presence of zinc ions, further to hexamers.[13] Monomers and dimers diffuse into fiber readily, whereas hexamers diffuse very poorly. Hence, absorption of insulin solution containing a high proportion of hexamers is delayed and slow. During chemisorption process, one has to take care of insulin activity and has to consider that a breaking of disulfide bridges causes immediate loss of insulin activity.

The chemisorption process comprises the following three stages:

- adsorption of the insulin by the fiber external surface,
- diffusion of the insulin inside the fibrous material, and
- chemical bonding of the insulin and fibrous material.

The external diffusion limitation of insulin macromolecules in solution is neglected because of good mixing pattern at the macrolevel.

Chemisorption progresses slowly. In practice, 1 hour or even more is required for the sorption of the insulin from the solution by fibrous ionites. The process beginning by the adsorption of the insulin on the external surface of the fiber and equilibrium is achieved practically in several seconds. The fixation of the insulin on the fiber, by bonding of insulin molecules to macromolecules of the fibrous material, in present case is a momentary process. The chemisorption rate is determined by the rate of insulin diffusion into the pores from the external surface of the fiber. The rate of insulin diffusion into the fiber depends on the size of the insulin particles as well as on structure of the fiber.

The degree of equilibrium sorption depends on chemisorption conditions and, particularly, on the temperature and insulin concentration.

In this article, the mathematical model describes the chemisorption process using fractional kinetics equations of diffusion. Chemisorption process has been widely considered to find the optimal experimental conditions. Some attempts have been made to optimize the performance of the fibers, ensuring the high insulin concentration. Also, attention has been paid to incorporate insulin conformation dynamics into transport phenomena including overdamped effects. In high concentration of insulin solution, insulin molecules have tendency to make molecule association, clusters, or agglomerates. It has significant impact on chemisorption dynamics as well as provokes effects of insulin anomalous transport through the fibrous matrix. Subdiffusion is a kind of anomalous diffusion problem, which includes overdamped effects.[14–19] Overdamped effects are caused by polymer conformational dynamics. The aim of this consideration is to determine the diffusion coefficients of insulin as well as overdamped exponents for corresponding experimental conditions.

EXPERIMENTAL

Materials

- Cation-exchanged PAN fibers with ion-exchanged capacity 1.7 mmol g^{-1} and linear density 6.4 dtex, obtained in Laboratory of Fibers, Faculty of Technology and Metallurgy, Department of Textile Engineering, Belgrade, Serbia
- Human Zn-insulin (approx. 24 I.U. per mg), Novo Nordix, Denmark
- Acetate buffer, pH 3.5
- Sodium hydroxide (NaOH) 5%

Obtaining complex ion-exchange fibers–insulin

Insulin was bonded to the fiber by a chemisorption reaction on ion-exchange PAN fibers under the following conditions:

- Ion-exchange fibers, 200 mg
- Insulin concentration, 0.16, 0.20, 0.31 g dm^{-3}
- Liquor ratio 1 : 500 (1 g of fiber: 500 dm^3 of insulin solution)
- Time of chemisorption 1–120 min and 24 h
- Temperature 24°C
- pH 3.5–5.5

The preparation of the fibrous insulin delivery system by insulin chemisorption by an ion-exchange acrylic fiber is described in details in our previous papers.[8–12]

Insulin concentration measurements—UV spectrophotometric method

Insulin chemisorption from insulin solutions by an ion-exchange acrylic fiber was monitored by UV Spectrophotometry, Shimadzu UV-260 UV–vis spectro-

photometer. UV spectrums of the solutions of insulin were recorded in the range of 200–400 nm and during 10, 20, 30, 40, 50, 60, 70, 120, and 2400 min. The concentration of insulin in the solution during chemisorption was determined on the basis of maximum UV absorption at the wavelength of 275 nm.

Scanning electron microscopy

The morphology and topography of fibers were studied by scanning electron microscopy (JEOL JSM-T20 i JEOL JSM-35).

RESULTS AND DISCUSSION

Experimental results and model consideration

A fiber-based insulin delivery system was prepared in the Fibers Laboratory of the Faculty of Technology and Metallurgy, Belgrade. In our previous paper,[10–12] the preparation of a fibrous insulin delivery system followed by insulin chemisorption by an ion-exchange acrylic fiber (PAN) is described.

The fibrous complexes cation-exchange fiber–insulin were formed under static conditions. The bonded amount of insulin was calculated based on the change in insulin concentration in the solution. The insulin concentration change was monitored and determined in assigned time intervals. In this way, the kinetics of the chemisorption reaction was studied. The intensity of the expected maximum absorbing for insulin decreases in time, indicating the decrease in concentration of the insulin in bath.

Porous fiber structure enables the diffusion of insulin into the polymer matrix and its bonding to ionic groups of fiber. The influence of the porous structure, size and geometry of pores, as well as size and geometry of insulin in mathematical model is expressed by means of diffusion coefficient of insulin molecule through the fiber.

Ion-exchange PAN fiber is characterized by an important ζ-potential and it enables a polyfunctional cooperation of sorbent and insulin to be established. In a schematic, simplified form, chemisorption of insulin by cation-exchanging fibers may be presented by following reaction:

$$Fiber\text{—}COOH + {}^{+}NH_3\text{—}R\text{—}COO^{-} \rightarrow -COO^{-}\,{}^{+}NH_3\text{—}R\text{—}COOH,$$

in which hydrogen from carboxyl group of sorbent moves to the carboxyl group of the zwitterion, i.e., in the absorption process the dipole ion transforms in cation.

Previous experimental research of the chemisorption process of insulin has shown that this reaction depends directly on the type and forms of fibrous ionite, static ion-exchange capacity, concentration of insulin solution, pH value, temperature and duration of the contact between insulin and fiber, bath modulus, etc.[10,12]

Interaction between insulin and fibers is chemical in nature. There is neither physical nor surface adsorption of insulin, which is confirmed in an attempt of insulin sorption by polyacrilonytrile fiber not containing functional groups.

Results of kinetics of insulin chemisorption by cation-exchange PAN fibers depending on the concentration are shown in Table I.

Each value, given in Table I, represents the average value of 10 experimental results. All results are within the range of experimental error allowed for the measuring method used with variation coefficient lower than 5% and SD less than 0.07.

Obtained results show high exhaustion degree and intensive flow of insulin chemisorption by cation-exchange PAN fibers. In higher concentrations of the insulin solution, sorption is impeded on account of the molecule association to agglomerates or clusters. Insulin in the monomer form has the molecular mass equal to 6000 Da. The tendency to agglomerate is expressed in highly concentrated solutions, as well as on certain pH values.

TABLE I
Kinetics of Insulin Chemisorption (Humane Zn-insulinum) by Sample (200 mg) of PAN Ionite in Na-form in Dependence on the Concentration of the Insulin Solution (pH solution 4.8–5.5, liquor ratio 1 : 500, T = 24°C)

Concentration of starting insulin solution 0.16 g dm^{-3}									
Time [min]	10	20	30	40	50	60	70	180	2400
Bonded insulin[a] [mg g^{-1}]	56.1	64.5	74.2	75.9	78.5	80.7	81.7	81.7	81.7
Concentration of starting insulin solution 0.20 g dm^{-3}									
Time [min]	10	20	30	40	50	60	70	180	2400
Bonded insulin [mg g^{-1}]	54.5	63.6	72.0	80.1	88.5	94.1	101.2	104.6	108.2
Concentration of starting insulin solution 0.31 g dm^{-3}									
Time [min]	10	20	30	40	50	60	70	180	2400
Bonded insulin [mg g^{-1}]	56.2	71.6	86.3	101.2	115.1	121.3	128.3	132.0	137.5

[a] Amount of insulin bonded to the fiber, mg of insulin per gram of fiber.

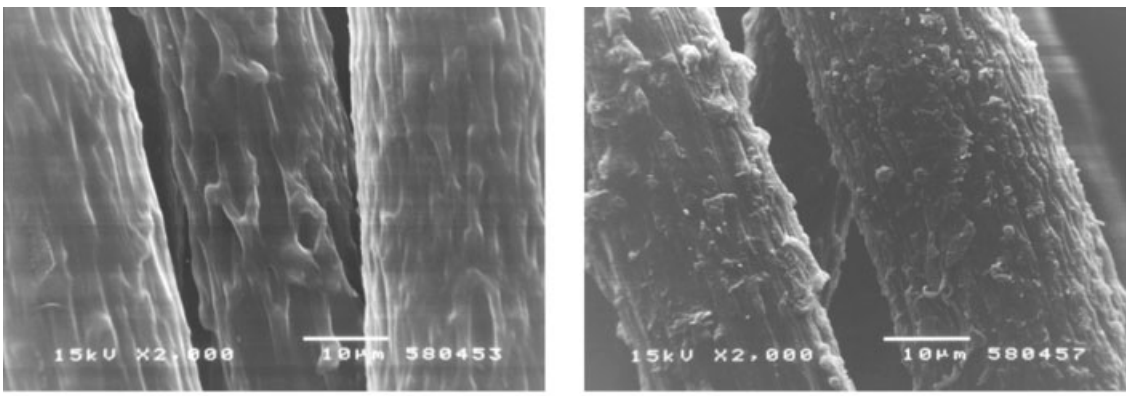

Figure 1 Scanning electron microscopy images of ion-exchange PAN fiber (a) and artificial insulin store (b).

To obtain artificial insulin depot with large quantity of insulin, sample of fibrous ionite could be submerged in the fresh insulin solution several times, up to the maximal exhaustion of the insulin solution. Our previous results of obtaining insulin artificial depot showed that it is possible to obtain fibrous depot with a significant amount of chemically bonded insulin (about 800 mg insulin per gram of polyacrilonitrile fiber).[10–12]

Changes in topography of the fibers, as evidential result of the insulin chemisorption, are presented on the scanning electron microscopy images (Fig. 1).

In Figure 1(b), realistic appearance of the obtained fibrous artificial store of insulin is shown, and specific structural details could be noticed. These structural details on the fiber surface could come from insulin agglomerates or clusters. The appearance of agglomerates on the surface may be caused by establishment of coordinative bonds between Zn^{2+} ion from insulin and residual, nonmodified —CN groups from fiber.

Our experiment (Table I) proved that the chemisorption from solution with higher insulin concentration flows more intensively, and fibers bond a bigger amount of insulin per gram of fiber.

Diffusion process into the fibers could be approximated as mass transport process in the very long cylindrical body with radius R. The processes of mass transport in polymers have a mutual dependence on the presence of void and defect structures and on the nature of polymer chain segmental motions.

A model of the chemisorption process could be established in relation to the change of insulin amount within the observed solution volume, or in relation to the change of the amount or concentration of insulin bonded to the fiber, depending on the conditions and duration of chemisorption.

The principle of this model is illustrated in Figure 2. The model describes the change of insulin concentration in a swollen fiber cross section.

Fractional kinetics equations of diffusion were proposed with an aim to include the overdamped effects into the dynamics of insulin transport into the porous structure of fibers. The consequence of insulin conformation ordering in flow could be described as overdamped effects. Such models offer the possibility to separate the overdamping effects from other insulin structural changes that affect the value of diffusion coefficient as insulin cluster formation, interactions between insulin macromolecules, and fiber matrices.

Equations that described the balance of the insulin concentration in fiber and into solution, during the time, are given by formulae (1) and (2).

Balance of insulin in fiber:

$$\frac{\partial^{\beta}\Delta c_f}{\partial t^{\beta}} = D_e \frac{1}{r} \times \frac{\partial}{\partial r}\left[r\frac{\partial \Delta c_f}{\partial r}\right]$$
$$\Delta c_f = c_{f_{eq}} - c_f \qquad (1)$$

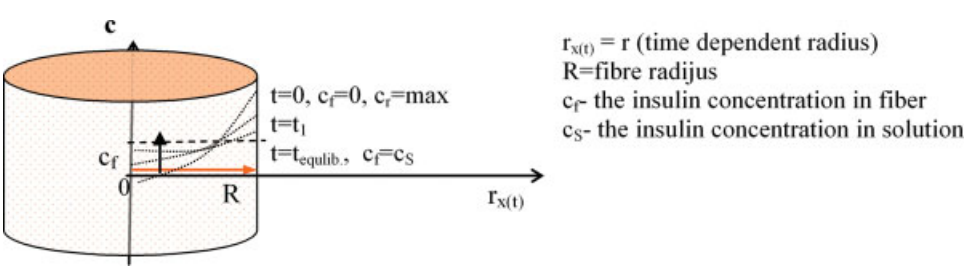

Figure 2 Cross-section change of the insulin concentration along the fiber radius during the time. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

Balance of insulin in solution:

$$V_r \frac{\partial^\beta \Delta c_S}{\partial t^\beta} = NP_{ef}\left[-D_e \frac{\partial \Delta c_f}{\partial r}\Big|_{r=R}\right]$$
$$\Delta c_S = c_S - c_{S_{eq}} \quad (2)$$

where c_f is the insulin concentration in the fiber; c_S, insulin concentration in the solution; D_e, diffusion coefficient; r, radius of a swollen fiber (time dependent radius); V_r, volume of insulin solution; N, total number of fibers; H, length of a fiber; P_{ef}, surface of a real, swollen fiber = 2 πRH; $c_{f_{eq}}$, equilibrium insulin concentration into the fiber; c_S, equilibrium insulin concentration in the solution; and β, overdamping exponent, which is $\beta \leq 1$. If the overdamped exponent is equal to one, such dynamics could be explained by classical diffusion equations.

The boundary conditions for insulin sorption by the fibrous material are as follows:

1. $r = 0$, $t = 0$, $c_f(0,0) = 0$
2. $r = R$, $t = 0$, $c_f(R,0) = c_{\text{fmax}}$
3. $r = R$, t, $c_f(R,t) = \alpha(t)\ c_S(t)$

where the concentration ratio parameter is introduced and expressed as $\alpha(t) = (c_f(R,t))/(c_S(t))$. The proposed model introduced the assumption that for $r < R$ the initial concentration of insulin in fiber is approximately $c_f(r,0) \approx c_f(0,0)$. Parameter $\alpha(t)$ at equilibrium, for pure physical sorption, is much lower than for chemisorption. Physically, the parameter $\alpha(t)$ represents the intensity of chemisorption. For our model interpretation, additional boundary condition is introduced:

4. $t = 0$, $\alpha(0) = (c_f(R,0))/(c_{s\ \max})$
5. $t = t_{\text{eq}}$, $\alpha(t_{\text{eq}}) = c_{f_{\text{eq}}}/c_{S_{\text{eq}}}$, where t_{eq} is equilibrium time.

On the bases of experimental research related to the forming of the artificial depot, an assumption is imposed that the initial concentration of insulin on the fiber surface is much higher than the initial concentration of insulin in solution, $(c_f(R,0) \gg c_s(0))$; that is, because of the electrokinetic potential influence, an accumulation on insulin molecules on the surface happened. As the chemisorption process is a fast one, a certain number of insulin molecules will be bonded to the fiber surface in a short time. The layer of insulin on the fiber surface presents a barrier to diffusion of insulin molecules from the solution toward the center of the fiber. This barrier, on the one hand, presents partial decrease of effective dimensions of PAN fiber pores in the surface layer of fiber, and on the other hand, the influence of electrostatic repellent interaction of certain chemical groups of insulin is also present.

External diffusion limitation is neglected because of good mixing pattern in the macrolevel, which corresponds to boundary conditions 2 and 3. Internal diffusion inside the fibers is considered, while the presence of boundary layer around the fibers is neglected.

Solution of the formulae (1) and (2) is possible by Fourier division of the variables, as well as Bessel's functions.

$$\Delta c_f = x(t) \cdot y(r) \quad (3)$$

$$\frac{\partial^2 y}{\partial r^2} + \frac{1}{r}\frac{\partial y(r)}{\partial \cdot r} + \frac{\lambda^2}{D_e} y(r) = 0 \quad (4)$$

$$\frac{\partial x(t)}{\partial t} + \lambda_a^2 D_t^{1-\beta} \cdot x(t) = 0 \quad (5)$$

$$x(t) = C_1 E_{1,\beta}(-\lambda^2 \cdot t^\beta)$$

where ${}_aD_t^{1-\beta}$ represents operator of nonintegers differentiation.[18,20]

The final solution of formula (1) describes the spatiotemporal change of insulin concentration in the fiber:

$$c_f = c_{fx} - \left\{ \begin{array}{l} C_1\left[1 - \frac{(ra)^2}{4} + \frac{(ra)^4}{64} - \frac{(ra)^6}{2304}\right] + \\ C_2\left[\frac{(ra)^2}{4} - \frac{(ra)^4}{64}\left(1+\frac{1}{2}\right) + \frac{(ra)^6}{2304}\left(1+\frac{1}{2}+\frac{1}{3}\right)\right] \\ \qquad \cdot E_{1,\beta}(-\lambda^2 t^\beta) \end{array} \right\} \quad (6)$$

where parameter a is expressed as $a = \sqrt{\frac{\lambda^2}{De}}$, λ represents the specific rate of insulin concentration decrease in solution and could be determined from the experimental data, and De is the internal diffusion coefficient of insulin.

The change of insulin concentration in the solution as a function of time is

$$c_S = c_{S_{eq}} + (c_{S_0} - c_{S_{eq}}) \cdot E_{1,\beta}(-\lambda^2 t^\beta)^* \quad (7)$$

Constants C_1 and C_2 were determined from the boundary conditions (1–3).

$$C_1 = -c_{f_{eq}} \quad (8)$$

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* $E_{1,\beta}(-\lambda^2 t^\beta)$ – Mittag – Leffler function.[14–18]

$$E_{1,\beta}(-\lambda^2 t^\beta) = \sum_{n=0}^{\infty} \frac{(-\lambda^2 t^\beta)^n}{\Gamma(\beta n + 1)},$$

where Γ represent gamma function.

$$C_2 = \frac{c_{f_{eq}} - c_{S_0} + c_{f_{eq}}\left[1 - \frac{(Ra)^2}{4} + \frac{(Ra)^4}{64} - \frac{(Ra)^6}{2304}\right]}{\left[\frac{(Ra)^2}{4} - \frac{(Ra)^4}{64}\left(1+\frac{1}{2}\right) + \frac{(Ra)^6}{2304}\left(1+\frac{1}{2}+\frac{1}{3}\right)\right]} \quad (9)$$

Further, diffusion coefficient could not be experimentally obtained. However, diffusion coefficient could be calculated using proposed model. By incorporating the formulae (6) and (7) into the model formula (2), following functional form is expressed:

$$V_s \frac{(c_{Sa} - c_{S_{eq}})}{N \cdot P_{ef}} = \frac{1}{2}R(C_2 - C_1) + \frac{1}{16}R^3a^2\left(C_1 - \frac{3}{2}C_2\right) + \frac{1}{384}R^5a^4\left(C_2\left(1+\frac{1}{2}+\frac{1}{3}\right) - C_1\right) + \cdots \quad (10)$$

where V_s is volume of insulin solution; P_{ef}, effective fiber surface area; N, total number of fibers; and R, the fiber radius that is experimentally obtained.

Discussion of experimental results using proposed mathematical model

Above discussed modeling approach was used for calculating the diffusion constants and overdamped exponent for various experimental conditions. The change of insulin concentration in solution during the chemisorption, for various initial concentrations, is shown in Figures 3(a–c), together with model curves calculated using the formula (7).

The parameter λ decreases with the increase of initial insulin concentration in solution. Higher initial insulin concentration resulted in the formation of higher-sized clusters in solution. Transport of such clusters from fiber includes the internal diffusion limitation through the fiber. External diffusivity limitation is neglected because of good mixing pattern in the macrolevel. The consequence of this phenomenon is calculated lower value of parameter λ. The overdamped exponent β is also determined by fitting procedure and is shown in Table II. All calculated values of exponent β are near to the one that means that overdamped effects do not affect the dynamics of insulin transport significantly. The lowest value of exponent β corresponds to the highest initial value of insulin concentration in solution. Overdamped effects affected the dynamics of insulin transport for higher initial insulin concentration. Insulin exists in solution (depending on concentration and pH) as monomers or dimers and in rhombohedral crystals as hexamers. At higher concentrations at acid or neutral pH (in the absence of zinc) the insulin monomer self-associates to form dimers and (in the presence of zinc) hexamers.[13] Under solution conditions where the native state is destabilized, the largely helical polypeptide hormone insulin readily aggregates to bigger aggregates or clusters. Conformational insulin molecule order in the flow from solution to the area inside the fiber depends on cluster sizes. Higher-sized clusters represent the more rigid structural units than do smaller-sized clusters.

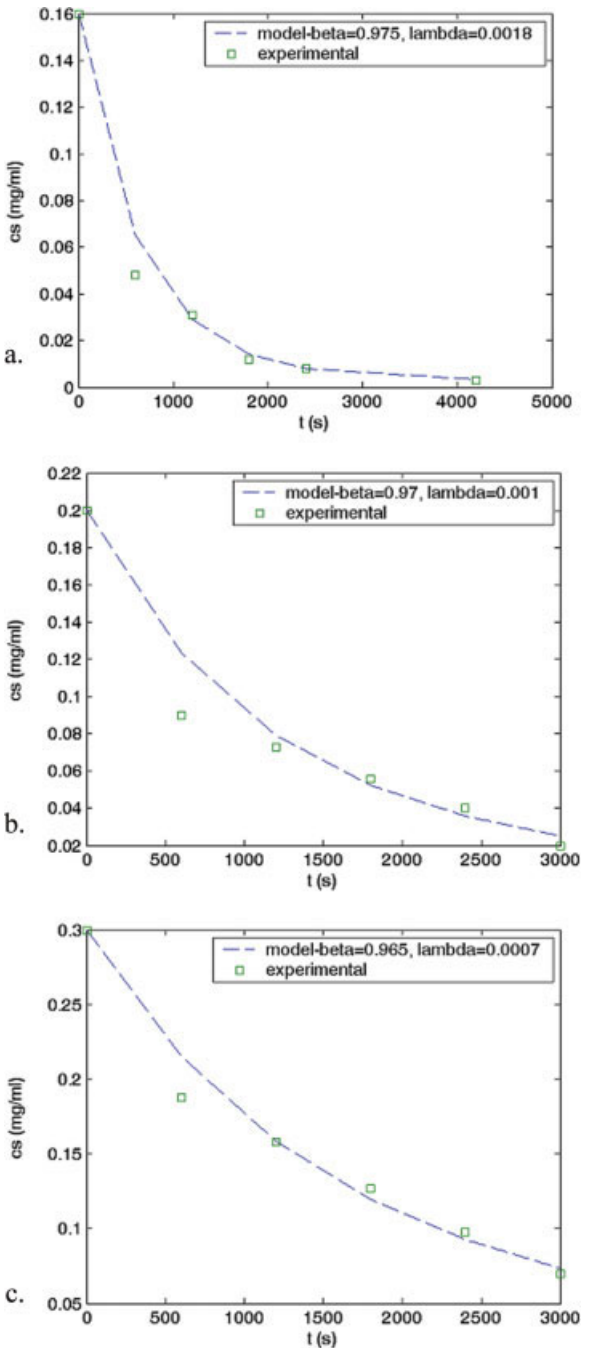

Figure 3 The change of insulin concentration in solution during the chemisorption as well as model curves of overdamped exponent β determined by fitting of experimental data. Initial insulin concentrations: (a) $c_s = 0.16$ mg/mL (b) $c_s = 0.2$ mg/mL (c) $c_s = 0.31$ mg/mL. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

Corresponding values of λ (Table II) are introduced to the eq. (10) on the account of diffusion coefficients calculation. The coefficient of insulin diffusion was determined by the mathematical model, taking all the

TABLE II
Values of Specific Decrease Rate of Insulin Concentration in Solution, Overdamped Exponent, As Well As Insulin Diffusion Coefficient for Various Initial Insulin Concentrations

Insulin concentration [g dm^{-3}]	λ	β	D_e [cm^2/s]
0.16	0.0018 ± 0.0002	0.975 ± 0.01	(2.6317 ± 0.2) × 10^{-13}
0.20	0.0010 ± 0.0002	0.970 ± 0.01	(1.5176 ± 0.2) × 10^{-13}
0.31	0.0070 ± 0.0002	0.965 ± 0.01	(1.1382 ± 0.2) × 10^{-13}

relevant conditions regarding this experiment into consideration. The mathematical model showed changes in the coefficients of insulin diffusion depending on insulin concentration. The insulin diffusion coefficient for insulin solution concentration 0.31 mg/mL is approximates half the size of the insulin diffusion coefficient for 0.16 mg/mL.

These values of diffusion coefficient for insulin chemisorption by polyacrylonitrile fibers show that diffusion of insulin through PAN fiber progresses very slowly. The values obtained for insulin diffusion coefficient through ion-exchange fiber are of the same grade with the results from literature related to coefficients of diffusion of giant molecules as γ-globulin, lysosomes, ovalbumin, etc., through fibrous forms (0.4×10^{-13} to 1.13×10^{-13} m^2/s).[21] In comparison with coefficient of water diffusion coefficient $D = 1.2361 \times 10^{-10}$ cm^2/s for PAN found in the literature,[22] diffusion of insulin molecules is much slower than water molecules through PAN fiber. The slow insulin diffusion through polymer could be explained by the tendency of insulin molecules tend to make agglomerates that do not easily pass through pores of fibers.

Calculated value of diffusion coefficient is further introduced into the model eq. (6) to determinate the concentration profile of insulin in fiber, which is schematically represented in Figure 2. In addition, we introduced the assumption that for experimental initial concentrations of insulin in solutions, i.e., $c_s = 0.16$ g dm^{-3}, $c_s = 0.20$ g dm^{-3}, $c_s = 0.30$ g dm^{-3}, corresponding initial insulin concentration on fiber surfaces $c_f(R,0)$ are 120, 180, and 210 g dm^{-3}, respectively. The results of calculation profiles of insulin concentrations in fiber for various experimental conditions are shown in Figure 4.

As shown in Figure 4, the equilibrium state is reached faster for lower initial concentration of insulin because of lower value of previously calculated diffusivity coefficient.

The concentration ratio parameter, α, with respect to time for various initial insulin concentrations in solution is shown in Figure 5. The parameter α could be explained as the measure of chemisorption efficiency in regard to bonded quantity of insulin into the fiber. Experimental results have shown that normalized parameter α_0/α increases during the time from 1 to equi-

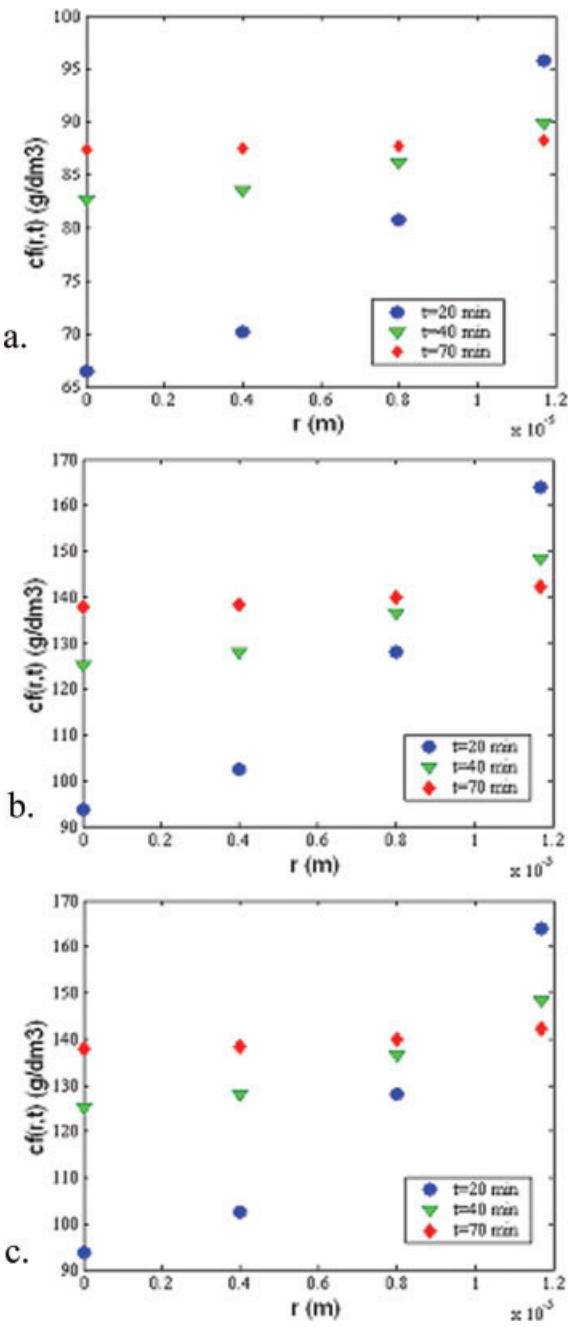

Figure 4 Profile of insulin concentration in the fiber depending on insulin concentration and time of sorption: (a) $c_s = 0.16$ mg/mL (b) $c_s = 0.2$ mg/mL (c) $c_s = 0.31$ mg/mL. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

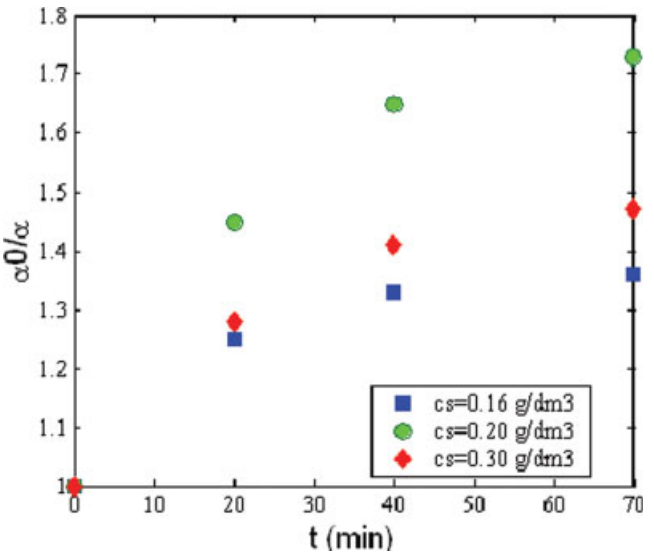

Figure 5 Change of the concentration ratio parameter. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

librium value. The equilibrium value of parameter α is in the range of 7.8–8.3.

In general, mathematical model has shown that in investigated range of insulin concentration, parameter α is not significantly clear on change of initial insulin concentration into the solution.

CONCLUSIONS

Mathematical model was developed on the basis of experimental results. A model of the chemisorption process was established in relation to the change of insulin amount within the observed solution volume. Mathematical model gives some detailed information about chemisorption process, such as profile of insulin concentration change in the fiber, as well as the diffusion coefficient of insulin into the fiber, overdamped exponent β, and the specific concentration rate parameter.

Higher initial insulin concentration resulted in the formation of higher-sized clusters in solution. Transport of such clusters from solution to fiber includes the internal diffusivity limitations while the external diffusivity limitation is neglected because of the good mixing pattern at the macrolevel. The consequence of this phenomenon is calculated lower value of parameter λ and overdamped exponent β. Conformational insulin molecule ordering in the flow depends on the cluster sizes. Higher-sized clusters represent the more rigid structural units then smaller-sized clusters.

The value of the diffusion coefficient, calculated according to concentration of the insulin solution 0.16 mg/mL, gives $De = 2.6317 \times 10^{-13}$ cm^2/s, for concentration of insulin solution of 0.2 mg/mL, $De = 1.5176 \times 10^{-13}$ cm^2/s, and finally for concentration 0.31 mg/mL, $De = 1.1382 \times 10^{-13}$ cm^2/s. The slow insulin diffusion through polymer is because the insulin molecules tend to make agglomerates that do not easily pass through pores of fibers.

Proposed model approach could be used to make the prediction of optimal experimental initial insulin concentration in the solution. Higher initial insulin concentration is desired to achieve the higher equilibrium insulin concentration inside the fiber. However, higher initial insulin concentration included the various anomalous transport phenomena as diffusion limitations and overdamped effects.

Also, proposed modeling approach is useful and can be applied for the description of transport dynamics in different complex systems as polymer transport through the porous matrices, which are governed by anomalous diffusion.

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