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ADSORPTION KINETICS OF DIBUCAINE AND TETRACAINE AT THE BENZENE/WATER INTERFACE STUDIED BY PENDANT DROP METHOD

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ABSTRACT. Dynamic interfacial tensions have been measured at the benzene/water interface in order to study the adsorption behavior of some local anesthetics, *namely* dibucaine and tetracaine, from the aqueous bulk solutions at the interface with pure benzene. For this purpose the pendant drop method was used. To describe the adsorption kinetics of these anesthetics at liquid interface, *a new theoretical approach* has been developed for the diffusion controlled adsorption of surfactants at the benzene/water interface. Therefore, various kinetic equations are tested and a *new diffusion controlled kinetic equation* is proposed, based on the Ward and Tordai diffusion equation associated with the two dimensional van der Waals state equation. This analysis provides a better understanding of the interfacial properties of adsorbed anesthetics layers at liquid interfaces. Diffusion coefficients, subsurface concentrations and molecular interaction parameters are derived from the experimental data and discussed in terms of the local anesthetics molecular structure.

Key words: adsorption kinetics at liquid interfaces; local anesthetics; dibucaine; tetracaine; diffusion coefficient; intermolecular interaction parameters

INTRODUCTION

The adsorption kinetics of various surfactants at liquid interfaces frequently plays a major role in many diverse processes, with a substantial scientific and technological impact, such as interfacial turbulence, foaming and wetting, as well as in biological processes [1-3]. Thus, the modeling [1-13] of the adsorption kinetics represents a key step to understand and improve processes which involve the stabilization of interfaces, such as the production of emulsions, drug delivery systems, pharmaceuticals and cosmetics, lubrication and oil recovery. Moreover, for basic research, the kinetics and mechanisms of the surfactant adsorption are also powerful tools to investigate the structure of adsorbed layers of surfactants [14-21] and the molecular interactions at the liquid interfaces [18-20].

If an interface is generated between a bulk aqueous solution, containing a surfactant, and a pure non-polar solvent, the adsorption of the surfactant at the interface occurs. This adsorption is not instantaneous since it implies the diffusion of surfactant molecules from the bulk solution towards the interface and at the interface the adsorption itself takes place by traversing a potential adsorption barrier. The time dependence of surfactant adsorption is complicated also by desorption processes.

If the rate of adsorption and desorption processes is high as compared to the diffusion, the adsorption may be considered as being diffusion-controlled. On the other hand, if the diffusion is assumed to be fast as compared to the transfer between the subsurface and interface, the process will be kinetic-controlled or barrier-controlled [1-3]. Both steps are taken into account in mixed kinetic controlled models.

Local anesthetics are widely used in the anesthesia processes and the molecular mechanism of their action is not fully understood. However, the anesthesia mechanism has been generally based on the anesthetics interactions with biological membranes. Several properties of plasma membranes seem to be modulated by anesthetics, such as, the lipid membrane structure [18-25], where the adsorption of anesthetics molecules at liquid interfaces is an essential step.

One of the goals of this study is to develop a kinetic model and to apply it to the adsorption of the two local anesthetics, namely dibucaine and tetracaine, from aqueous bulk solutions to the interface with pure benzene. The interest for this type of studies is recently increased because the oil/water interface (*e.g.,* benzene/water) is generally considered as a model for biological membranes.

THEORETICAL MODELS FOR ADSORPTION

Diffusion Controlled Adsorption Kinetics

The quantitative model for the adsorption kinetics controlled by diffusion of surfactants from the bulk solution to the freshly formed liquid interface was proposed first by the Ward and Tordai [4]:

$$\Gamma(t) = 2\left(\frac{D}{\pi}\right)^{1/2}\left\{c_0 t^{1/2} - \int_0^{t^{1/2}} c_s(t-\tau)\,d\tau^{1/2}\right\} \qquad (1)$$

where $\Gamma(t)$ represents the surfactant adsorption at the time t, D is the diffusion coefficient, π is 3,1415…, c_0 is the bulk solution concentration far from the liquid interface, c_s represents the subsurface concentration and τ is a dummy variable ranging from 0 to t.

The direct application of this theory is rather complicated. However, some *asymptotic approximations* were derived and commonly used [5], namely:

for t → 0, a *short time approximation* results:

$$\Gamma(t) = 2\ c_0 \left(\frac{D}{\pi}\right)^{1/2} t^{1/2} \tag{2}$$

and for t → ∞, a *long time approximation* [5 - 9] was derived, called also the *Joos relationship*:

$$\Delta\sigma(t)_{t\to\infty} = \sigma(t) - \sigma_e = \frac{RT\Gamma^2}{2c_0}\left(\frac{\pi}{Dt}\right)^{1/2} \tag{3}$$

Joos equation can be also written as:

$$\left[\frac{d\sigma(t)}{d\left(1/\sqrt{t}\right)}\right]_{t\to\infty} = \frac{RT\,\Gamma^2}{2\,c_0}\sqrt{\frac{\pi}{D}} \tag{4}$$

where R is the gas law constant, T is the temperature, $\sigma(t)$ and σ_e are the dynamic and the equilibrium surface tensions, respectively. The Eq. (3) is the theoretical basis for the extrapolation $\sigma_e = \sigma\ (t^{-1/2})_{t\to\infty}$ and the intersection with the ordinate is frequently used as the equilibrium interfacial tension value. The linear relationship between $\sigma(t)$ and $1/\sqrt{t}$ remains valid only for a restricted period of time and it indicates that the adsorption process is controlled by diffusion.

Eq. (1) takes into account only the diffusion process and as boundary condition the conservation of mass at the interface. Since the subsurface concentration c_s is unknown, Eq. (1) is not alone suitable to predict the surfactant adsorption with time. Frequently, one assumes a local equilibrium between the liquid interface and the *subsurface (i.e.,* the *adjacent layer* only a few angstroms away from the interface and still belonging to the bulk phase).

Usually, it has been assumed that the relation between the experimental interfacial pressure and the surfactant adsorption curves is better described by the *Frumkin isotherm* than by the *Langmuir isotherm*. It is argued that the *Langmuir isotherm* does not consider mutual interactions [9] among the adsorbed molecules, and therefore, the *Frumkin isotherm* might be better to describe the experimental curves because it introduces such intermolecular interactions [12].

On the other hand, it is well known that the surfactant adsorption can be transformed into the mean molecular area of the surfactant. Keeping this in mind, we can conclude that the experimental curves of the interfacial pressure as a function of the mean molecular area can be quite well described by the surface state equations because they introduce the intermolecular interactions within the adsorbed layers at liquid interface as an adjustable parameter [26-31].

Langmuir Adsorption Kinetics

In some cases it is found that experimental data cannot be understood by a simple diffusion and one must drop the boundary condition of the local equilibrium and replace it by the *Langmuir kinetic equation* [10, 11]:

$$\frac{d\Gamma}{dt} = k_1 c_s\left(1-\frac{\Gamma}{\Gamma_\infty}\right) - k_2\frac{\Gamma}{\Gamma_\infty} \qquad (5)$$

where, k_1 is the adsorption rate constant, k_2 is the desorption rate constant, and Γ_∞ represents the maximum adsorption or the maximum surface coverage by the surfactant molecules at the liquid interface.

In Eq. (5) the adsorption rate is presumed to be directly proportional with the subsurface concentration c_s and with the free interface. Also, Eq. (5) takes into account a desorption process, with a rate directly proportional with the interface occupied by the surfactant. The kinetic Eq. (5) assumes an ideal localized layer [10].

Eq. (5) is valid also at equilibrium, when $\frac{d\Gamma}{dt} = 0$, $\Gamma = \Gamma_e$ and $c_s = c_0$. With these equilibrium conditions Eq. (5) can then be rewritten as:

$$k_1 c_0 = \frac{k_1 c_0 + k_2}{\Gamma_\infty}\Gamma_e = k\Gamma_e \qquad (5')$$

For some cases, with surfactant concentration high enough, a diffusion equilibrium can be thought to be established, involving $c_s = c_0$. In this case, the combination [11] of Eqs. (5) and (5') results in:

$$\frac{d\Gamma}{dt} = -k(\Gamma - \Gamma_e)$$

relationship and by its integration yields:

$$\Delta\Gamma = \Delta\Gamma_0 e^{-kt} \qquad (6)$$

with $\Delta\Gamma = \Gamma - \Gamma_e$, $\Delta\Gamma_0 = \Gamma_0 - \Gamma_e$, where Γ_0 stands for the adsorption at t = 0, i.e. $\Gamma_0 = 0$.

In the situation that, the increase of adsorption is proportional to the decrease of interfacial tension, Eq. (6) may be written as:

$$\Delta\sigma = \Delta\sigma_0 \cdot e^{-kt} \qquad (6')$$

or in a logarithmic form gives:

$$\ln\frac{\Delta\sigma_0}{\Delta\sigma} = \ln\frac{\sigma_0 - \sigma_e}{\sigma - \sigma_e} = kt \qquad (7)$$

where σ, σ_e and σ_0 stand for the actual, for the equilibrium interfacial tension, and for the interfacial tension in the absence of the surfactant, respectively.

In the present paper two local anesthetics, viz. dibucaine and tetracaine have been studied by measuring dynamic interfacial tension values at the benzene/water interface and for the beginning Eq. (7) has been tested.

EXPERIMENTAL

The two local anesthetics used, dibucaine (2-butoxy-N-[2-(diethylamino) ethyl]-4-quinoline carboxamide hydrochloride) and tetracaine (4-butyl amino) benzoic acid 2-(dimethyl amino)ethyl ester hydrochloride), both synthetic commercial products of high purity (minimum 99%) were purchased from Sigma. Benzene pro-analysis was purchased from Merck. All chemicals were used without further purification. Twice-distilled water of pH 2 was used, containing 0.01 mole dm^{-3} hydrochloric acid. Volumetric aqueous solutions of HCl pro-analysis were purchased from Reactivul Bucharest.

In order to study the anesthetic adsorption at the same liquid interface the benzene/water of pH 2 systems were chosen. At pH 2, dibucaine and tetracaine may exist in three forms: uncharged (free base) and charged ones, *i.e.,* monocation (mono-protonated) and dication (diprotonated) molecules. The calculations show at pH 2, that the dibucaine is almost in mono-protonated form, and the tetracaine is a mixture of monocation (45%, mono-protonated) and dication (55 %, di- protonated) molecular species [32]. At pH 2, the molecular species of anesthetics existing in the aqueous solutions are completely insoluble in the bulk benzene phase. Therefore, any transport across the benzene/water interface can be neglected. The pH of aqueous solutions was constant during all experiments and it was measured by an MV-84 type pH-meter by using a glass electrode.

Dynamic interfacial tensions in the time range from 1 minute up to 90 minutes for the aqueous solutions (pH 2) of various anesthetic concentrations at the interface with pure benzene were measured by pendant drop method described by us elsewhere[21, 33]. The shape of drops was recorded on a highly quality film in order to determine the characteristic drop diameters. By using a computer program in Basic language the dynamic interfacial tension values were finally determined.

Experimental data obtained by the pendant drop technique were compared with the data obtained by ring method, that was described by us previously [34-36]. The agreement between the two methods is excellent and the deviations do not exceed the error of the individual method. The accuracy of interfacial tension measurements was ± 0.1 mN/m, in agreement with literature data [1,6]. All measurements were performed at constant temperature of 20 ± 0.1 ^{o}C.

RESULTS AND DISCUSSION

Dynamic interfacial tension values, together with the equilibrium values are presented in Tab. 1

In order to test the validity of Eq. (7), the left hand side, denoted as y, has been calculated by using experimental σ values presented in Tab. 1 as well as their equilibrium values σ_e corresponding to t = ∞, and by taking σ_0 = 34.7 mN/m.

The plot of y *vs*. t exhibits a quite good linearity, although the straight lines do not pass through the origin of the coordinate system, *i.e*., actually Eq. (7) is of the following form:

$$y = \ln\frac{\sigma_0 - \sigma_e}{\sigma - \sigma_e} = a + kt \qquad (7')$$

By performing a linear regression, the parameters *a* and *k* have been determined. Results are presented, together with the correlation coefficient, in Table 2. In the last column n indicates the number of experimental points used in the linear regression.

Table 1

Dynamic interfacial tensions (mN/m) at the benzene/water interface

Anesthetics t, min	Dibucaine			Tetracaine		
	C_o, mole dm^{-3}					
	0.001	0.005	0.010	0.001	0.005	0.010
1	31.9	28.7	26.4	32.8	31.1	29.9
2	31.1	27.1	24.25	31.85	30.53	28.95
3	30.2	25.4	22.2	31.7	29.2	27.5
4	29.7	24.6	20.8	31.3	28.75	27.0
5	29.2	23.5	20.0	31.1	28.2	26.2
6	28.8	23.1	19.2	30.8	27.72	25.9
7	28.4	22.1	18.6	30.7	27.5	25.3
8	28.1	21.85	18.15	30.5	27.2	25.1
9	27.8	21.2	17.5	30.3	27.0	24.7
10	27.5	20.9	17.3	30.1	26.7	24.5
11	27.3	20.4	16.8	30.0	26.6	24.3
12	27.0	20.1	16.6	29.9	26.4	24.0
13	26.9	19.7	16.2	29.8	26.3	23.9
14	26.6	19.4	16.0	29.6	26.1	23.8
15	26.5	19.2	15.8	29.5	26.0	23.7
∞	26.0	18.6	15.6	29.3	25.6	23.3

Table 2.

The *a* and *k* parameters of Eq. (7').

Anesthetics	C_0 mole dm^{-3}	a	k min^{-1}	r	n
Dibucaine	0.001	0.152	0.169	0.9932	15
	0.005	0.202	0.190	0.9918	15
	0.010	0.284	0.234	0.9909	14
Tetracaine	0.001	0.342	0.154	0.9966	13
	0.005	0.340	0.176	0.9974	14
	0.010	0.330	0.199	0.9984	15

As seen from Tab. 2, the a values are rather far from zero. This means that the *basic hypothesis* used at the deriving of Eq. (7) is not perfectly valid, presumably the diffusion equilibrium is not yet established and the boundary condition $c_s = c_0$ is not fulfilled. Nevertheless, from the k values reported in Tab. 2, some conclusions can be drawn. As seen, with the increasing C_0 the obtained k values are also increased. According to Eq. (5') written as follows:

$$k = \frac{k_1}{\Gamma_\infty} C_0 + \frac{k_2}{\Gamma_\infty} \tag{8}$$

it is clear that the plot of k *vs*. C_0 exhibits indeed an acceptable linearity. The k_1/Γ_∞ and k_2/Γ_∞ values and the corresponding correlation coefficients are presented in Table 3.

Table 3.

Relative adsorption and desorption rate constants derived from *k* values, given in Table 2.

Anesthetics	k_1/Γ_∞ $dm^3\ mole^{-1}\ min^{-1}$	k_2/Γ_∞ min^{-1}	r
Dibucaine	7.25	0.159	0.9914
Tetracaine	4.99	0.149	0.9988

Inspection of Tab. 3 shows the quite good agreement with Eq. (8). The relative rate constant values are rather reasonable. The k_1 values are much higher than the k_2 ones, pleading for a high interfacial activity of these local anesthetics in good agreement with their behavior at liquid interfaces.

In the Ward and Tordai Eq. (1) the second term, the back diffusion integral being neglected, one obtains:

$$\Gamma = 2\left(\frac{D}{\pi}\right)^{1/2} \cdot c_0 t^{1/2} \tag{9}$$

It is to be noted that the Eq. (9) coincides with the *short time approximation* given by the Eq. (2).

At the other hand, by performing an integration by parts of Eq. (1), and by neglecting the remaining integral, one obtains:

$$\Gamma = 2(c_0 - c_s)\left(\frac{D}{\pi}\right)^{1/2} t^{1/2} \tag{10}$$

Clearly, both Eqs. (9) and (10) suggest a proportionality of the adsorption with $t^{1/2}$.

In order to establish a correlation between the adsorption and the interfacial tension σ or the interfacial pressure Π, frequently, the surface state equation:

$$\Pi A = kT \text{ or } \Pi = \Gamma kT \tag{11}$$

is used, which is the two dimensional analog of the perfect gas state equation. A represents the molecular area (A = 1/Γ) and Γ is the surfactant adsorption expressed in molecules per unit interface.

By combining Eq. (11) with Eqs. (9) and (10), respectively, one obtains:

$$\Pi = 2kT\left(\frac{D}{\pi}\right)^{1/2} c_0 t^{1/2} \tag{12}$$

and

$$\Pi = 2kT\left(\frac{D}{\pi}\right)^{1/2} (c_0 - c_s)\, t^{1/2} \tag{13}$$

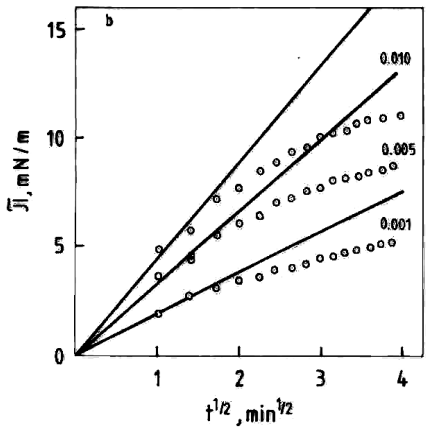

Fig. 1. Experimental dynamic interfacial pressures of dibucaine aqueous solutions as a function of $t^{1/2}$ at the interface benzene/ water. Figures indicate the dibucaine bulk concentration C_0 in mole dm^{-3}.

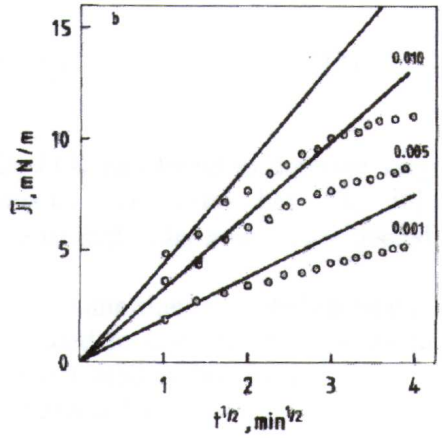

Fig. 2. Experimental dynamic interfacial pressures of tetracaine aqueous solutions as a function of $t^{1/2}$ at the benzene/water interface. Figures indicate the tetracaine bulk concentration C_0 in mole dm^{-3}.

In order to test the validity of Eqs. (12) an (13) we performed an analysis of the experimental Π vs. $t^{1/2}$ data. Experimental Π values, calculated from σ_0 and from σ values given in Tab. 1, are presented in Figs. 1-2, plotted vs. $t^{1/2}$ values, for dibucaine and tetracaine, respectively.

If the relations (12) or (13) were valid, the Π *vs.* $t^{1/2}$ curves would exhibit a linear portion at least at small t values. This is why the tangency to the curve for t = 0 was constructed in Figs. 1 and 2. It is to be noted that the experimental curves exhibit an important negative deviation from these straight lines. This means that a better approach is needed to describe the behavior of anesthetics at the oil/water interfaces.

Deriving of a New Diffusion Controlled Kinetic Equation

Eqs. (12) and (13) have been obtained by presuming the state equation (11) to be valid. But interfacial monolayers do not obey Eq. (11). One of the best state equations [21, 26-31] proposed for the surfactant monolayers at the liquid interfaces is of the following form:

$$\left(\Pi + \frac{\alpha}{A^{3/2}}\right)(A - A_0) = kT \tag{14}$$

where A stands for the mean molecular area. Eq. (14) was found to describe very well the compression isotherms of miscellaneous monolayers [21, 28, 30], especially if the interaction parameter α and the own molecular area A_0 are treated as adjustable parameters.

Because the equilibrium data for another local anesthetics, *namely* procaine [30], are well described by the Eq. (14) we decided to consider this model to describe the experimental data for the local anesthetics used in this study.

From the state equation (14), Π may be expressed as:

$$\Pi = \frac{kT}{A - A_0} - \frac{\alpha}{A^{3/2}} = \frac{kT\Gamma}{1 - \Gamma A_0} - \alpha\Gamma^{3/2} \tag{15}$$

Let us denote:

$$x = 2(c_0 - c_s)\left(\frac{D}{\pi}\right)^{1/2} \tag{16}$$

Eq. (10) may be written as $\Gamma = xt^{1/2}$. Thus, by combining Eqs. (10), (14) and (16), one obtains:

$$\Pi = \frac{kTxt^{1/2}}{1 - A_0 xt^{1/2}} - \alpha x^{3/2} t^{3/4} = kTx\left[\frac{t^{1/2}}{1 - A_0 xt^{1/2}} - \frac{\alpha x^{1/2}}{kT} t^{3/4}\right] \tag{17}$$

One may expect Eq. (17) to describe better the time dependence of Π, than Eq. (13) does.

In order to study the properties and possibilities of Eq. (17), let us introduce a reduced time scale. If in an experiment Π has been followed from t = 0 up to a maximum time t_m, a reduced time can be defined as:

$$\tau = \frac{t}{t_m} \tag{18}$$

By combining Eqs. (17) and (18) one obtains:

$$\Pi = kTxt_m^{1/2}\left[\frac{\tau^{1/2}}{1-A_0xt_m^{1/2}\tau^{1/2}} - \frac{\alpha x^{1/2}}{kT}t_m^{1/4}\tau^{3/4}\right] \tag{19}$$

This equation may be written as:

$$\Pi = a\left[\frac{\tau^{1/2}}{1-b\tau^{1/2}} - c\tau^{3/4}\right] = a\varphi(\tau) \tag{20}$$

with:

$$a = 2kT(c_0 - c_s)\left(\frac{Dt_m}{\pi}\right)^{1/2}$$

$$b = 2A_0(c_0 - c_s)\left(\frac{Dt_m}{\pi}\right)^{1/2}$$

$$c = \frac{2^{1/2}\alpha(c_0 - c_s)^{1/2}}{kT}\left(\frac{Dt_m}{\pi}\right)^{1/4}$$

From the Eq. (20), of the parameters *a*, *b* and *c*, one obtains:

$$D = \left[\frac{a}{2kT(c_0 - c_s)}\right]^2 \frac{\pi}{t_m};\ A_0 = \frac{kTb}{a};\ \alpha = \frac{c}{a^{1/2}}(kT)^{3/2} \tag{21}$$

It is clear that, if $t = t_m$, one has $\tau = 1$ and Eq. (20) becomes:

$$\Pi_m = a\varphi(1) = a\left[\frac{1}{1-b} - c\right] \tag{22}$$

Let us introduce also for the interfacial pressure a reduced scale:

$$\Pi^* = \frac{\Pi}{\Pi_m} \tag{23}$$

which according to Eqs. (20) and (22) can be expressed as:

$$\Pi^* = \frac{\Pi}{\Pi_m} = \frac{\varphi(\tau)}{\varphi(1)} \tag{24}$$

Thus one obtains finally for the time dependence of the interfacial pressure:

$$\Pi = \frac{\Pi_m}{\varphi(1)}\varphi(\tau) \tag{25}$$

By comparing Eq. (25) with Eq. (20) it is obvious that:

$$a = \frac{\Pi_m}{\varphi(1)} \tag{26}$$

In order to check the possibilities of Eq. (25), we studied the influence of the parameters *b* and *c* upon the shape of the Π/a *vs*. τ and Π^* *vs.* τ curves. For this purpose theoretic curves have been constructed. Some examples are given in Fig. 3.

In Fig. 3 the influence of parameter *c* upon the shape of the $\Pi/\underline{a} = \varphi(\tau)$ *vs*. τ curves is illustrated, by taking the *b* = 0.1, as a constant value. The dashed line curve is the $\tau^{1/2}$ *vs.* τ plot, corresponding to the validity of Eqs. (12) or (13).

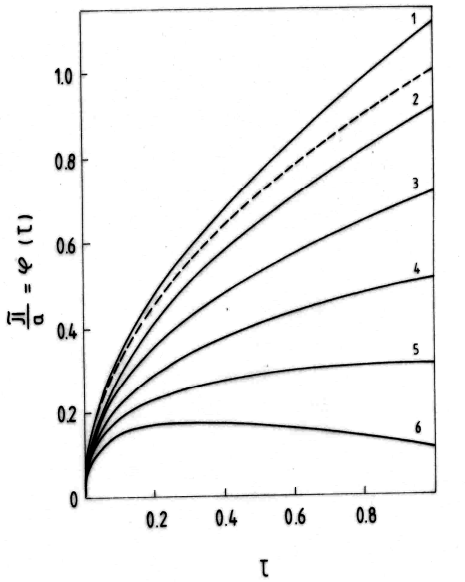

Fig. 3. Influence of the c parameter upon the theoretical $\varphi(\tau)$ *vs*. τ curves; b = 0.1; curve (1): c 0; (2) 0.2; (3) 0.4; (4) 0.6; (5) 0.8; (6) 1.0. Dashed line curve: b = c = 0.

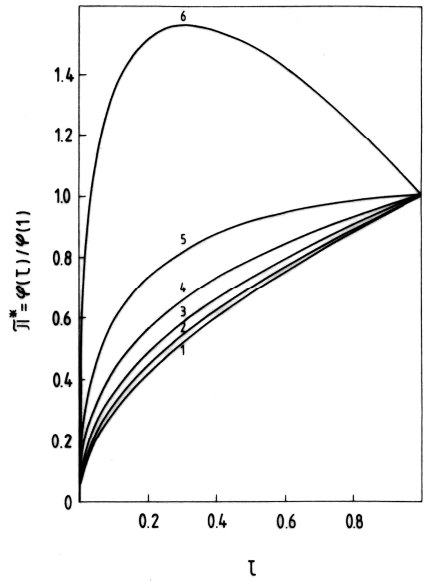

Fig. 4. Influence of the c parameter upon the theoretical Π^* *vs*. τ curves. b and c values as in Fig. 3

Since parameters *b* and *c* influence also the $\varphi(1)$ value, the shift of the theoretical curves makes their comparison more difficult. The influence of these parameters is more clear if the $\Pi^* = \varphi(\tau)/\varphi(1)$ *vs.* τ curves are constructed. This is shown in Fig. 4.

It is worth mentioning that for *b* = 0.1 and *c* = 1.0 both $\varphi(\tau)$ and Π^* exhibit a maximum for about $\tau = 0.3$. This would imply the appearance of a maximum interfacial pressure at a certain time, followed by the diminution of Π. This is of course unrealistic. It is obvious that not all *b* – *c* pairs can describe real adsorption kinetics. Although not all $\varphi(\tau)$ functions correspond to real behavior of surfactants the main feature is that in the case of diffusion controlled adsorption the own molecular area A_0 and the intermolecular interactions expressed by the parameter α may account for both positive and negative deviations from the $t^{1/2}$ law.

The deviation of the reduced surface pressure from the $t^{1/2}$ law may be expressed by the function:

$$\Delta = \frac{\varphi(\tau)}{\varphi(1)} - \tau^{1/2} \tag{27}$$

The influence of the *c* parameter upon the theoretical Δ *vs.* τ curves is illustrated in Fig. 5.

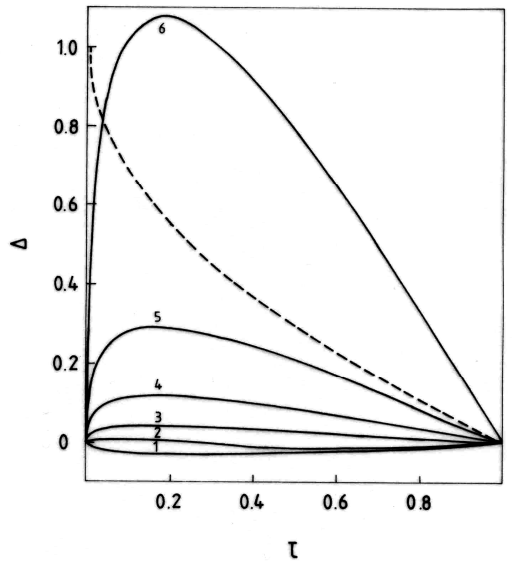

Fig. 5. Influence of the c parameter upon the theoretical Δ *vs*. τ curves.
b and c parameters as in Fig. 3.

It is obvious that both positive and negative Δ values may appear and the deviation from the $t^{1/2}$ law may be very important.

In real systems, as seen in Figs. 1 and 2 with increasing time negative deviations from the $t^{1/2}$ law appear. In a Π^* *vs.* τ plot this means that the curve is more convex as compared to $\tau^{1/2}$, *i.e.* Δ has positive values. Consequently, negative Δ values indicate unrealistic theoretical curves. Even

the positive values have an upper limit, it is easy to see that the Π vs. t curve passes through a maximum if $\Delta > 1 - \tau^{1/2}$. The dashed line curve in Fig. 5 indicates this upper limit $\Delta = 1 - \tau^{1/2}$.

Adsorption Dynamics of Dibucaine and Tetracaine at the Benzene/ Water Interface

In order to derive the parameters *a*, *b* and *c* we adopted the following procedure of working up the experimental data given in Tab. 4. We choose t_m = 15 min in the case of both local anesthetics and calculated for each experimental point the reduced parameters τ and Π^*. Further we calculated, for the found τ values, the theoretical Π^* values by taking certain b – c pairs. In the *first approach* we took *b* = 0 and calculated theoretical Π^* values for different c ones. In the case of each *c* value the *standard deviation* (noted Δ) of the experimental Π^* values from the theoretical ones was calculated. By means of a systematic variation of *c* the minimum standard deviation was sought for.

Calculations were repeated, then, for other *b* values too. Thus, a *double minimization* of the standard deviation has been performed and the *b – c* pair ensuring the least value for the standard deviation has been taken for the most realistic parameter values. This calculation procedure is visualized in Fig. 6, for the aqueous solution of tetracaine for C_0 of 0.001 mole dm^{-3} at the interface with pure benzene.

Curve 1 gives the minimum standard deviation obtained for different *b* values presumed and curve 2 indicates the corresponding *c* value. Let us take *e.g. b* = 0.062. Eq. (24) allows us to calculate theoretical Π^* values corresponding to *b* = 0.062 and to different *c* values. In each case, *i.e.* with each *c* value presumed, the standard deviation:

$$\Delta = \sqrt{\frac{1}{n}\sum (\Pi_t^* - \Pi_e^*)^2} \qquad (28)$$

is calculated where n stands for the number of points used, Π_t^* and Π_e^* stand for the theoretical and for the experimental reduced interfacial pressure, respectively. By trying different c values, one observes that the standard deviation will be the less for *c* = 0.559, *viz*. it will be equal to Δ = 0.00473. Thus, we obtained a point on curve 1 and a point on curve 2.

By repeating these calculations for other b values, eventually one obtains the whole curves 1 and 2. As seen, curve 1 has a minimum (indicated by a downward vertical arrow), corresponding to *b* = 0.0697; this *minimum of* the Δ value is ensured by the *c* value equal to 0.571 (indicated on the curve 2 by an upward vertical arrow).

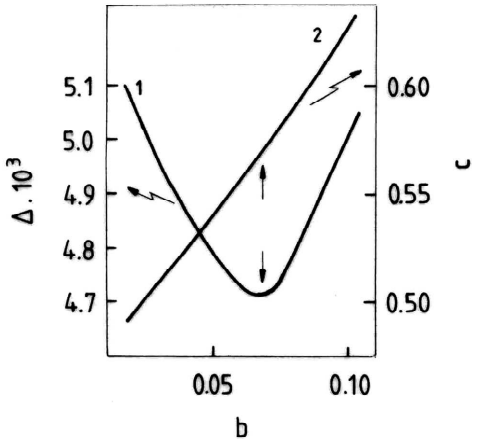

Fig. 6. Deriving of b and c parameters for tetracaine aqueous solution of C_0=0.001 mole dm^{-3} at the interface with pure benzene.

Table 4.

Parameters of Eq. (20) derived from our experimental data. C_0 is expressed in mole dm^{-3}.

Anesthetics	C_0	t_m min	Π_m mN/m	φ(1)	a	b	c	Δ mN/m
	0.001	15	8.2	0.5926	13.84	0	0.407	0.0028
Dibucaine	0.005	15	15.5	0.4863	31.87	0.0039	0.518	0.0029
	0.010	15	18.9	0.4096	46.14	0	0.590	0.0014
	0.001	15	5.2	0.5042	10.31	0.0697	0.571	0.0047
Tetracaine	0.005	15	8.7	0.4328	20.10	0.0465	0.616	0.0025
	0.010	15	11.0	0.4135	26.60	0	0.586	0.0028

By using the obtained *b* and *c* values, φ(1) may be easily calculated according to Eq. (22), as well as the parameter *a* by means of Eq. (26). Results obtained by means of this procedure are presented in Tab. 4.

The parameter values given in Tab. 4 allow us to construct by means of Eq. (20) theoretical Π *vs*. t curves. These curves are given in Figs. 7 and 8 as full line curves. Thus, it is clear that Eq. (20) describes very well the experimental curves.

Inspection of Tab. 4 shows that with a given anesthetic the *a* parameter increases with increasing bulk concentration C_0. The *c* parameter shows also a clear increasing tendency. The *b* parameter has very small values, frequently vanishing ones and cannot be correlated with C_0 values.

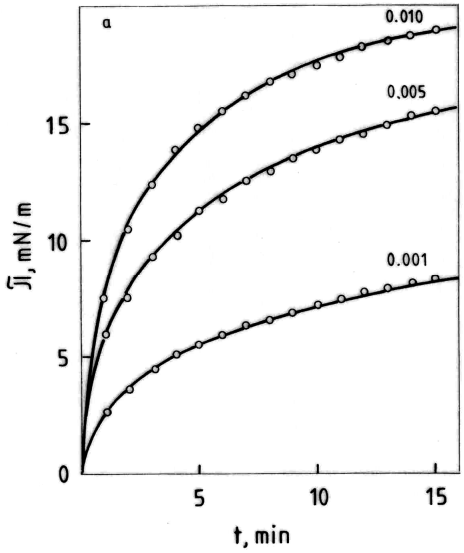

Fig. 7. Data as in Fig.1 represented function of time.

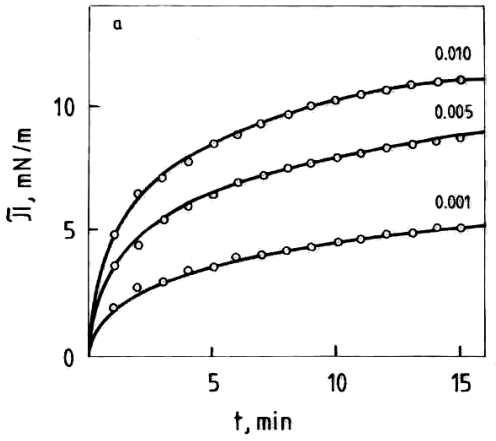

Fig. 8. Data as in Fig. 2 represented as a as a function of time.

With respect to the meaning of the parameter *a*, according to Eq. (21), it allows us to calculate the diffusion coefficient D. Let us assume as a *first approach* that $C_s = 0$ at all bulk concentrations C_0. By taking into account that c_0 represents the bulk concentration expressed in molecules cm^{-3}, and C_0 is given in mole dm^{-3}, one has $c_0 = C_0 \cdot 10^{-3} N_A$, where N_A stands for Avogadro's constant. Thus, Eq. (21) becomes:

$$D = \left(\frac{a}{2kT \cdot 10^{-3} \cdot N_A \cdot C_0} \right)^2 \frac{\pi}{t_m} \qquad (29)$$

The diffusion coefficients calculated by means of Eq. (29) and by using the a values given in Tab. 4, are presented in Tab. 5.

By inspecting the D values (Tab 5) one can see that the D values are of the same order of magnitude and show a slight decreasing tendency with increasing bulk concentration. Moreover, in the case of aqueous anesthetic solutions of the same anesthetic concentration of 0.001 mole dm^{-3}, the D value of dibucaine is less than two times higher than that of tetracaine.

Table 5.

Diffusion coefficients D, subsurface concentrations C_s and interaction parameters α calculated from the *a* and *c* parameters of Eq. (20).

Anesthetics	C_0 mole dm^{-3}	$D \cdot 10^{10}$ $cm^2 \cdot s^{-1}$	$D_0 \cdot 10^{10}$ $cm^2 \cdot s^{-1}$	$C_s \cdot 10^3$ mole dm^{-3}	$\alpha \cdot 10^{22}$ dyne·cm^2
Dibucaine	0.001	2.84	2.84	0	8.90
	0.005	0.602		2.70	7.46
	0.010	0.316		6.67	7.07
Tetracaine	0.001	1.58	1.58	0	14.4
	0.005	0.240		3.05	11.2
	0.010	0.105		7.42	9.25

As a *second approach* we shall presume that this relation $C_s = 0$ is valid only in the case of anesthetic aqueous solutions of $C_0 = 0.001$ mole dm^{-3} and that the C_s value increases with increasing bulk concentration C_0, but the diffusion coefficient remains the same D_0 as obtained from the *a* value for the aqueous anesthetic solution of 0.001 mole dm^{-3}. In this assumption C_s may be calculated from Eq. (21) and one obtains:

$$C_s = C_0 - \frac{\pi^{1/2} \cdot a}{2kT \cdot 10^{-3} \cdot N_A \cdot D_0^{1/2} \cdot t_m^{1/2}} \qquad (30)$$

Results are presented in the same Tab. 5. The C_s values obtained seem to be quite realistic and the C_s values increase systematically with increasing C_0 values.

Eq. (21) allows also the calculation of the interaction parameter α from the parameters *a* and *c* of Eq. (20). Results are presented also in Tab. 5. As seen one does not obtain the same value in the case of differing bulk concentrations, *viz.* a decreasing tendency is observed with increasing C_0. This might be due to experimental errors, to the interfacial active impurities, and/or to the imperfection of the model. However, by calculating the mean α values, some properties of the adsorbed monolayers of anesthetics at the benzene/water interface can be evidenced. Therefore, the mean α value is calculated; for dibucaine is $\alpha = 0.78.10^{-21}$ dyne·cm^2, and for tetracaine is $\alpha = 1.16.10^{-21}$ dyne·cm^2.

The higher α value of tetracaine as compared to that of dibucaine seems to be reasonable. Inspecting their molecular structures one can see that with dibucaine steric factors hinder the close packing of the molecules, consequently the intermolecular attraction will be weaker as compared to tetracaine. At the other hand the polar headgroup of dibucaine has a higher

polarity than that of tetracaine. This can be seen from the acidity constant of the protonated species. In the case of tetracaine one has pK = 8.15 but with dibucaine pK = 10.19 [32]. This means that the polar headgroup of dibucaine anchored into the water phase, due to its higher proton affinity will be more hydrated as compared to the tetracaine, entailing a weaker intermolecular attraction.

CONCLUSIONS

The diffusion controlled kinetics Eq. (20) proposed by us seems to describe very well the adsorption dynamics of dibucaine and tetracaine at the benzene/water interface. Because, the deviations of the experimental points from the calculated curves (Figs 7 and 8.) are within the limit of experimental accuracy, this refinement was further pursued.

Finally, the Eq. (21) allows us to obtain the diffusion coefficients, the subsurface concentrations and the interaction parameters α, for the adsorption dynamics of dibucaine and tetracaine at the benzene/water interface.

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