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Surface modification of silica particles by a cationic surfactant: adsolubilization of steroids from aqueous solutions

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Abstract

The incorporation of three steroids, progesterone, testosterone and hydrocortisone onto fine silica particles surfaces as induced by the adsorption of a cationic surfactant, cetyltrimethylammonium bromide at the solid/water interface, has been studied below and above the surfactant critical micelle concentration (cmc). It is shown that the binding of the steroids is at a maximum at the equilibrium cmc and decreases above this concentration. This effect is due to the competing effects of drug adsolubilization in the adsorbed aggregates and the solubilization into the free micelles above the cmc. At higher surfactant concentrations complete desorption of the drugs from the silica/water interface is observed. Analytical expressions have been derived for the adsorption and the desorption processes. It is shown that at low drug concentration the partition coefficients of the steroids are equal in the surface adsorbed surfactant aggregates and in the micellar solutions. The analytical expressions enable the calculation of the surfactant concentration required for the complete desorption of the drugs from the silica surface. At higher drug concentrations, the same effects are observed, but the mathematical analysis is then complicated by drug adsorption onto silica in the absence of surfactant.

Keywords: Adsolubilization; Adsorption isotherms; Cationic surfactants; Partition coefficients; Silica dispersion; Steroids

1. Introduction

Some surfactants adsorb at solid/water inter-

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faces thereby modifying considerably the properties of the solid surface. This phenomenon has been extensively studied for dispersed particles, in particular with reference to processes such as the flottation of minerals, soil remediation or the formation of thin films on solids (O'Haver et al., 1995). Applications have been also found in the pharmaceutical industry. The research group of Rupprecht has made particular emphasis on the importance of the modification of solid substrate surfaces by surfactants for the incorporation of various drugs such as codeine (Strnadova et al., 1995), propantheline bromide (Daniels and Rupprecht, 1985), acetylsalicylic acid (Daniels et al., 1986) at silica/water interfaces. In effect, silicas have been recommended for a long time as drug supports due to their negligible physiological and intersting physicochemical properties. Other investigations have concerned for example, hydrocortisone (Zimmer et al., 1994), pilocarpine (Harmia et al., 1986) and model propellant devices (Clarke et al., 1993) with various solid substrate/surfactant systems. The ease of elution of proteins such as flubiprofen from silica surfaces by cationic surfactants may also be considered as the same area of research although the aims could be different (Wahlgren et al., 1993). The retention of various antibiotic and antithrombic agents on vascular grafts use essentially the same physicochemical ingredients (Yao and Strauss, 1992). Finally the rate of drug release may be increased by the presence of surfactants at solid surfaces (Buckton et al., 1991). The increased wettability of the solid particles as the surfaces are covered by the surfactants, may be an important parameter in drug release investigations.

The rational which governs these studies is the following. It is well known that as surfactants adsorb on a solid hydrophilic surface, they form aggregates such as admicelles or bilayers depending upon the solid surface coverage. These structures may incorporate ionic or nonionic solutes by a mechanism very similar to ion-exchange or to solubilization as it occurs in the classical micellar solutions. This phenomenon has been coined adsolubilization (Harwell et al., 1985) to emphasize that it concerns surfactants adsorbed at solid/liquid interfaces. However, as the surfactant concentration is increased above the critical micelle concentration (cmc) and the solid surface is saturated, free micelles must form in the solution. Therefore, an equilibrium will be established between the fraction of the solute adsorbed at the solid/liquid interface and the fraction which is solubilized in the free micelles (Monticone and Treiner, 1995a; Favoriti et al., 1996a,b). It is the purpose of the present investigation to quantify both effects and, more particularly, to study the conditions for the desorption of the solutes from the solid/water interface.

In recent investigations, the incorporation of three steroids at various solid/water interfaces was studied, namely, progesterone, testosterone and Hydrocortrisone. The solid substrates were alumina (Jansen et al., 1994) above its isoelectric point, i.e. positively charged particles and negatively charged polystyrene latex (Jansen et al., 1996). With both substrates, a nonionic surfactant was used: Triton X-100. In the present study, the same steroids have been be studied in the presence of the cationic surfactant, cetyltrimethylammonium bromide (CTAB) adsorbed onto a hydrophilic silica. Analytical expressions are used in order to allow comparison on a quantitative basis of the adsorption and the desorption of the solutes from the solid/water interfaces.

2. Materials and methods

Hydrocortisone, testosterone and progesterone were obtained from Sigma (St. Louis, MO). CTAB was a pure compound from Sigma. It was used as received. The cmc was considered as a criterion of purity. It was determined from conductivity experiments using the conventional conductivity versus concentration plot. An automatic Wayne-Kerr bridge (model 6542) was used. The conductivity cell (Philips) had platinized electrodes. The experiments were performed in a water-bath at 25 ± 0.05°C. The cmc was found to be 8.8×10^{-4} mol/l, in agreement with literature values.

The substrate was a hydrophilic non porous silica: Aerosil 200 from Degussa-France. The BET

surface, as determined by the manufacturer, was 200 ± 25 m^2/g. The surface was negatively charged above its isoelectric point (iep) which is, in the present case, equal to 2.8. Thus, cationic surfactants could be easily adsorbed onto the particles.

The batch-method was used throughout 0.1 g of solid was dispersed into 10 ml of solution in screw-top tubes. As the solubility of the testosterone and progesterone are very small, the compounds were solubilized in pure ethanol and a portion of the solution was diluted into water. Thus all solutions contained 10 weight per cent of ethanol. 0.15 mol/l of NaBr was added to the solution, in order to increase the adsorption of the surfactant and maintain a constant thermodynamic activity in the system. The tubes were equilibrated in a water-bath at 37.00 ± 0.05°C for at least 24 h with protection from light.

After ultracentrifugation at 20000 rpm for 1 h, the supernatant was analyzed using a spectrometer (Perkin-Elmer $\lambda 5$). In the case of CTAB, a slight excess of the dye, Orange II (2-naphthobenzene sulfonic acid from Sigma), was added to the supernatant and the resulting 1-1 complex was extracted using chloroform. The complex concentration was analysed at 486 nm ($\varepsilon = 22470$). For the steroids, the maximum wavelength employed were, respectively 247.4, 248.9 and 247.0 nm for hydrocortisone, testosterone and progesterone.

The pH of the solutions was maintained at 6.5 for all experiments. A combined glass-electrode was used to measure the pH.

The adsolubilization experiments were performed at constant steroid concentration and variable surfactant concentration: two solute concentrations were studied: 1.0×10^{-4} and 1.0×10^{-3} mol/l. For convenience, the corresponding results will be discussed separately.

Some micellar solubility experiments were also performed in the absence of solid at the same constant concentration of ethanol and added salt as for the adsolubilization experimental conditions. The classical method of solubility experiments was used: an excess of steroid concentration was added at various CTAB concentrations. After filtration, the supernatant solutions were analyzed spectrometrically.

3. Results and discussion

3.1. Surfactant adsorption isotherm and the adsolubilization experiments at low steroid concentrations

3.1.1. Description of the isotherms

Fig. 1 shows on the same graph the surfactant adsorption isotherm and the adsolubilization curve in the case of progesterone. The surfactant isotherm is presented in the familiar scale of mol/m^2 as a function of free surfactant concentration. The coadsorption of the drug is presented in mol/l of coadsorbed progesterone as a function of free surfactant concentration in order to emphasize the fact that the adsolubilization phenomenon will be discussed in terms of partition coefficients as shown below, i.e. as a ratio of concentrations. Furthermore this representation enables an easy evaluation of the percentage of coadsorbed drug, knowing the total concentration C_t (on Fig. 1, $C_t = 1.0 \times 10^{-4}$ mol/l).

The surfactant adsorption isotherm presents a classical profile. There is an accepted scenario for

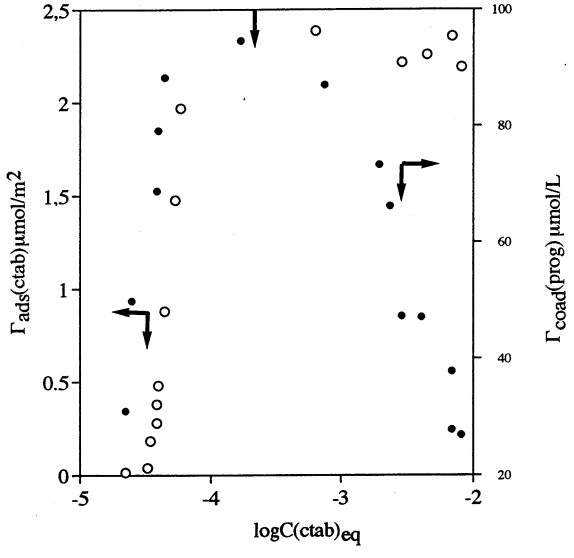

Fig. 1. Adsorption of cetyltrimethylammonium bromide (left scale) and adsolubilization of progesterone (right scale) as a function of the equilibrium surfactant concentration: 1% silica for all figures. The arrow indicates the position of CTAB critical micelle concentration.

the interpretation of this type of isotherm. At low concentrations, the surfactant adsorbs as individual monomers lying flat on the silica surface. As the concentration increases, it is generally accepted that for a hydrophilic silica above the isoelectric point, patches of small double-layer aggregates, sometimes called admicelles, are formed due to favorable interactions between the surfactant hydrophobic chains, above a surface coverage of about 20%. These admicelles grow in size with total surfactant concentration until at some concentration which depends upon the pH of the solution, the reactivity of the ionic sites of the solid particles and the presence of salt, a saturation occurs with, consequently, an adsorption plateau. It is admitted that only surfactant monomers adsorb onto the solid surface so that as the plateau is attained, free micelles are formed in the solution. Thus, the occurence of the plateau often coincides with the surfactant cmc. This is the case here. It is to be noted that the presence of salt or ethanol does not change the overall profile of the surfactant adsorption isotherm (Jansen et al., 1994).

The adsolubilization curve at constant solute concentration can easily be interpreted qualitatively from the above description. As admicelles form and grow onto the silica particles, the steroid molecules which do not adsorb on these silica particles at low concentrations are increasingly incorporated into the surfactant aggregates much as in the similar case of micellar solubilization. As the surfactant plateau appears and free micelles are formed, the steroid molecules are distributed between the admicelles and the free micelles. At concentrations higher than the cmc, the admicelle concentration remains constant but the concentration of free micelles increases. Therefore, the steroid molecules are preferentially solubilized by the free micelles and their concentration in the admicelles decreases. Eventually, the steroid will be completely desorbed from the admicelles. This mechanism is very similar to an extraction process.

Under the present experimental conditions the maximum steroid uptake was equal to 94, 80 and 55%, respectively for progesterone, testosterone and hydrocortisone. No attempt was made to optimize these values.

3.1.2. Quantitative analysis

It was thought important to further describe the above phenomena using a quantitative approach. The incorporation of the steroid into the adsorbed admicelles could be described using a partition model. The solubilization mechanism which was supposedly occuring above the cmc could be analyzed using the same approach. Thus, the effect of the structure of the aggregates on the incorporation of the steroids could be discussed on a quantitative basis: planar bilayers in the case of admicelles and spherical aggregates for the free micelles in equilibrium with the admicelles. This approach was used previously in the case of naphthalene derivatives (Favoriti et al., 1996a,b). Only the basic equations will be recalled here.

Let us consider first the increasing portion of the adsolubilization curve of Fig. 1, i.e. in the region where the solute is distributed between the aqueous (ethanolic) solution and the adsorbed admicelles.

Assuming the pseudo-phase model, one can write, in the mole fraction basis:

$$P_{ads} = 55.5 \frac{C_{ads}}{\Gamma_s \cdot C_w} \quad (1)$$

where C_{ads} is the concentration of adsorbed steroid; C_w is the concentration of free steroid in the solution; and Γ_s is the concentration of adsorbed surfactant.

Likewise, above the cmc, one can write the following relation:

$$P_{mic} = 55.5 \frac{C_{mic}}{(C_s - \text{cmc})C_w} \quad (2)$$

where C_s is the total surfactant concentration and C_{mic} is the concentration of steroid solubilized into the free micelles.

From Eqs. (1) and (2), one can get Eq. (4) where C_t is the total concentration of steroid introduced in each vial at the various CTAB concentration investigated, e.g. 1.0×10^{-4} mol/l, and C_{ads} is the experimental adsorbed steroid concentration with:

$$C_t = C_{ads} + C_{mic} + C_w \quad (3)$$

$\Gamma_{s,max}$ is the surfactant concentration at the adsorption plateau. In the present case an average

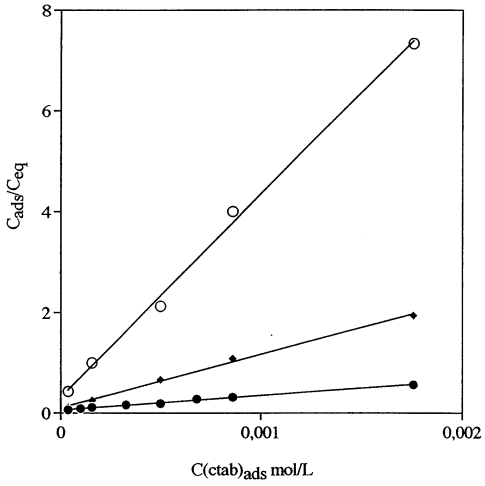

Fig. 2. Determination of P_{ads}: ratio of adsolubilized to equilibrium steroid concentrations as a function of surfactant adsorption concentration (Eq. 1): ● progesterone; ◆ testosterone; ○ hydrocortisone.

value of $\Gamma_{s,max} = 5.0 \times 10^{-3}$ mol/l was taken for the three steroids:

$$C_{ads} = \frac{C_t}{1 + \dfrac{(1 + P_{mic}(C_s - cmc))}{P_{ads} \cdot \Gamma_{s,max}}} \quad (4)$$

P_{ads} may be obtained from a plot of the ratio of adsorbed to free steroid concentration as a function of adsorbed surfactant concentration following Eq. (1). Then, the only unknown quantity in Eq. (4) is P_{mic}, the micellar solubilization constant, as all other quantities are obtained experimentally. If a unique P_{mic} value may describe the decreasing portion of the adsolubilization curve of Fig. 1, one may conclude that the present model is correct, i.e. that the decreased adsolubilization is due to a classical micellar solubilization effect.

Fig. 2 presents an illustration of Eq. (1) using the adsolubilization experiments below the cmc for the three steroids. A good straight-line is obtained in all three cases. From the slopes of these lines, a partition coefficient of adsorption may be calculated. The results are displayed on Table 1. Note that all partition coefficients in the Table were expressed in the molarity scale $P(c)$. Thus the experimental values, which were obtained in the molality scale $P(m)$ were transformed by the classical relationship:

Table 1
Molar partition coefficients of adsolubilization P_{ads}, desorption P_{mic} and micellar solubilization P_{sol} of three steroids with cetyltrimethylammonium bromide at 37°C in 10% ethanolic aqueous solutions with 0.15 mol/l of salt

Steroid	$P^{a}_{sol,b35}$	$P^{b}_{sol,ctab}$	$P^{b}_{mic,ctab}$	$P^{b}_{ads,ctab}$
Hydrocortisone	115	—	75	105
Testosterone	750	130	330	385
Progesterone	1570	940	1560	1455

[a] Reference: Tomida et al. (1978): pure water.
[b] In the presence of 10% ethanol and 0.15 mol/l of salt.

$$P(c) = V_s P(m) \quad (5)$$

where V_s is the surfactant monomer partial molar volume. In the case of CTAB, V_s is taken as equal to 0.35 l/mol (De Lisi et al., 1988).

Figs. 3–5 illustrate the application of Eq. (4). Here on the ordinate, the adsorbed solute concentrations is expressed in the practical scale of mol/l. Each full curve was calculated with a unique P_{mic} value and the P_{ads} data just obtained. It is clear that the model used is correct, i.e. that the decreasing adsolubilization concentration must be due solely to the incorporation of the steroids to the free micelles above the equilibrium cmc. The results are shown on Table 1.

These results show that the concentration of surfactant added to such systems must be carefully calculated if the effect of surfactant adsorption with respect to the uptake of an additive compound is to be rationalized. In particular,

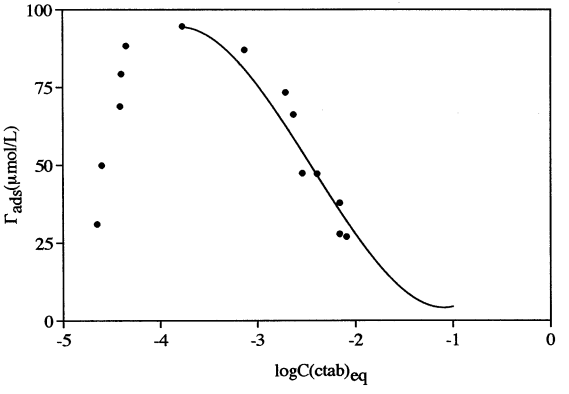

Fig. 3. Determination of P_{mic}: adsolubilization of progesterone ($C_t = 1.0 \times 10^{-4}$ mol/l) full line: calculated values: Eq. 4.

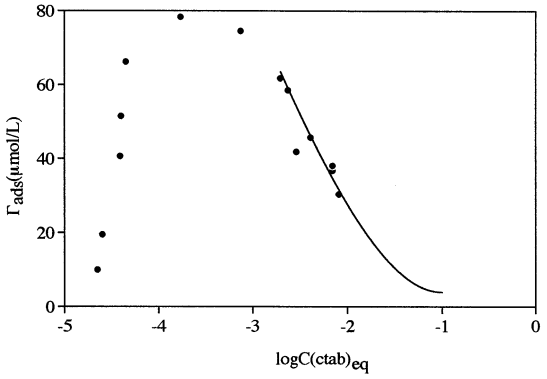

Fig. 4. Determination of P_{mic}: adsolubilization of testosterone ($C_t = 1.0 \times 10^{-4}$ mol/l) full line: calculated values: Eq. 4.

adding surfactant above the cmc may have no effect on the particle/surfactant uptake of a drug, as the drug may be completely desorbed from the solid/water interface and solubilized into the free micelles (Harmia et al., 1986). Also, Eq. (4) may be useful for the evaluation, at a given solute concentration, knowing its micellar partition coefficient, of the concentration of solute remaining adsolubilized at the solid/water interface.

3.1.3. Comparison between adsolubilization and solubilization constants

The data of Table 1 show that within experimental uncertainty, one can write:

$$P_{ads} = P_{mic} \tag{6}$$

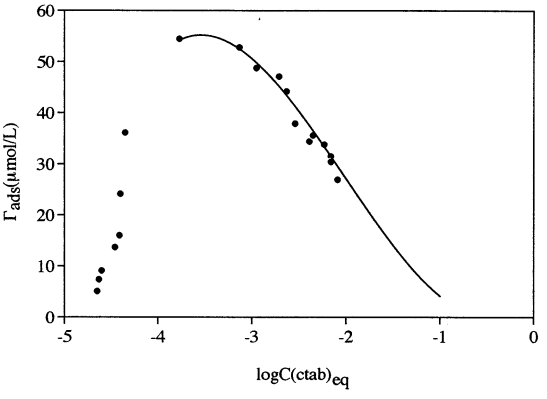

Fig. 5. Determination of P_{mic}: adsolubilization of hydrocortisone: full line: ($C_t = 1.0 \times 10^{-4}$ mol/l) calculated values: Eq. 4.

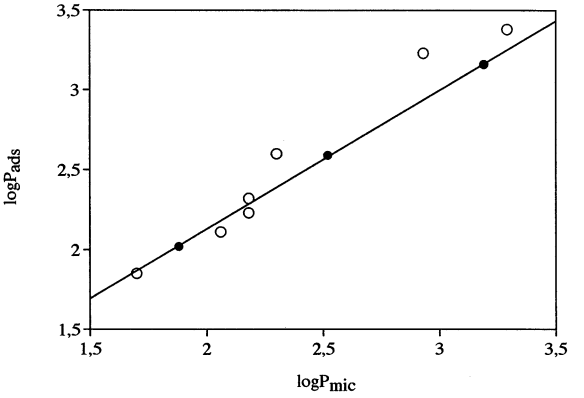

Fig. 6. Correlation between adsolubilization and desorption constants for various solutes on silica with cetyltrimethylamonium bromide. From bottom to top: phenoxyethanol, hydrocortisone, 3-phenoxypropanol, 1,4 benzoquinone, 1,4-naphthoquinone, 1,4-nitroaniline, testosterone, 1-naphthylamine, progesterone, 2-naphthol, 2-naphthalene, ethanol.

This is an interesting conclusion. Firstly, it implies that the concentration of adsorbed solute can be calculated below and above the cmc for different compounds provided that the solubilization partition coefficient and the surfactant plateau value are known. From Eq. (4), the concentration of surfactant necessary for complete desorption of the steroids from the solid particles can be evaluated. Secondly, Eq. (6) implies that the type of structure of the surfactant aggregate plays a minor role, if any, on the incorporation of these solutes. This is important in view of the numerous publications which have dealt with the question of relating the curvature of a particular aggregate (spherical, cylindrical or else) to its solubilization capabilities. The reason is that solutes such as steroids do not penetrate the aggregates but are simply adsorbed at their surface. In that case, the radius of curvature of the aggregates is an irrelevant parameter.

The question may also be asked to what extent Eq. (6) is of any generality. The number of systems for which P_{ads} and P_{mic} have been determined is small. Fig. 6 displays such results in log P units.

The line of equal of partition constants goes through those solutes which are not ionized: alcohols, quinones and the three steroids. For those

solutes which can be ionized (under the present experimental conditions, the pH of the solutions was two units above the pK values of the solutes), P_{ads} is systematically larger than P_{mic} by a factor of 2 to 3. It is the case with amines or phenols (Favoriti et al., 1996a,b). Thus, one should consider for the time being that Eq. (6) applies only to non ionized solutes.

3.2. Adsolubilization experiments at higher steroid concentrations

The very small solute concentration used above enables to consider the adsolubilization phenomenon under thermodynamically ideal conditions as far as concentration effects are concerned. It was considered as important to evaluate the adsolubilization phenomenon at larger solute concentrations. A concentration of 1.0×10^{-3} mol/l was chosen for that purpose. Save for that parameter, the experimental conditions were the same that for the experiments at lower concentrations. Fig. 7 presents the results obtained for the three steroids.

A very different picture is displayed by progesterone and testosterone when compared to the results of Figs. 4 and 5: the two drug molecules are adsorbed onto Aerosil 200 particles in the absence of surfactant. As CTAB is added to the system, the concentration of adsorbed steroid does not vary until the cmc is attained. Above the cmc, the adsorbed concentration decreases as in the case of the lower concentrations discussed above. One may infer that the same effect is observed: partitioning of the steroids in favor of the free micelles as the consequence of their solubilization.

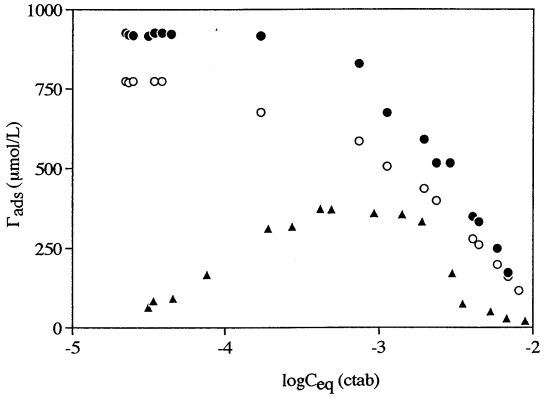

Fig. 7. Adsolubilization of three steroids ($C_t = 1.0 \times 10^{-3}$ mol/l) as a function of CTAB equilibrium concentration: ● progesterone; ○ testosterone; ▲ hydrocortisone.

This behaviour has been noted before in the case of naphthalene below the solubility limit of 2.7×10^{-4} mol/l in the presence of CTAB adsorbed on a porous silica (Sorbsil C30). This hydrocarbon is adsorbed on the silica surface in the absence of CTAB (Monticone and Treiner, 1995b). Addition of surfactant does not change the adsorption until the equilibrium cmc is attained just as in the case of the two most hydrophobic steroids. Desorption begins above the equibrium cmc. Naphthalene as well as progesterone or testosterone adsorption onto silica in the absence of surfactant could be related to the presence on portions of the silica surface of siloxane groups which may be considered as hydrophobic, thus favoring the adsorption of hydrophobic solutes at higher concentrations. Whatever the reason, this adsorption complicates the analysis of the data along the lines suggested above as three different equilibrium should then be taken into account: (i) solute/solid particle; (ii) solute/adsorbed aggregates; and (iii) solute/free micelles.

The case of hydrocortisone on Fig. 7 seemed easier to analyze because of its similarity with the previously analyzed systems. Fig. 8 compares the results obtained by applying Eq. (1) to the adsolubilized effect at the two concentrations investigated. A curvature appears at higher surfactant concentration for the data at 1.0×10^{-3} mol/l. However if only the lower concentrations are used in the analysis for both set of data, then a single curve may be drawn through all the experimental points leading to an unique value for P_{ads}.

If one considers the relative uptake of steroid at the two concentrations studied, the results are very similar: One gets from a total concentration of 1.0×10^{-3} mol/l the following numbers: 92, 77 and 37%, for progesterone, testosterone and hydrocortisone respectively. These numbers should be compared to the values of 94, 80 and 55% from a total steroid concentration of 1.0×10^{-4} mol/l

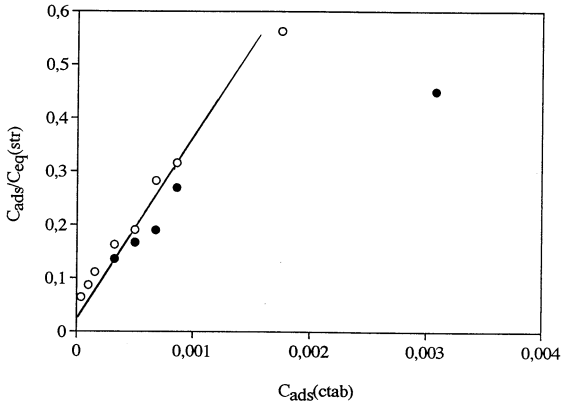

Fig. 8. Determination of P_{ads} for hydrocortisone at two steroid concentrations (Eq. 1): ○ $C_t = 1.0 \times 10^{-4}$ mol/l; ● $C_t = 1.0 \times 10^{-3}$ mol/l.

as stated above. Only hydrocortisone displays a slightly different behaviour at the two concentrations investigated.

These observations should be applicable to other pH values. In effect, it is well known that by increasing the pH of the silica dispersion, the number of ionic sites increases and therefore the concentration of cationic surfactant adsorbed increases. It has been recently shown that, neither the change of pH nor the change of ionic strength has any important effect on the adsorption partition coefficient (Monticone and Treiner, 1995a,b). The reason for this behaviour may be looked upon as a straightforward analysis of Eq. (1). As the pH, for example, increases, the CTAB concentration also increases with a simultaneous increase of solute uptake. As a result, P_{ads} remains approximately constant in a large pH range. The same observation was made in the case of the uptake of a hydrophobic alcohol from solution where the ionic strength was increased from 2×10^{-2} to 2×10^{-1} mol/l, P_{ads} remained constant in the whole range of ionic strengths.

Thus, it appears that the above considerations should apply to a large range of pH and ionic strengths for neutral drugs in the presence of an adsorbed cationic surfactant on a hydrophilic silica.

Finally, the most notable difference which may be noted between the results obtained at the two solute concentrations investigated is that the rate of change of solute desorption with surfactant addition is larger for the largest solute concentration. As an example, it may be deduced from inspectations of the curves corresponding to progesterone and testosterone that at, say, an equilibrium CTAB concentration of 1×10^{-2} mol/l, the desorption is about half of the maximum steroid adsorption in the case of a steroid concentration of 1.0×10^{-4} mol/l, whereas at 1.0×10^{-3} mol/l, the desorption is about one fifth of the maximum steroid concentration.

One of the possible interpretation of this result is that the highest steroid concentration, corresponds to a saturation concentration. Therefore the decrease of solute adsorption is partly due to the excess solute which is solubilized in the free micelles. This fraction of solute is readily available to micellar solubilization. The fraction of the solute which is adsolubilized in the adsorbed surfactant structures would not be as easily transferred to the free micelles. This should be considered as an ad hoc hypothesis which needs some confirmation. Note that the same observation has been made in the case of progesterone and testosterone at $C = 1.0 \times 10^{-3}$ mol/l on polystyrene latexes in the presence of adsorbed Triton X-100 (Jansen et al., 1996).

3.3. Comparisons with similar systems

It has been recalled above that the adsolubilization of steroids had been studied before on two different substrate systems: alumina (Jansen et al., 1994) and polystyrene latex nanoparticle surfaces (Jansen et al., 1996) modified by the same nonionic surfactant, Triton X-100. In both cases, the same aqueous solution was employed, i.e. it contained 0.15 mol/l of added salt and 10% ethanol. In all cases the total steroid concentration was constant and equal to 1.0×10^{-4} mol/l. Furthermore, they did not adsorb on the solid particles in the absence of surfactant. Thus, the influence of the substrate could be discussed. Note that the polystyrene latex presents sulfate surface groups, which makes it a negatively charged colloid.

It must be emphasized that the adsorption of Triton X-100 on alumina is very small. However,

the shape of the surfactant adsorption isotherm is qualitatively the same than that observed on silica. It is only the height of the adsorption plateau which is much smaller with alumina. Nevertheless, the molar fraction of steroid at the interface, i.e. the ratio of the number of mole of steroid divided by the total number of mole of steroid and Triton X-100, is large. For progesterone, testosterone and hydrocortisone, the values of x_s were respectively: 0.84, 0.79 and 0.84. In the case of the polystyrene latex, the values of x_s obtained under the same experimental conditions were: 0.92 and 0.48 for progesterone and hydrocortisone, respectively. The most straightforward interpretation of these results would be to assume that under these experimental conditions, the presence of only patches of adsorbed surfactant molecules which do not cover the entire particle solid surfaces have changed the properties of the solid alumina surface from a hydrophilic to a hydrophobic surface. This would be sufficient for allowing adsolubilization of the steroid molecules.

Thus, the general conclusion seems to be that the electric charge or the nature of the substrate does not play an important role on the adsolubilization phenomenon. It is the hydrophobicity of the neutral solute molecules which governs its behavior towards the particles. The necessary condition for adsolubilization being however that the particle surface has been made sufficiently hydrophobic by surfactant adsorption. This may be obtained with a rather small surfactant coverage as shown by the case of alumina with Triton X-100.

This observation has been noted before by consideration of the partition coefficient of selected solutes in widely different surfactant systems: a short chain alcohol, 1-pentanol and a barbituric acid, butobarbital: the general conclusion is that the charge, the type of head-group or the hydrocarbon chainlength N (for $N > 12$) play a minor role on the degree of incorporation of neutral solutes in micellar systems, at least at solute concentrations below the solubility line (Treiner, 1995). This conclusion indicates that for many surfactant/drug systems, an evaluation of the solubilization constant may be used for application to the adsolubilization phenomenon.

Finally, it was also of interest to compare the solubilization data obtained from the desorption portion of the Figs. 2–5 with direct micellar solubility results. The corresponding partition coefficients P_{sol} were obtained from the slope of the linear variation of a plot of steroid solubility versus surfactant concentration in the presence of ethanol and salt (not shown). Again the results were calculated in the molar basis. They are to be found in Table 1. Although the solubility results are somewhat lower than those deduced from Eq. (4), they are indeed of the same order of magnitude. In fact, even these differences may be interpretable within the framework of thermodynamic solutions. The P_{mic} data as deduced from the desorption experiments should be compared to partition experiments as they are performed using the semi-equilibrium dialysis method. In both cases the solute molecule is studied below the saturation concentration. It is known that under these experimental conditions, the partition coefficients are larger than those deduced from solubility experiments because of activity coefficient effects.

The micellar solubilization results for the same steroids in surfactant solutions of alkylpolyoxyethylene (Brij35) aqueous solutions are also presented in Table 1 for the sake of comparison (Tomida et al., 1978). They are amazingly similar to those deduced from the present study. This observation confirms the points made earlier: in the absence of specific interactions between the drugs and the surfactants, it is the hydrophobicity of the drug molecules which governs the adsolubilization or the micellar solubilization behaviour and not the structural properties of the surfactants.

4. Conclusions

Hydrophobic drugs may easily be retained at the surface of silica particles in the presence of adsorbed CTAB molecules. This phenomenon has been coined adsolubilization. The maximum adsolubilization occurs at the equilibrium cmc of the surfactant. The presence of free micelles decreases the steroid incorporation into the CTAB aggre-

gates as the result of micellar solubilization. A pseudo-phase model has been successfully applied to the two phenomenon. It has been shown that the partition coefficients of adsolubilization and solubilization are equal for the three studied steroids. The model enables the calculation of the surfactant concentration necessary to desorb the drugs from the adsorbed surfactant aggregates. These conclusions may be extended to other substrate/surfactant systems.

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