Adsorption 10: 19–28, 2004

Retention of Progesterone by an Activated Carbon: Study of the Adsorption Kinetics

CRISTOBAL VALENZUELA-CALAHORRO, ANTONIO NAVARRETE-GUIJOSA,
MOSTAFA STITOU AND EDUARDO M. CUERDA-CORREA
Departamento de Quimica Inorganica, Facultad de Farmacia, Universidad de Granada,
Campus Universitario de Cartuja S/N E-18071, Granada, Spain
cvalen@ugr.es
nguijosa@ugr.es
mostitou@fst.ac.ma
emcc@unex.es

Received August 22, 2002; Revised May 29, 2003; Accepted September 5, 2003

Abstract. The process by which progesterone in an ethanol solution is retained by Merck granular activated carbon involves a reversible mechanism that conforms to a kinetic equation of unity partial order in both the progesterone concentration in solution, the coverage fraction (θ) of the adsorbing surface and $(1-\theta)$. Over the temperature range 10–40°C, the specific adsorption rate varies from $5.8 \cdot 10^{-5}$ to $1.3 \cdot 10^{-4}$ s^{-1}. The thermodynamic activation functions for the process are $\Delta H^* = 41.6$ kJ/mol and $\Delta S^* = -0.20$ kJ/K· mol. The rate of the adsorption-desorption process is primarily determined by diffusion of progesterone molecules in the pores of the sorbent.

Keywords: adsorption, activated carbon, kinetics, progesterone

1. Introduction

A physico-chemical knowledge of solid surfaces is interesting both for purely scientific reasons and for their practical implications. A number of processes including adsorption (Kentish and Stevens, 2001; Bessarabov, 1999), ion exchange (Kentish and Stevens, 2001) and catalysis (Hart et al., 2002; Sinfelt, 2002; Weiss and Ranke, 2002) possess technological interest. In the past thirty years, such processes have found uses in pharmacology and the pharmaceutical industry (Lam et al., 2001; Queiroz et al., 2001; Raffa et al., 2000).

Ever since the concept of modified-release pharmaceutical forms was established (Zaffaroni, 1980), a large number of active principles have been administered in such forms. Also, theoretical studies on such systems and their preparation have substantially grown in number and variety (Sutani et al., 2002; Zhang et al., 2002; Lee et al., 2001; Einmahl et al., 1999).

Prolonged-release forms with a physically or chemically based action (viz. matrix systems and poorly soluble complexes such as ion-exchange resins, respectively) are very frequently encountered in the literature (Maggi et al., 2002; Muhlbacher et al., 2001, Obaidat and Obaidat, 2001; Genc et al., 1999; Cuna et al., 2000) and in pharmaceutical practice. On the other hand, forms involving a physico-chemical interaction with active sites on a solid surface are uncommon; this function can be served, among others, by carbonaceous materials such as carbon black and activated carbon.

A proper study of the behaviour of the solid-drug system must deal with its kinetic, equilibrium and thermodynamic aspects, in relation to both the action of the drug in biological fluids and the previous preparation of solid-drug systems when a long-acting oral solid pharmaceutical form is to be developed.

In any of the above-described cases, studies are usually restricted to the behaviour of a solid-liquid system and, in relation to physical and/or chemical retention-release (adsorption-desorption and ion exchange), to those occurring at the solid/liquid interface.

This paper reports the kinetic results of the study of a system consisting of activated carbon and progesterone in an ethanol solution, from which an adsorbate (in the pharmaceutical sense of this word) might be obtained that could theoretically be used as the starting material for the preparation of long-acting oral solid pharmaceutical forms.

2. Material and Methods

One gram of Merck granular activated carbon (average particle size $\phi = 2.48$ mm), henceforward referred to as AC-Merck, was used as sorbent. This activated carbon had previously been thoroughly characterized (Gonzalez-Martin et al., 1991). The adsorbate employed was progesterone (pregn-4-en-3,20-dione), supplied in analytical-reagent grade by Guinama (Valencia, Spain) and dissolved in pro-analysis ethanol from Panreac (Barcelona, Spain). A volume of 250 mL of solution was used in each experiment.

A 500 mL Pyrex Erlenmeyer flask furnished with a stopper and an inlet for sample collection was used. The system was thermostated and stirred at 200 rpm in a Gallenkamp stirrer throughout each experiment.

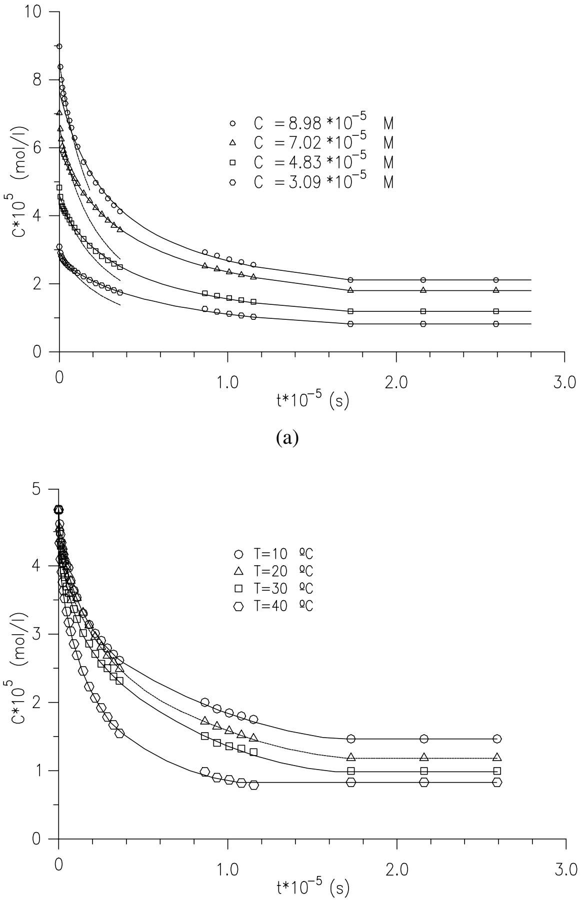
The concentration of the solution in contact with the solid was determined by using a spectrophotometric method to measure the absorption of light of $\lambda = 241$ nm at preset time intervals.

3. Results

Two different experiment batches were conducted. In the first, a temperature of 20°C and four progesterone solutions of known concentration, C, were used; the results obtained are shown as C vs. t kinetic curves in Fig. 1(a). The second experiment series, which involved the use of a $5 \cdot 10^{-5}$ M progesterone solution, was performed at 10, 20, 30 and 40°C; the results are shown in Fig. 1(b).

4. Discussion

4.1. Kinetic Equation: Specific Rate and Thermodynamic Activation Functions



(a)

(b)

Figure 1. Retention of progesterone by an AC-Merck activated carbon at 20°C (a) and Kinetics of progesterone retention by AC-Merck activated carbon (b).

4.1.1. First Experiment Series. The experiments of the first series were conducted in such a way as to facilitate the determination of the partial orders of the overall retention process in the adsorbate concentration in solution (C), the fraction of free (adsorbate-accessible) sorbent active sites ($1 - \theta$) and that of sites occupied by adsorbate (progesterone) molecules (θ). Of these three variables, only C could be determined in a direct manner, θ and ($1 - \theta$) being calculated from it. Consequently, only the partial order of the process in C could be directly determined from the experimental results; those in θ and ($1 - \theta$) were obtained by fitting the experimental results to the equations for previously reported models.

The results obtained in the experiments are shown in Fig. 1(a).

The overall process by which an adsorbable solute, A, in solution is retained by a solid sorbent, S, can be formulated as follows:

$$S(s) + A(dis.) \rightleftharpoons S - A(s) \tag{1}$$

the kinetic equation for which is

$$\frac{-d[A]}{dt} = \frac{-dC}{dt} = k_1 \cdot C^{n_1} \cdot (1-\theta)^{n_2} - k_2 \cdot \theta^{n_3} \tag{2}$$

n_1 in the previous equation was determined using the so-called "differential method" (Letort, 1937, 1942), based on which $\theta = 0$ and $(1 - \theta) = 1$ at $t = 0$ and any value of n_2 and n_3. Therefore, Eq. (2) simplifies to

$$\left(\frac{-dC}{dt}\right)_0 = k_1 \cdot C_0^n \tag{3}$$

where $n = n_1$, so $n = 1$.

The goodness of the n_1 value thus determined was assessed and the most likely values for n_2 and n_3 were determined using the so-called integral method (Valenzuela, 1994), which compares experimental results with those provided by an iterative procedure involving application of the equation resulting from integration of Eq. (2) at different n_2 and n_3 values, and $n_1 = 1$. The best results were obtained with $n_1 = n_2 = n_3 = 1$, at which Eq. (2) can be rewritten as

$$\frac{-dC}{dt} = k_1 \cdot C \cdot (1-\theta) - k_2 \cdot \theta \tag{4}$$

From this it follows that, at equilibrium,

$$k_1 \cdot C_e \cdot (1-\theta) = k_2 \cdot \theta \tag{5}$$

where C_e denotes the progesterone concentration at equilibrium ($t \geq t_{\mathrm{eq}}$).

If, on the other hand, one assumes $\theta = 1$ at equilibrium, then

$$\theta = \frac{C_0 - C}{C_0 - C_e} \tag{6}$$

$$1 - \theta = \frac{C - C_e}{C_0 - C_e} \tag{7}$$

Substitution of Eqs. (5)–(7) into (4), and rearrangement, yields (Stitou, 1998)

$$\begin{aligned}\frac{-dC}{dt} &= \frac{k_1}{C_0 - C_e} \cdot \left(C^2 - 2 \cdot C_e \cdot C + C_e^2\right) \\ &= \frac{k_1}{C_0 - C_e} \cdot (C - C_e)^2 \end{aligned} \tag{8}$$

From Eq. (8) it clearly follows that, even though $n_1 = n_2 = n_3 = 1$, experimental (C, t) data—or at least some of them—occasionally can be satisfactorily fitted to a kinetics of $n_1 = 2$:

$$\frac{-dC}{dt} = k_1 \cdot C^2 \cdot (1-\theta) - k_2 \cdot \theta \tag{9}$$

This has been found in examining many processes such as that studied in this work, both by other authors and by us. In theory, this seemingly anomalous fitting to Eq. (9) is especially likely in the initial portion of the (C, t) curve (where $C \sim C_0$) and in the immediate vicinity of equilibrium (Stitou, 1998) (where $C \sim C_e$). Integration of Eq. (8) between 0 and t (t values), and from C_0 to C, yields

$$C = \frac{C_0 + k_1 \cdot C_e \cdot t}{1 + k_1 \cdot t} \tag{10}$$

from which the following expression can be readily derived:

$$\sqrt{\frac{1}{(-dC/dt)}} = \sqrt{\frac{1}{k_1 \cdot (C_0 - C_e)}} + \sqrt{\frac{1}{(C_0 - C_e)}} \cdot t \tag{11}$$

Based on Eq. (11), plotting experimental $[1/(-dC/dt)]^{1/2}$ vs. t data should give a single straight line. However, our experimental values at the shorter times exhibit a negative deviation from the straight lines predicted by Eq. (11) in all cases; this suggests that either the overall process conforms to a kinetics other than that of Eq. (4) or the points in question deviate for some reason exclusively due to this particular sorbent that lacks practical significance with others (e.g. in the retention of progesterone by carbon black (Stitou, 1998)), especially at long times.

Equation (11) allows one to calculate k_1, which was used as the starting point to fit the experimental (C, t) results to Eq. (10). The fitting, carried out using an iterative procedure, provided refined k_1 values that resulted in closer agreement between calculated and experimental C values. Fitting to Eq. (10) provided the results shown as a solid line in Fig. 1; as can be seen, such a line only fitted properly the C values obtained at the longer times; those found at the shorter times (broken line) fitted to the following equation more closely:

$$\frac{1}{C} + \frac{1}{C_e} \cdot \ln\left(\frac{C - C_e}{C}\right) = \frac{1}{C_0} + \frac{1}{C_e} \cdot \ln\left(\frac{C_0 - C_e}{C_0}\right) - \frac{k_1 \cdot C_e}{C_0 - C_e} \cdot t \qquad (12)$$

This expression was obtained by integrating the expression resulting from substitution of $(1 - \theta)$ by its value in Eq. (7) into the expression for an irreversible adsorption process with $n_1 = 2$:

$$\frac{-dC}{dt} = k_1 \cdot C^2 \cdot (1 - \theta) \qquad (13)$$

Equation (13) can be derived from Eq. (9) on the assumption that, at very short times, the product $k_2 \cdot \theta$ will be zero. Various potential sources of this behaviour were examined and the most plausible explanation was found to be the previous one, i.e. that, in specific cases and conditions, the experimental (C, t) results—or part thereof—for a reversible adsorption process of order $n_1 = 1$ fit a rate equation with $n_1 = 2$.

The first portion of the (C, t) kinetic curves (Fig. 1(a)) was found to actually fit Eq. (13) better than Eq. (9), which corresponds to a reversible process of partial order $n_1 = 2$.

The irreversible character suggested by the fact that the (C, t) data for the initial portion of the kinetic curves conform to Eq. (13) leads us to believe that—under our working conditions—the desorption rate is negligible compared to the adsorption rate. This might be the result of the formation of very strong S—A bonds (through chemical reaction or strong chemisorption) and/or the diffusion of adsorbed A molecules to the outside of the solid sorbent (i.e. chemisorption and/or diffusion) being strongly hindered.

4.1.2. Second Experiment Series. The second series of experiments was intended to provide information about the equilibrium time (t_{eq}), specific rates of adsorption (k_1), thermodynamic activation functions for the adsorption process and the factors determining the adsorption kinetics.

The experiments provided the results shown in Fig. 1(b). As can be seen, the (C, t) kinetic curves—particularly that obtained at 10°C—exhibit a potentially significant slope change at intermediate times the origin of which might be the apparent change in n_1 with increase in θ.

As can also be seen from Fig. 1(b), the (C, t) kinetic curves never intersect because, on equal t, C decreases with increasing temperature. This suggests that the adsorption process is endothermal—which is confirmed by the equilibrium isotherms, n^s vs. (C/C_0)—, probably as a result of a marked contribution of adsorbate diffusion through sorbent pores to the adsorption process.

The kinetic curves of Fig. 1(b) were used to calculate the parameters described in the following sections, which were in turn employed to derive the information described in each.

4.1.2.1. Equilibrium Time. Table 1 lists the adsorption-desorption equilibrium times obtained.

4.1.2.2. Specific Adsorption Rate (k_1) and Thermodynamic Activation Functions. Using the same procedure as in Section 4.1.1 on the assumption of a reversible process with $n_1 = 1$ in C, Eqs. (10) and (11) provided the k_1 values given in Table 2; the apparent specific rates for a hypothetical process conforming to Eq. (13) were calculated in order to fit the initial portion of each kinetic curve but are not shown in the Table.

The adsorption rate values thus calculated, k_1, were used to derive the thermodynamic activation functions for the process. To this end, the following equation, based on Eyring's theory of the transition state (Levine,

Table 1. Adsorption-desorption equilibrium time.

	t_e	
T (°C)	(s)	(h)
10	170000	47.2
20	168000	46.6
30	166000	46.1
40	150000	41.6

Table 2. Specific adsorption rate (k_1).

T (°C)	$k_1 \cdot 10^{+4}$ (s^{-1})
10	0.58
20	0.79
30	0.99
40	1.31

Table 3. Thermodynamic activation functions for the adsorption process.

T(°C)	ΔH^* (kJ/mol)	ΔS^* (kJ/K·mol)	ΔG^* (kJ/mol)
10	41.6	−0.2	97.6
20			99.5
30			101.5
40			103.5

1996) was employed:

$$k = \frac{R \cdot T}{N \cdot h} \cdot e^{\left(\frac{\Delta S^*}{R}\right)} \cdot e^{\left(\frac{-\Delta H^*}{R \cdot T}\right)} \tag{14}$$

from which it follows that

$$\ln \frac{k}{T} = \ln \frac{R}{N \cdot h} + \frac{\Delta S^*}{R} - \frac{\Delta H^*}{R} \cdot \frac{1}{T} \tag{15}$$

Based on Eq. (15), the k_1 values in Table 2 were used to construct a ln (k_1/T) vs. $(1/T)$ plot. Analytical fitting of the data to the corresponding regression line allowed us to determine the ΔH^* and ΔS^* values listed in Table 3, which also includes ΔG^* values (calculated from the expression $\Delta G^* = \Delta H^* - T \cdot \Delta S^*$).

From the results of Table 3 it follows that, as usual, the formation of the activated species involved in the adsorption process is an endothermal, exoentropic step; because $\Delta S^* < 0$, the progesterone molecule in the activated species possesses fewer degrees of freedom than in solution (where it is in solvated form). On the other hand, the likelihood of the activated species being formed decreases with increasing temperature.

4.2. *The Potential Influence of Diffusion on the Kinetics of the Adsorption-Desorption Process*

4.2.1. Retention Rate Expressed as $d\theta/dt$. Consequences. The rate equation for process (1) can be formulated indifferently either as in Eq. (4) or as follows:

$$\frac{d\theta}{dt} = k_1' \cdot C \cdot (1 - \theta) - k_2' \cdot \theta \tag{16}$$

which is related to Eq. (4) via

$$\frac{d\theta}{dt} = \frac{1}{C_0 - C_e} \cdot \left(\frac{-dC}{dt}\right) \tag{17}$$

an expression that is the derivative of Eq. (6) with respect to t. Substitution of Eq. (4) into (17) yields

$$\frac{d\theta}{dt} = \frac{1}{C_0 - C_e} \cdot [k_1 \cdot C \cdot (1 - \theta) - k_2 \cdot \theta] \tag{18}$$

Substituting $k_1 \cdot \theta$ in Eq. (18) by its value in Eq. (5) and rearranging yields:

$$\frac{d\theta}{1 - \theta} = \frac{k_1}{C_0 - C_e} \cdot (C - C_e) \cdot dt \tag{19}$$

Equation (10) is solved for $(C - C_e)$. This is substituted into Eq. (19), subsequent integration of which from 0 to θ and from 0 to t yields:

$$\frac{1}{\theta} = 1 + \frac{1}{k_1} \cdot \frac{1}{t} \tag{20}$$

derivation of which yields:

$$\frac{1}{(d\theta/dt)} = \frac{1 + 2 \cdot k_1 \cdot t + k_1^2 \cdot t^2}{k_1} = \frac{1}{k_1} + 2 \cdot t + k_1 \cdot t^2 \tag{21}$$

Equation (21) allows one to draw two significant conclusions, namely:

> A plot of $[1/(d\theta/dt)]$ vs. t will be a curve of second order in t the intercept and the slope of the last portion (long times) of which will increase and decrease, respectively, with increasing k_1.
> At very small k_1 values, the intercept of the previous plot will be very high (especially at very short times) and the influence of the product $k_1 \cdot t^2$ will result in the points seemingly defining a straight line.

Based on these conclusions, the portion of the $[1/(d\theta/dt)]$ vs. t plot at short times may occasionally be assimilated to a straight line; at long times, however, the plot clearly corresponds to a second-order potential function. Therefore, the $[1/(d\theta/dt)]$ vs. t plot for reversible adsorption processes conforming to Eq. (16) occasionally consists of a "roughly straight" initial portion followed by an exponential (second-order polynomial) one. However, if virtually all active sites on the sorbent surface are free -which is the case at very short times—and exhibit a high affinity for the adsorbate, then retention rate $(d\theta/dt)$ may be anomalously high and $[1/(d\theta/dt)]$ anomalously low, giving rise to a negative deviation (with respect to a straight line) the magnitude of which will increase with increasing t. Occasionally, the—usually short—portion close to the inflection (intersect) point between the initial branch (the upper limit of the deviation) and that corresponding to strict fulfillment of Eq. (21) might seem a straight line, so the $[1/(d\theta/dt)]$ vs. t plot would apparently consist of up to three distinct portions, namely: an initial segment concave with respect to the x-axis, a straight segment and a convex one. These portions coincide with those hypothesized by Aharoni and coworkers (Aharoni and Ungarish, 1976, 1977a, 1977b; Aharoni et al., 1979; Aharoni and Suzin, 1982a, 1982b, 1982c) for the $[1/(d\theta/dt)]$ vs. t plot corresponding to a highly complex process.

The first of the previous portions—when present—fits the equation of Bangham (Bangham and Burt, 1924; Bangham and Sever, 1925), which can be formulated indifferently as

$$\ln \frac{1}{1-\theta} = k_b \cdot t^m \tag{22}$$

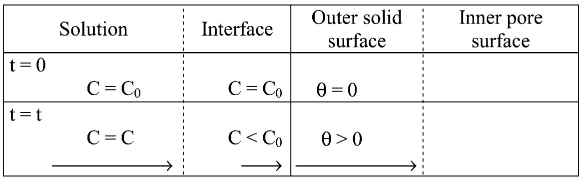
or

$$\theta = k_b \cdot t^m \tag{23}$$

based on which

$$\frac{d\theta}{1-\theta} = m \cdot k_b \cdot t^{m-1} \cdot dt \tag{24}$$

According to Bangham, when exponent m equals 0.5, the adsorption of further molecules inevitably entails their diffusion to the inside of the solid. However, Aharoni (1984) suggests that, in practice, the process can be assumed to be essentially diffusive in nature at $0.65 < m < 0.70$. m values below 0.5 are frequently encountered in chemisorption processes. Because the Bangham equation takes account of the influence of diffusion on the kinetics of the retention process, it should be considered in studying experimental results as adsorption processes always involve some diffusion—which is clearly apparent from Fig. 2.



	Solution	Interface	Outer solid surface	Inner pore surface
$t = 0$	$C = C_0$	$C = C_0$	$\theta = 0$	
$t = t$	$C = C$	$C < C_0$	$\theta > 0$	

Figure 2. Diffusion steps in a process involving adsorption alone.

In fact, Fig. 2 clearly reveals that, whether or not experimental (θ, t) data exhibit the above-described deviation at short times, at least the values obtained at the shorter times could be fitted to the Bangham equation; this would allow one to calculate m, which, according to Aharoni (1979), would provide a clue as to whether adsorption would take place essentially in a non-porous solid or—because it would occur in a porous one—it would be determined largely by diffusion. The second—seemingly straight—portion in the curve conforms to the empirical equation of Elovich (Low, 1960a, 1960b; Aharoni and Tompkins, 1970).

$$\theta = A + \frac{1}{b} \cdot \ln(t_0 + t) \tag{25}$$

where A, b and t_0 are three constants the last of which corresponds to a negative value of t where the adsorption rate has an infinite value.

According to Aharoni (Aharoni and Ungarish, 1976), the Elovich equation usually holds for the results of processes involving the chemisorption of an adsorbate on a sorbent with a heterogeneous surface. According to other authors, however, the Elovich equation cannot be applied unless other processes preceding those which obey such an equation are considered; in the light of this assertion, Taylor and Thon (1952) assumed the presence of a so-called pre-Elovich process of infinite rate starting and ending at $t = 0$. Also, Aharoni and Tompkins (1970) assumed the presence of pre-Elovich adsorption at an infinite rate that gradually evolved to an Elovich process. The previous two hypotheses are intended to account for the fact that the θ vs. ln $(t_0 + t)$ plot exhibits a convex deviation at the beginning of the process; physico-chemically, however, the previous assumptions (viz. an infinite rate) should be taken with caution. It should be borne in mind that the Elovich equation, in all its forms, is an empirical equation of limited validity—as admitted by Aharoni (1984) in the above-mentioned review—intended as an approximate substitute for Eq. (20) over an interval of relatively low values of t: in the absence of segment 1, $0 < t < t_p$; in its presence, $t_i < t < t_p$. To our minds, segment 2 suggests that the process develops consistently with the Langmuir equation and that it should be fitted to Eq. (20) (together with the data obtained at the longer times) rather than to Eq. (25).

Segment 3 can be assumed to appear when the retention process takes place in an irreversible manner, in conformance with the kinetic requirements that lead to the Langmuir equation; under these conditions, the

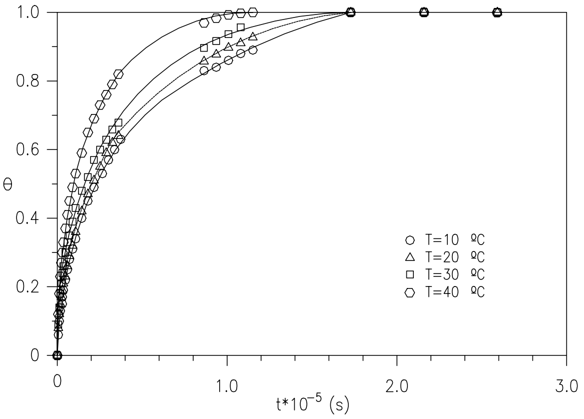


Figure 3. Plot of θ vs. t.

rate equation is given by Eq. (18), and the relationship between $[1/(d\theta/dt)]$ and time by Eq. (21).

Based on the foregoing, the results of Fig. 1(b) were used to calculate the corresponding θ, $(1/\theta)$ and $[1/(d\theta/dt)]$ values, which were employed to construct Figs. 3–5.

As can be seen from Fig. 3, the adsorption rate increases with increasing temperature; the fact that all (θ, t) curves converge at $\theta = 1$ is a result of using $\theta_e = (C_0 - C_e)/(C_0 - C_e) = 1$ in every single experiment. Based on Eq. (20), a plot of $1/\theta$ vs. $1/t$ (Fig. 4) should consist of straight lines the slopes of which will increase with increasing temperature; this can be assumed to indicate that adsorption takes place in a reversible manner and conforms to the Langmuir equation. With AC-Merck (a highly porous, essentially microporous solid), some of the points obtained at the shorter times exhibit a negative deviation from the straight line observed at the longer times; such points could be studied in the light of the Bangham equation in order to derive complementary information. The shapes of the lines in Fig. 5 are consistent with a polynomial function of second order in t [Eq. (21)]. The negative deviations observed at the shorter times might arise from the fact that AC-Merck is a highly porous solid—an essentially microporous one- so it must result in a substantial contribution of diffusion to the retention kinetics. All other information provided by Fig. 5 virtually coincides with that contained in the previous one. As noted earlier, fitting the experimental results to the Bangham Eq. (22) allows one to determine m (Table 4), which provides and indication of the influence of diffusion on the adsorption process.

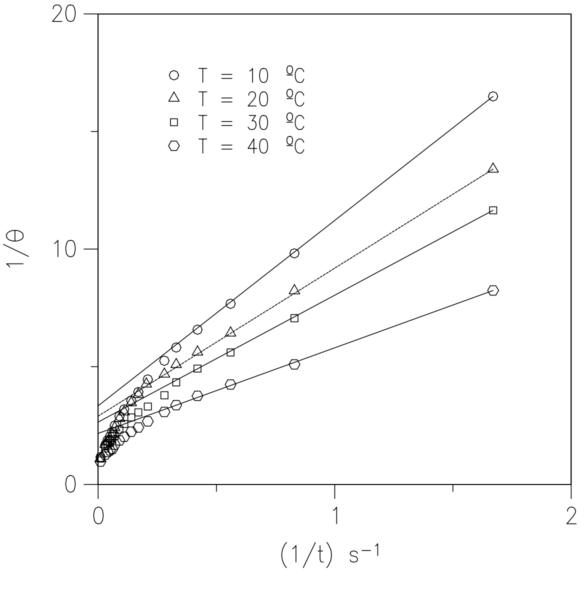


Figure 4. Plot of $1/\theta$ vs. $1/t$.

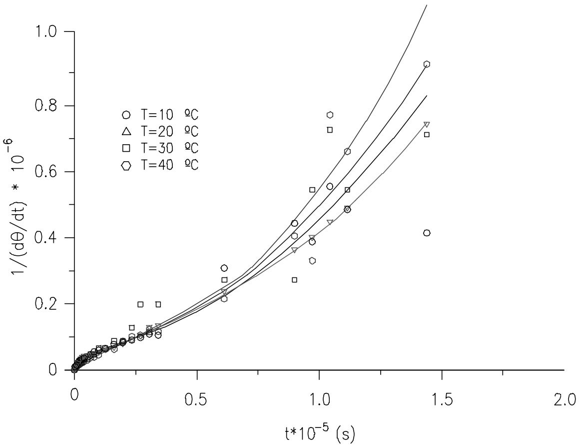


Figure 5. Plot of $[1/(d\theta/dt)]$ vs. t.

Based on the m values thus calculated, diffusion must exert a substantial effect on the kinetics of progesterone adsorption by AC-Merck. Also, m decreases with increasing temperature, consistent with the fact

Table 4. Values for coefficient m in Eq. (22) at different temperatures.

T	m	R^2
10	0.65	0.9970
20	0.61	0.9941
30	0.59	0.9964
40	0.59	0.9985

that the diffusion coefficient, D, and the diffusion rate, increase in the same direction, thereby—seemingly—diminishing the influence of diffusion—and of the solid porosity—on the adsorption kinetics.

The behaviour of AC-Merck in our experiments can be considered to be typical of an essentially microporous solid. This assertion is supported by several arguments. Thus, Eq. (22) was used by Espinola-Lara (1994) to study the retention of xanthine derivatives by activated carbons (AC-Merck included); this author found m values above 0.5 in all cases ($0.5 \leq m \leq 0.79$). According to Aharoni et al. (1979), this may indicate that diffusion of adsorbate molecules (xanthine derivatives) decisively influences the adsorption kinetics. Similar conclusions were reached by these authors in their study of the retention of phosphate ions by alumina; they obtained a value of 0.7 for coefficient m.

4.2.2. Diffusion of Adsorbate Molecules in Sorbent Particles. In order to examine the potential influence of diffusion on the retention kinetics we fitted our experimental data to the following equations:

Banerjee et al. (1997)

$$\frac{n_t^s}{n_e^s} = 1 - \left(\frac{6}{\pi^2}\right) \cdot \sum_{n=1}^{\infty} \frac{1}{n^2} \cdot \exp\left(-\frac{n^2 \cdot t}{\tau}\right) \tag{26}$$

where:

n_t^s = Moles of progesterone retained by adsorbent mass unity at a time, t.

n_e^s = Moles of progesterone retained by adsorbent mass unity at equilibrium ($t \geq t_e$).

and

$$\tau = \frac{r^2}{\pi^2 \cdot D} \tag{27}$$

r = Thickness of the slab or radium of the sphere through which diffusion takes place.

D = Diffusion coefficient.

Carman and Haul (1954)

$$\frac{n_t^s}{n_e^s} = (1+\alpha) \cdot \left\{1 - \frac{\nu_1}{\nu_1+\nu_2} \cdot e.erfc\left[\frac{3\cdot\nu_1}{\alpha} \cdot \left(\frac{D\cdot t}{a^2}\right)^{1/2}\right] - \frac{\nu_2}{\nu_1+\nu_2} \cdot e.erfc\left[\frac{-3\cdot\nu_2}{\alpha} \cdot \left(\frac{D\cdot t}{a^2}\right)^{1/2}\right]\right\} \tag{28}$$

where:

$$\nu_1 = \frac{1}{2} \cdot \left[\left(1 + \frac{4\cdot\alpha}{3}\right)^{1/2} + 1\right] \tag{29}$$

$$\nu_2 = \nu_1 - 1 \tag{30}$$

$$e.erfc(Z) = \exp(Z^2) \cdot erfc(Z) \tag{31}$$

$$\alpha = \frac{3 \cdot V}{4 \cdot \pi \cdot r^3} \tag{32}$$

and

r = Thickness of the slab or radium of the sphere through which diffusion takes place.

n_t^s = Moles of progesterone retained by adsorbent mass unity at a time, t.

n_e^s = Moles of progesterone retained by adsorbent mass unity at equilibrium ($t \geq t_e$).

Aharoni and Suzin (1982b)

$$\frac{n_t^s}{n_\infty} = 0.449 + \frac{1}{3.535} \cdot \ln\left(\frac{t}{t_p} + 0.333\right) \tag{33}$$

being

$$t_p = 0.349 \cdot \tau \tag{34}$$

$$\tau = \frac{r^2}{\pi^2 \cdot D} \tag{35}$$

r = Radium of the sphere through which diffusion takes place.

D = Diffusion coefficient.

The results provided by all these equations were consistent; by way of example, Table 5 gives those provided by that of Banerjee et al. (1997).

Table 5. Diffusion coefficients as determined using the equation of Banerjee et al. (1997).

	Initial segment		Final segment	
T (°C)	$D \cdot 10^{+8}$ (cm^2/S)	R^2	$D \cdot 10^{+8}$	R^2
10	5.37	0.9745	1.78	0.9932
20	6.37	0.9400	2.20	0.9914
30	15.90	0.9781	2.84	0.9902
40	20.85	0.9641	5.98	0.9941

As can be seen, the diffusion coefficient increased with increasing temperature, as the likely result of diffusion being activated by an increased temperature and a potential decrease in the size of the diffusing adsorbate molecules through partial solvation.

4.2.2.1. Activation Energies for the Diffusion Process. Provided it remains constant throughout the working temperature range, the activation energy, E_a, for the diffusion process can be calculated from

$$D = D_0 \cdot e^{\frac{-E_a}{R \cdot T}} \tag{36}$$

A plot of ln D vs. $1/T$ allowed us to calculate the activation energy and the frequency factor, D_0, which were found to be $E_a = 25.1$ kJ/mol and $D_0 = 8.3 \cdot 10^{-5}$ cm^2/s with the sphere model and $E_a = 26.9$ kJ/mol and $D_0 = 7.3 \cdot 10^{-4}$ cm^2/s with the layer model. It should be noted that the E_a values for the diffusion process are fairly close to those of the enthalpy of activation (ΔH^*) for the adsorption process (Table 3). This, again, suggests that the kinetics of progesterone adsorption by the sorbents used may be primarily determined by diffusion.

Nomenclature

AC	Activated carbon.
λ	Wavelenght (nm).
C	Solute concentration (mol$\cdot L^{-1}$)
t	Time (s).
θ	Fraction of sorbent active sites occupied by adsorbate molecules.
S	Solid sorbent.
A	Adsorbate solute.
k_1	Adsorption specific rate.
k_2	Desorption specific rate.
n_1	Partial order of the overal retention process in the adsorbate concentration in solution.
n_2	Partial order of the overal retention process in the fraction of free sorbent active sites.
n_3	Partial order of the overal retention process in the fraction of occupied sorbent active sites.
C_e	Adsorbate concentration in solution at equilibium time (mol$\cdot L^{-1}$).
C_0	Initial adsorbate concentration in solution (mol$\cdot L^{-1}$).
t_{eq}	Equilibrium time (s).
k	Adsorption rate.
R	Molar gas constant (J$\cdot$mol$\cdot$ K^{-1}).
T	Temperature (K).
N	Avogadro's number (mol^{-1}).
h	Plank's constant (J$\cdot$s^{-1}).
ΔS*	activation entropy (kJ$\cdot$mol$^{-1}\cdot$K^{-1}).
ΔH*	activation enthalpy (kJ$\cdot$mol^{-1}).
ΔG*	activation Gibbs free energy (kJ$\cdot$mol^{-1}).
k_b	specific rate in Bangham equation.
t_i	initial time (s).
t_p	inflection point in the $[1/(d\theta/dt)]$ curve (s).
E_a	activation energy (kJ$\cdot$mol^{-1}).
D_0	frequency factor (cm$^2\cdot$s^{-1}).

References

Aharoni, C. and F.C. Tompkins, *Adv. Catalysis*, **21**, 1 (1970).
Aharoni, C., *Adsorption Sciences & Technology*, **1**, 1–29 (1984).
Aharoni, C. and Y. Suzin, *J. Chem. Soc. Faraday Trans. I*, **78**, 2313–2320 (1982a).
Aharoni, C. and Y. Suzin, *J. Chem. Soc. Faraday Trans. I*, **78**, 2321–2327 (1982b).
Aharoni, C. and Y. Suzin, *J. Chem. Soc. Faraday Trans. I*, **78**, 2329–2336 (1982c).
Aharoni, C. and M. Ungarish, *J. C. S. Faraday Trans. I*, **72**, 400–408 (1976).
Aharoni, C. and M. Ungarish, *J. C. S. Faraday Trans. I*, **73**, 456–464 (1977a).
Aharoni, C. and M. Ungarish, *J. C. S. Faraday Trans. I*, **73**, 1943–1950 (1977b).
Aharoni, C. et al., *J. Chem. Techn. Biotechnol.*, **29**, 404–412 (1979).
Banerjee, K. et al., *Wat. Res.*, **31**, 249–261 (1997).
Bangham, D.H. and F.P. Burt, *Proc. Royal Soc.*, A**105**, 481 (1924).
Bangham, D.H. and W. Sever, *Phil. Mag.*, **49**, 938 (1925).
Bessarabov, D.G., *Membrane Technology*, **107**, 9–13 (1999).
Carman, P.C. and R. Haul, *Proc. Roy. Soc.*, **222A**, 109 (1954).
Cuna, M. et al., *Int. J. Pharm.*, **199**, 151–158 (2000).
Einmahl, S. et al., *Int. J. Pharm.*, **185**, 189–198 (1999).
Espinola-Lara, A., "Retencion de derivados de la xantina en carbones activos," PhD Thesis, University of Granada, 207, 1994.
Genc, L. et al., *Pharm. Acta Helv.*, **74**, 43–49 (1999).
Gonzalez-Martin, M.L., et al., *Langmuir*, **7**, 1296–1298 (1991).
Hart, M. et al., *J. Mol. Catal.*, **182/183**, 439–445 (2002).
Kentish, S.E. and G.W. Stevens, *Chemical Engineering Journal*, **84**, 149–159 (2001).
Lam, A. et al., *Micropor. Mesopor. Mater.*, **49**, 157–162 (2001).
Lee, B. et al., *Int. J. Pharm.*, **188**, 71–80 (2001).
Letort, M., *J. Chem. Phys.*, **34**, 206–210 (1937).
Letort, M., *Chim. France*, **9**, 1–8 (1942).
Levine, N.I., *Physical-Chemistry*, 4th ed., McGraw-Hill. Madrid, pp. 910–920, 1996.
Low, M.J.D., *Chem. Rev.*, **60**, 267 (1960).
Low, M.J.D., *Can. J. Chem.*, **38**, 588 (1960).
Maggi, L. et al., *Biomaterials*, **23**, 1113–1119 (2002).
Muhlbacher, J. et al., *J. Control. Release*, **76**, 51–58 (2001).
Obaidat, A.A. and R.M. Obaidat, *Eur. J. Pharm. Biopharm.*, **52**, 231–235 (2001).
Queiroz, A.C. et al., *Biomaterials*, **22**, 1393–1400 (2001).
Raffa, R.B. et al., *J. Phar. Toxic. Methods*, **43**, 205–210 (2000).
Sinfelt, J.H., *Surf. Sci.*, **500**, 923–946 (2002).

Stitou, M., “Retencion de progesterona por negros de carbon *y* por un carbon activado,” PhD Thesis; University of Granada, **55**, 1998.

Sutani, K. et al., *Radiat. Phys. Chem.*, **64**, 331–336 (2002).

Taylor, H.A. and N. Thon, *J. Amer. Chem. Soc.*, **74**, 4169 (1952).

Valenzuela, C., *Quimica General. Introduccion a la Quimica teorica.* pp. 419–445, Ed. Universidad de Salamanca, 1994.

Weiss, W. and W. Ranke, *Progress in Surface Science*, **70**, 1–151 (2002).

Zaffaroni, A., “New Approaches to Drug Administration,” Abstract of papers presented at the *31st International Congress of Pharmaceutical Sciences*, pp. 19–20, 1980.

Zhang, X. et al., *Int. J. Pharm.*, **235**, 43–50 (2002).