Kinetics Study of Isothermal Nicotine Release from Poly(acrylic acid) Hydrogel

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ABSTRACT: The isothermal kinetic of the release of nicotine from a poly(acrylic acid) (PAA) hydrogel was investigated at temperature range from 26°C to 45°C. Specific shape parameters of the kinetic curves, the period of linearity and saturation time were determined. The change in the specific shape parameters of the kinetic curves with temperature and the kinetic parameters of release of nicotine E_a and ln A were determined. By applying the "model fitting" method it was established that the kinetic model of release of nicotine from the PAA hydrogel was $[1 - (1 - \alpha)^{1/3}] = k_M t$. The limiting stage of the kinetics release of nicotine was found to be the contracting volume of the interaction interface. The distribution function of the activation energy was determined and the most probable values of activation energies of 25.5 kJ mol^{-1} and 35 kJ mol^{-1} were obtained. Energetically heterogeneity of the interaction interface was explained by the existence of the two different modes of bonding the nicotine molecules onto the hydrogel network by hydrogen bond and electrostatic forces. © 2010 Wiley Periodicals, Inc. J Appl Polym Sci 119: 1805–1812, 2011

Key words: hydrogels; drug delivery systems; kinetics

INTRODUCTION

Hydrogels are three-dimensional crosslinked polymeric structures that are able to swell in an aqueous environment. Due to its characteristic properties such as swellability in water, hydrophilicity, biocompatibility and intoxicity, hydrogels have been used in a wide range of biological, medical, pharmaceutical and environmental applications.[1,2] One of the most powerful applications of hydrogels is to act as controlled release systems for targeted delivery of drugs to specific areas of the body. The swelling ability of hydrogels allows them to absorb and release high quantities of drugs.[3,4]

The transdermal delivery of drugs can offer substantial advantages over the more traditional oral and parenteral routes. The development of new transdermal devices is therefore an integral part of the current general research effort aimed at controlling and sustaining the delivery of drugs, so that the predictability and reproducibility of their release kinetics and their bioavailability are improved. There are a number of successful transdermal drug delivery systems commercially available at present but the need remains to extend their operating parameters so that more sustainable and variable delivery regimes can be achieved. Polymeric matrix or reservoir transdermal delivery patch for the controlled release of nicotine comprising an amount of nicotine or a pharmaceutically acceptable salt or solvate thereof effective to treat symptoms associated with tobacco smoking cessation and an amount of an anti-pruritic effective to treat the pruritis associated with transdermal delivery of nicotine, in a pharmaceutically acceptable carrier.[5]

Bannon et al. reports the results of a series of investigations in which a range of ion exchange resins with different characteristics were incorporated into the hydrogel vehicle of a thoroughly-studied transdermal system originally designed to deliver nicotine.[6] The kinetics of the release of nicotine from two types of sulphonic acid-based ion exchange resins held in a hydrogel was investigated and found that the rate of nicotine release from the complex vehicles was controlled primarily by diffusion through the hydrogel matrix.[7] Conaghey et al. established the principles that govern the iontophoretically-assisted delivery of nicotine-loaded vehicles based on a hydrogel containing particles of an ion-exchange resin into which the drug has been previously loaded. The use of an iontophoretic current has been shown to enhance the rates of delivery from these vehicles over the corresponding passive transport. In the case of human skin these enhanced rates mean that the vehicles could potentially be used in an electrically assisted transdermal drug delivery system.[8]

The glucose responsive nicotine release composite membrane was prepared and tested for the intelligent release functions with anti-smoking effect, as well as the temperature-responsive nicotine release membrane for comparison.[9] The interactions of the nicotine, nicotinic acid, nicotinamide, and niketha-mide with poly(acrylamide/maleic acid) hydrogels were examined.[10]

In this study, the isothermal kinetic of the nicotine release from the poly(acrylic acid) (PAA) hydrogel were investigated with aim to determine the kinetic parameters (E_a, ln A) and kinetic model of the nicotine release and to establish model for the mechanism of nicotine release from the hydrogel with intention to realize new generation of transdermal delivery systems.

MATERIALS AND METHODS

Materials

Materials for hydrogel synthesis

Acrylic acid (99.5%) (AA) was supplied by Merck KGaA, Darmstadt, Germany. The initiator, 2,2′-azo-bis-[2-(2-imidazolin-2-yl)propane] dihydrochloride (VA-044) (99.8%) was supplied from Wako Pure Chemical Industries, Osaka, Japan. The crosslinker, $N,N′$-methylene bisacrylamide (p.a) (MBA) was purchased from Aldrich Chemical, Milwaukee. Sodium carbonate (Na_2CO_3) (p.a) was obtained from Merck KGaA, Darmstadt, Germany. Nicotine (p.a) was purchased from Merck, KGaA, Darmstadt Germany.

Xerogel synthesis

The PAA hydrogel was synthesized using a one-pot process based on the radical polymerization of AA and crosslinking of the formed PAA in aqueous media using the following procedure.

A 20 wt % solution of AA was prepared and mixed with a 0.1 wt % solution of MBA. After stirring well to ensure homogeneity of the reaction mixture and nitrogen bubbling throughout the mixture for half an hour, the initiator solution (0.05 wt % of the monomer) was added and the reaction mixture was once again rapidly stirred and bubbled with nitrogen for a further 20 min. Immediately, the prepared reaction mixture was poured into glass moulds (plates separated by a rubber gasket 2 mm thick) and placed in an oven at 80°C for 5 h. Then, the obtained gel-type product was transformed into the Na^+ form (60 %) by neutralization with a 3% solution of Na_2CO_3. The resulting hydrogel was stamped into approximately equally sized discs and immersed in excess distilled water. The water was changed every 2–3 hours, except overnight, for 7 days to remove the sol fraction of polymer and unreacted monomer. Subsequently, the washed-out hydrogel was dried in an air oven in the temperature regime 80°C for 2 h, 90°C for 3 h and finally at 105°C until constant mass was attained. The obtained product (xerogel) was stored in a vacuum exicator until use.

Nicotine loading

The PAA xerogel sample (1g) was immersed in an excess of nicotine solution (100 mL of 5 wt % solution) and left to load at ambient temperature for 24 h. The loaded hydrogel was removed from the nicotine solution and dried air oven in the temperature regime 40°C for 6 h, 60°C for 4 h, 80°C for 2 h and at 105°C until constant mass was attained. Subsequently, the nicotine loaded PAA xerogel was obtained.

Nicotine release

Nicotine release was carried out by immersing the xerogel–nicotine loaded disks in distilled water at different temperatures with constant stirring at 400 rpm. The xerogel–nicotine loaded disks with an average weight of 0.20 g (±10%) were left to release nicotine in excess distilled water at the temperatures 26°C, 30°C, 36°C, 41°C or 45°C (±0.2°C).

At the beginning of each experiment, the xerogel disks (0.2 g) were weighed and then entirely immersed in excess distilled water (100 mL). At predetermined time intervals, the aliquots of external solution were taken out from the solution and analyzed by spectrometry. The released nicotine concentration in water solution was determined using the absorption at 259 nm, by the method ISO 2881.[11] This was done until the external solution attained constant nicotine concentration, i.e., until equilibrium was reached.

For each temperature, release measurements of at least three samples were performed and the mean values were used.

Degree of nicotine released (α) is calculated by Eq:

$$\alpha = \frac{c_i}{c_{max}} \tag{1}$$

where the c_i (g L^{-1}) is nicotine concentration released at time and the c_{max} (g L^{-1}) is equilibrium nicotine concentration.

KINETICS MODEL OF NICOTINE RELEASE FROM XEROGEL

Model-fitting method

Kinetic model of the nicotine release from xerogel was examined by the so-called model-fitting

TABLE I
Set of the Kinetic Reaction Models Used to Determine the Model of Nicotine Release Kinetic; $f(\alpha)$ is the Analytical Expression Describing the Kinetic Model and $g(\alpha)$ is the Integral Form of the Kinetics Model; $g(\alpha) = \int_0^\alpha \frac{d\alpha}{f(\alpha)} = kt$

Kinetics models	$f(\alpha)$	$g(\alpha)$
Power law	$4\alpha^{3/4}$	$\alpha^{1/4}$
Power law	$3\alpha^{2/3}$	$\alpha^{1/3}$
Power law	$2\alpha^{1/2}$	$\alpha^{1/2}$
Power law	$2/3\alpha^{-1/2}$	$\alpha^{3/2}$
Zero-order (Polany – Winger equation)	1	α
Phase – boundary controlled reaction (contracting area, i.e., bidimensional shape)	$2(1-\alpha)^{1/2}$	$[1-(1-\alpha)^{1/2}]$
Phase – boundary controlled reaction (contracting volume, i.e., tridimensional shape)	$3(1-\alpha)^{2/3}$	$(1-(1-\alpha)^{1/3}]$
First – order (Mampel)	$(1-\alpha)$	$-\ln(1-\alpha)$
Second – order	$(1-\alpha)^2$	$(1-\alpha)^{-1} - 1$
Third – order	$(1-\alpha)^3$	$0.5\,[(1-\alpha)^{-2} - 1]$
Avrami – Erofe' ev	$2(1-\alpha)(-\ln(1-\alpha)^{1/2}$	$(-\ln(1-\alpha)^{1/2}$
Avrami – Erofe' ev	$3(1-\alpha)(-\ln(1-\alpha)^{2/3}$	$(-\ln(1-\alpha)^{1/3}$
Avrami – Erofe' ev	$4(1-\alpha)(-\ln(1-\alpha)^{3/4}$	$(-\ln(1-\alpha)^{1/4}$
One-dimensional diffusion	$1/2\alpha$	α^2
Two-dimensional diffusion (bidimensional particle shape)	$1/[-\ln(1-\alpha)]$	$(1-\alpha)\ln(1-\alpha)+\alpha$
Three-dimensional diffusion (tridimensional particle shape), Jander equation	$3(1-\alpha)^{2/3}/2[1-(1-\alpha)^{1/3}]$	$[1-(1-\alpha)^{1/3}]^2$
Three-dimensional diffusion (tridimensional particle shape), Ginstling - Brounshtein	$3/2\,[(1-\alpha)^{-1/3}-1]$	$(1-2\alpha/3) - (1-\alpha)^{2/3}$

procedure. The model-fitting procedure is widely used to determine the suitability of various kinetic reaction models for solid state reaction.[12] According to the model-fitting method the kinetic reaction models, for any solid phase-reaction, generally occurring at a reaction interface are classified in five groups depending on the theoretical reaction mechanism: (1) power law reaction, (2) phase boundary controlled reaction, (3) reaction order, (4) reaction described by the Avrami equation, and (5) diffusion controlled reactions.

The model-fitting method is based on the following. The experimentally determined conversion curve $\alpha_{exp} = f(t)_T$ has to be transformed into the experimental normalized conversion curve $\alpha_{exp} = f(t_N)_T$, where t_N is the so-called normalized time. The normalized time, t_N, was introduced to normalize the time interval of the monitored process and was defined by the equation:

$$t_N = \frac{t}{t_{0.9}} \quad (2)$$

where $t_{0.9}$ is the moment in time at which $\alpha = 0.9$.[13] The kinetics model of the investigated process was determined by analytically comparing the experimentally normalized conversion curves with the normalized model's conversion curves. Based on that comparing, a theoretical kinetic model for which the

sum of squares of the residual from the experimentally normalized conversion curves is minimal was then chosen.

A set of the reaction kinetics models used to determine the model which best describes the kinetic of the nicotine release is shown in Table I, where: $f(\alpha)$ is the analytical expression describing the kinetic model and $g(\alpha)$ is the integral form of the kinetic model.

Differential isoconversion method

The activation energy of investigated nicotine release process for various degrees of nicotine release was established by the Friedman method[14] which is based on the follows. The rate of the process in condensed state is generally a function of temperature and conversion:

$$\frac{d\alpha}{dt} = f(T, \alpha) \quad (3)$$

i.e.,

$$\frac{d\alpha}{dt} = k(T) \cdot f(\alpha) \quad (4)$$

where, $d\alpha/dt$ is the reaction rate, α is the conversion degree, $k(T)$ the rate constant, t the time, T the temperature and $f(\alpha)$ is the reaction model associated

with a certain theoretical reaction mechanism. The dependence of the rate constant on temperature is ordinary described by the Arrhenius law:

$$k(T) = A \cdot \exp\left(-\frac{E_a}{RT}\right) \qquad (5)$$

where E_a is the activation energy, A is the pre-exponential factor and R is the gas constant.

Then we get the following equation:

$$\left(\frac{d\alpha}{dt}\right) = A \exp\left(-\frac{E_{a,\alpha}}{RT}\right) \cdot f(\alpha) \qquad (6)$$

According to the isoconversional principle the $f(\alpha)$ is not change with α, and then the eq. (6) can be easily transformed to:

$$\ln\left(\frac{d\alpha}{dt}\right)_\alpha = \ln[A \cdot f(\alpha)] - \frac{E_{a,\alpha}}{RT} \qquad (7)$$

That allows the evaluation of the activation energy for particular degree of conversion, i.e. nicotine release.

The normalized distribution curve of the activation energy

Muira and Maki[15] established a simple method for determination the density distribution function the activation energy $f(E)$. The basic principle of the method consists in accepting the fact that the investigated process can be described by the so-called distribution activation energy model (DAEM).[16] In that case, we can propose that following is valid:

$$\alpha = 1 - \int_0^\infty \Phi(E,T) f(E) dE \qquad (8)$$

where $\Phi(E,T)$ is equated to:

$$\Phi(E,T) = \exp\left(-\frac{A}{\beta}\int_0^T \exp\left(-\frac{E}{RT}\right) dT\right) \qquad (9)$$

when β is heating rate.

By using a variable $x = \frac{E}{RT}$, eq. (9) is rewritten as:

$$\Phi(E,T) = \exp\left\{-\frac{AE}{\beta R}\left(\frac{e^{-x}}{x} - \int_x^\infty \frac{e^{-x}}{x} dx\right)\right\}$$
$$= \exp\left\{-\frac{AE}{\beta R} p(x)\right\} \qquad (10)$$

where $p(x)$ is the so-called "p-function" that is well known in the field of thermal analysis. By employing an approximation $p(x) = \frac{e^{-x}}{x^2}$, we can write that:

$$\Phi(E,T) = \exp\left[-\frac{ART^2}{\beta E}\exp\left(-\frac{E}{RT}\right)\right] \qquad (11)$$

To estimate the $f(E)$ curve from the experimental data of α versus time, the possibility of an approximate representation for eq. (8) was examined. Since the $\Phi(E,T)$ function changes rather steeply with activation energy at a given temperature, it seems to be reasonable to assume $\Phi(E,T)$ by the step function U at an activation energy $E = E_s$ as:

$$\Phi(E,T) = U(E - Es) \qquad (12)$$

This approximation assumes that is only single reactions whose activation energy is E_s at given temperature T. Then eq. (8) is simplified to:

$$\alpha = 1 - \int_{Es}^\infty f(E) dE \qquad (13)$$

According to eq. (12) we can write that:

$$\alpha = 1 - \int_0^{Es} f(E) dE \qquad (14)$$

therefore, $f(E_s)$ is given by differentiating eq. (14) by E_s as:

$$f(E_s) = \frac{d\alpha}{dE_S} \qquad (15)$$

Actually, the density distribution function of activation energies could be directly obtained by the differentiating the experimentally determined relationship: α versus E.

RESULTS AND DISCUSSION

The isothermal kinetic curves of nicotine release from PAA hydrogel at different investigated temperatures are shown in Figure 1.

Three distinct range of the changes of the specific amount of nicotine released with time can be clearly observed on the presented kinetic curves, i.e., linear, nonlinear and saturation regions. To determine the temperature influence on the shape of those kinetic curves the so-called shape parameters of the kinetic curves are defined: period of linearity t_{in} and saturation time t_s. The period of linearity is the time interval within which the specific amount of nicotine release increases linearly with the time. The period of linearity is determined graphically.[17] The saturation time represents the time required to achieve the maximum concentration released nicotine in the
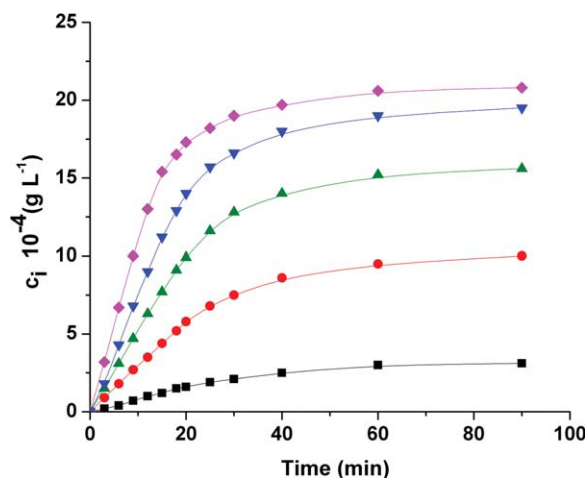
Figure 1 The isothermal kinetic curves of released nicotine from PAA hydrogel at 26°C (■), 30°C (●), 36°C (▲), 41°C (▼), and 45°C (◆). [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

solution at a given temperature and is also determined graphically from the kinetic curves. The kinetic curve parameters (t_{in} and t_s) at different temperatures are presented in Table II.

Based on the results given in Table II, it can be seen that that the values t_{in} and t_s decrease with the increase in temperature of the release process.

To determine the kinetic model of the investigated release process, the possibility of applying the most common kinetic models was examined. It was also assumed that the kinetics of the release process could be determined by the rate of diffusion of molecule nicotine through the hydrogel to external medium and by the concentration of nicotine in external medium.

In the case when the kinetics release is controlled by the rate of diffusion of nicotine molecules through the hydrogel, the dependence $\alpha^2 = f(t)$ would be the straight line which slope corresponds to the constant of nicotine release rate. Figure 2 shows the isothermal dependence $\alpha^2 = f(t)$ at different temperatures.

According to the results presented in Figure 2 it is easy to recognize that the plots of α^2 on time do not give the straights lines in the entire range of α, for

TABLE II
Change of Shape Parameters of the
Kinetic Curve with Temperature

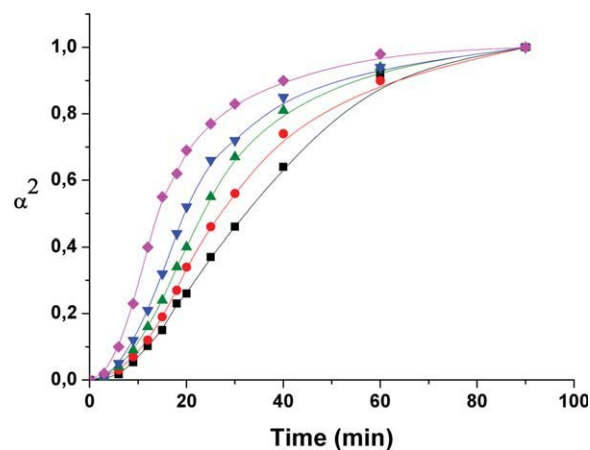| T (°C)	t_{in} (min)	t_s (min)
26	20	90
30	19	88
36	18	85
41	15	80
45	12	75

Figure 2 The isothermal dependence of α^2 on adsorption time at 26°C (■), 30°C (●), 36°C (▲), 41°C (▼), and 45°C (◆). [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

all of the investigated temperatures. That directly proves that the kinetic of nicotine release from hydrogel is not controlled by the rate of diffusion of the nicotine molecules.

When the adsorption kinetics is determined by the concentration of nicotine in external medium, the dependence of $-\ln(1-\alpha)$ versus time would give the straight line. The plots of the isothermal dependences $-\ln(1-\alpha) = f(t)$ for different temperatures are shown in Figure 3.

The isothermal dependence of $-\ln(1-\alpha)$ on the release time give straights lines only in limited ranges of α, in the range from 0.45 to 0.65 which depends on temperature. As temperature increase the range of linearity α increase also.

Bering in mind the previously obtained results, to determine the real kinetic model of nicotine release
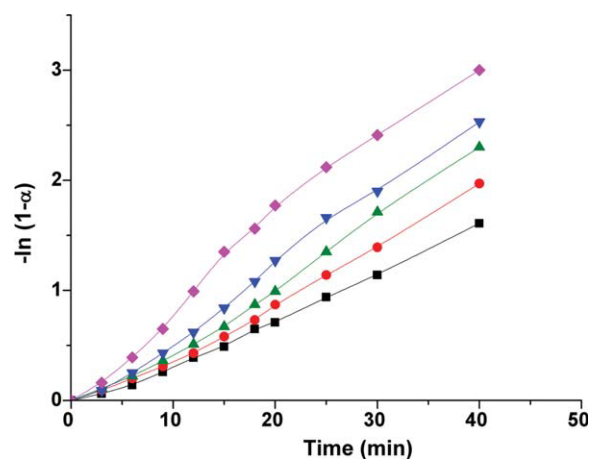

Figure 3 The plots of $-\ln(1-\alpha)$ versus nicotine release time for PAA hydrogel at: 26°C (■), 30°C (●), 36°C (▲), 41°C (▼), and 45°C (◆). [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]
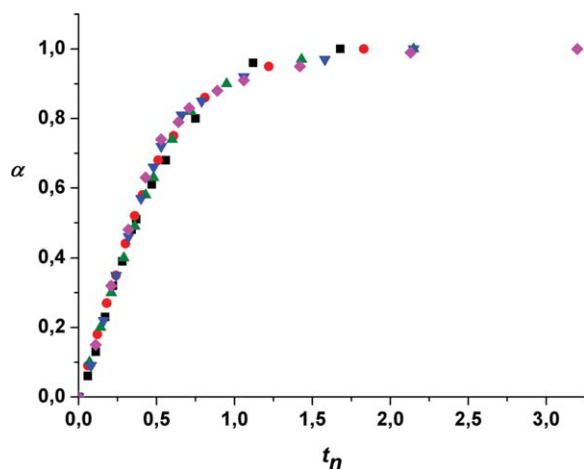
Figure 4 Experimentally normalized conversion curves for nicotine release at 26°C (■), 30°C (●), 36°C (▲), 41°C (▼), and 45°C (◆). [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

process the "model fitting method" was applied. Figure 4 shows the isothermal dependence of the degree of nicotine released on normalized time.

Experimentally normalized conversion curves of nicotine released process, at all of the investigated temperatures are identical by shape and all of them conform to a single kinetic model. Based on the normalized conversion curves $\alpha = f(t_N)$, by the use of the analytical method, with great degree of certainty (≥ 0.999) it can be stated that the kinetics of nicotine release from hydrogel at all the investigated temperatures can be best described by the theoretical kinetic model which is given by following equation:

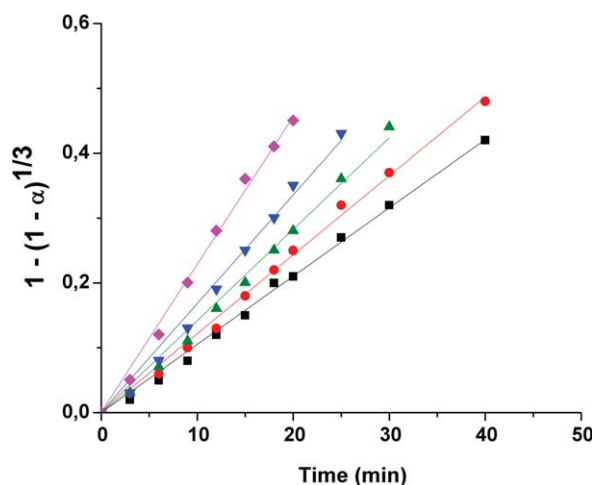$$\lfloor 1 - (1-\alpha)^{1/3} \rfloor = k_M t \qquad (16)$$

Figure 5 The isothermal dependences of $[1-(1-\alpha)^{1/3}]$ versus release time at 26°C (■), 30°C (●), 36°C (▲), 41°C (▼), and 45°C (◆). [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary. com.]

TABLE III
The Change of the Model Constant of Nicotine Release Rate with Temperatures and Kinetic Parameters E_a and $\ln A$

T (°C)	$k_M \cdot 10^{-2}$ (min^{-1})	R	Kinetic parameters
26	1.07 ± 0.01	0.999	
30	1.22 ± 0.01	0.998	E_a (kJ mol^{-1}) $= 28 \pm 1$
36	1.41 ± 0.02	0.998	$\ln A$ (min^{-1}) $= 8 \pm 1$
41	1.68 ± 0.03	0.996	$R = 0.966$
45	2.28 ± 0.04	0.998	

where k_M is the constant of the rate of nicotine release from the PAA hydrogel. This model is characteristic for the physicochemical processes which kinetic is determined by the rate of three-dimensional contracting of the interaction interface (phase – boundary controlled reaction, i.e contracting volume). The isothermal dependences of $[1-(1-\alpha)^{1/3}]$ versus time of nicotine release are shown in Figure 5.

Over almost whole range of the investigated nicotine release process, the dependence $[1-(1-\alpha)^{1/3}]$ on the release time is linear, which confirms that correct kinetic model was selected for describing the release of nicotine from the PAA hydrogel. The change of the model constant of nicotine release rate with temperatures is given in Table III. The kinetics parameters, activation energy (E_a) and pre-exponent factor ($\ln A$), of nicotine release from the PAA xerogel for this model were determined by applying the Arrhenius equation. The obtained results are also given in Table III.

Bearing in mind that the rate of initial nicotine release differed from the saturation nicotine release rate and that the rate of release of nicotine decreased with the increasing the degree of release, the Friedman iso-conversional method was applied to determine the dependence of the activation energy of the release of nicotine from the PAA hydrogel on the degree of released nicotine. By that method, activation energy for different degree of released nicotine was determined. Figure 6 presents the dependences $\ln v_\alpha = f(1/T)$ for different degrees of released nicotine from xerogel.

As can be seen from the obtained results presented in Figure 6, there was a linear relationship between the $\ln v_\alpha$ and the inverse temperature ($1/T$) for all of the degrees of released nicotine from hydrogel. From the slopes and intercepts of these straight lines the values of the kinetics parameters ($E_{a,\alpha}$ and $\ln A_\alpha$) for each value of the degree of nicotine released (α) have been obtained. The dependence of $E_{a,\alpha}$ versus α is shown in Figure 7.

On the curve of the dependence of activation energies on the different degrees of nicotine released, it may be distinguished three characteristic shapes of changes of activation energy with the increasing
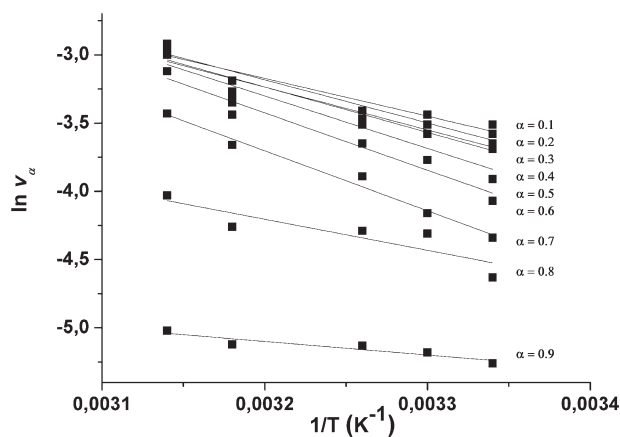
Figure 6 The dependences of ln v_α on inverse temperature $(1/T)$ for different degrees of nicotine released for PAA hydrogel.

Figure 8 The function of the density distribution $f(E_s)$ for nicotine release from PAA hydrogel.

degree of nicotine released. In the range of $\alpha \leq 0.4$, the values of activation energies are independent on the degree of nicotine released, i.e., the $E_{a,\alpha} = 25$ kJ mol^{-1} is until unchanged $\alpha = 0.4$. The increasing degree of nicotine released in the range of $0.4 \leq \alpha \leq 0.7$, leads to the increasing the values of activation energies and the maximal value of the $E_{a,\alpha} = 36$ kJ mol^{-1} is achieved for $\alpha = 0.65$. When the degree of nicotine release is higher then 0.7, $\alpha \geq 0.7$, the increase in the nicotine release leads to the abrupt decrease in the values of $E_{a,\alpha}$.

The value of activation energy calculated by applying the established kinetic model of the release of nicotine agree well with the values of activation energy calculated by the Friedman method $(E_{a,\alpha})$ in the range of $\alpha \leq 0.4$, which implies that this activation energy had dominant effect on the overall kinetics of the release of nicotine from the PAA hydrogel.

Bearing in mind that activation energy of the release of nicotine is proportional to the heat of nico-
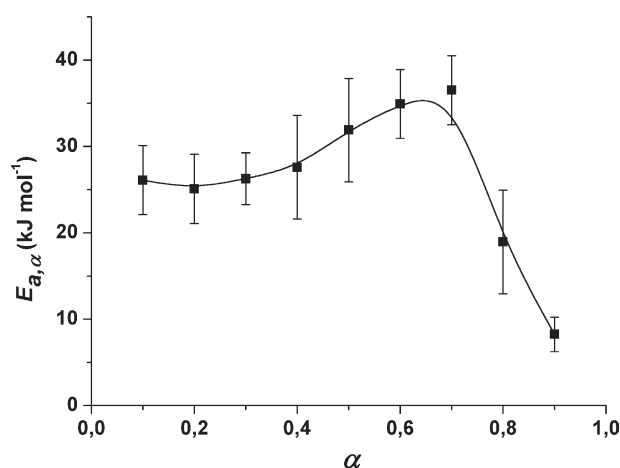
tine binding from water solution onto the hydrogel, one may conclude that the molecules of nicotine are bonded on hydrogel with different haet of binding, i.e. that the interface hydrogel bonded nicotine-external medium is energetically heterogeneous. With aim to precise define energetically heterogeneity of interface hydrogel bonded nicotine-external medium, by applying the Muira method the shape of the probability of distribution function of the activation energies was determined (Fig. 8).

The distribution function of activation energies of nicotine release has characteristic shape with easily distinguished two characteristic peaks. The first of them is well defined and sharp with clear maximum at the $E_{a,\alpha} = 25.5$ kJ mol^{-1}, while the second one is significantly broader with a maximum at the $E_{a,\alpha} = 35$ kJ mol^{-1}. The established value of activation energy determined by using the kinetic model is in well accordance with the value of activation energy of the first peak of the distribution function of activation energies. This decidedly confirms that suitability of the chosen model because the value of activation energy obtained by applying that model corresponds to the most probable activation energy of nicotine release on the distribution function. The energetically heterogeneity of the interactive interface is most

Figure 7 The dependence of $E_{a,\alpha}$ versus degree of released nicotine from PAA hydrogel.
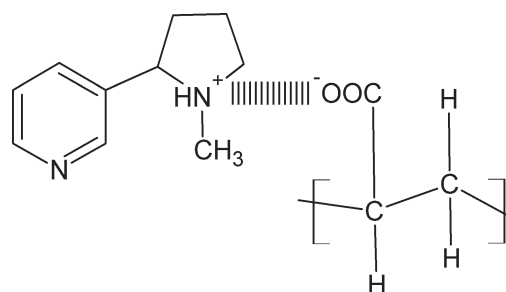
Scheme 1 Nicotine binding to PAA hydrogel by electrostatic forces.
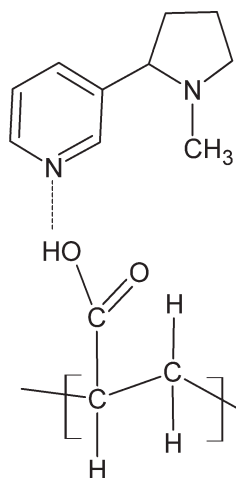
Scheme 2 Nicotine binding to PAA hydrogel by hydrogen bond.

probably associated with the two different modes of binding the nicotine molecules for active centers of the hydrogel. To these centers corresponds two different states of bonded nicotine. The first mode of binding, for which are characteristic lower values of heats of binding and lower activation energy of nicotine releasing, corresponds to the binding of nicotine molecules by electrostatic forces with the carboxyl groups in the hydrogel (Scheme 1).[10] The second one, for which are specific higher heats of nicotine bonding and high activation energy of nicotine releasing, corresponds to the binding of molecules of nicotine by hydrogen bonds (Scheme 2).[18]

CONCLUSION

The release of nicotine from the PAA hydrogel is not controlled by the diffusion, but with the rate of contracting volume of the interactive interface (nicotine bonded to hydrogel and external solution) and is described by the following kinetic model:

$[1-(1-\alpha)^{1/3}] = k_M t$. The activation energy of nicotine release from the PAA hydrogel changes with the changes in the degree of nicotine release. The shape of the distribution function of the activation energies, which showed two peaks with most probable values of the $E_{a,\alpha} = 25.5$ kJ mol^{-1} and $E_{a,\alpha} = 35$ kJ mol^{-1}, were established. The energetically heterogeneity of interactive interface is associated with the presence of two different modes of binding the nicotine molecules to the active centres of the hydrogel.

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