Effect of Various Parameters on Sodium Dodecyl Sulfate (SDS) Flux Through a Collagen Membrane

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The influence of various experimental parameters on the flux of sodium dodecyl sulfate (SDS) through a collagen membrane has been studied. The variables evaluated were donor concentration, time, temperature, pH and ionic strength. Data on the influence of both surfactant concentration and time on surfactant diffusion through the collagen film allow one to postulate a diffusion process mainly of the monomeric type. This diffusion mechanism based on surfactant monomers has been corroborated by studying the effect of ionic strength. This *in vitro* technique could be a useful tool to predict the effect of diverse experimental parameters on the percutaneous absorption of surfactants.

KEY WORDS: Collagen, diffusion, permeability, SDS, surfactant.

The human skin is a highly organized, heterogeneous and multilayered organ, which constitutes a living protective envelope surrounding the body. The skin is exposed to the action of surfactants as a result of the application of toiletries and cosmetic products. The percutaneous absorption of such surfactants is a function of a series of factors such as the chemical structure and physico-chemical characteristics of the surfactant, the composition of the formulation and the application conditions. Because the percutaneous absorption of a substance can be considered a passive diffusion process (1), it is possible to apply Fick's laws of diffusion to study the phenomenon. Direct measurement of percutaneous absorption is complex. Thus, the development of *in vitro* methods to predict the rate at which materials penetrate the skin would be useful in assessing potential toxicological hazards and in improving the way in which drugs are administered topically. *In vitro* techniques allow one to evaluate accurately the rate of absorption of a substance through specific membranes (2-5).

In the present study, the influence of several experimental parameters on the surfactant flux through a collagen membrane has been analyzed in order to predict the effect of such parameters on the percutaneous absorption of surfactants. This *in vitro* technique has been used because of the correlation found in a previous study (6) between the gradation in the diffusion values and the irritancy capacity of anionic surfactants. Sodium dodecyl sulfate has been selected for three main reasons: (i) it is an amphiphile of frequent use, (ii) it is available in high purity, and (iii) it possesses important denaturalizing and irritant powers.

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MATERIALS AND METHODS

Sodium dodecyl sulfate (SDS). It was a reagent-grade product from Merck (Darmstadt, Germany) and was used without further purification. Its purity was 99%.

Collagen film. A thin edible protein film (with a thickness of 15 microns), manufactured by extrusion of collagen dough and obtained from Naturin-Werck Becker & Co., Weinhein (Germany), was used.

Diffusion test device. The study of SDS diffusion through the collagen film was carried out in the device shown in Figure 1. The surfactant solution was introduced into one of the receptacles, and distilled water was placed in the second. Aliquots were drawn off to analyze the amount of surfactant diffused through the protein support. With this device, the influence of various factors on SDS diffusion through a collagen film was systematically studied, but first suitable experimental conditions were determined to obtain a negligible influence of the osmotic flux and to minimize the effect of the diffusion layers to the overall diffusion process.

Tensiometer. Surface tension values were determined by the ring method in a Lauda automatic tensiometer (Königshofen, Germany) (7). The apparent surface tension values obtained were corrected according to the Harkins-Jordan factors.

Surfactant analysis. The analysis of diffused SDS was carried out by the methylene blue spectrophotometric method (8).

RESULTS AND DISCUSSION

Influence of the concentration. A series of diffusion essays was carried out varying the SDS donor concentration. The temperature was maintained at 25°C. After 24 hr, the amount of surfactant diffused through the collagen film was determined. The diffusion results obtained against initial SDS concentration in the range from 0 to 40 mM are plotted in Figure 2. The surfactant flux remains nearly constant when the donor surfactant concentration exceeds the SDS critical micelle concentration (CMC) (7.5 mM). The CMC was obtained by plotting surface tension data *versus* the corresponding surfactant concentrations.

Diffusion rate. The diffusion rate curve for the permeation of SDS from solutions with a donor concentration of 25 mM is shown in Figure 3. These data are presented as cumulative surfactant penetrated (μmol/cm^2) as a function of time. For periods of time shorter than 100 hr, the amount of surfactant diffused increases linearly with time. When time of essay is longer than 100 hr, the linear relationship disappears and the curve becomes flat. The quantity of surfactant diffused at equilibrium was 160 μmol/cm^2, an amount that, considering both the membrane surface and the volume of the vessel, is equivalent to 8000 μmol/L.

The easiest way to determine which concentration gradient is the driving force between the solutions separated

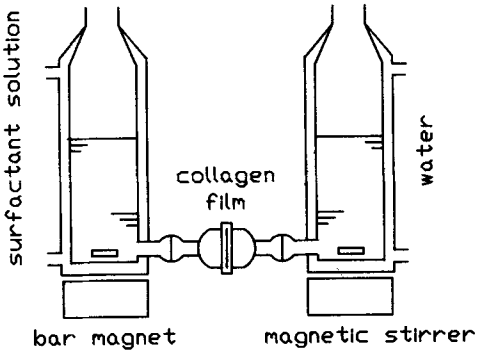

FIG. 1. Diffusion test device.

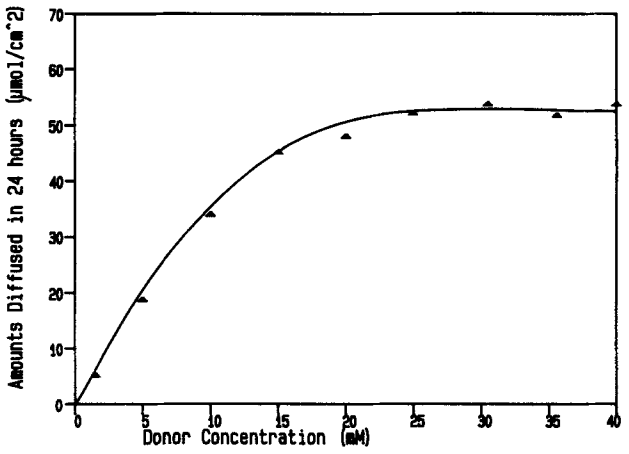

FIG. 2. Surfactant flux *versus* donor concentration.

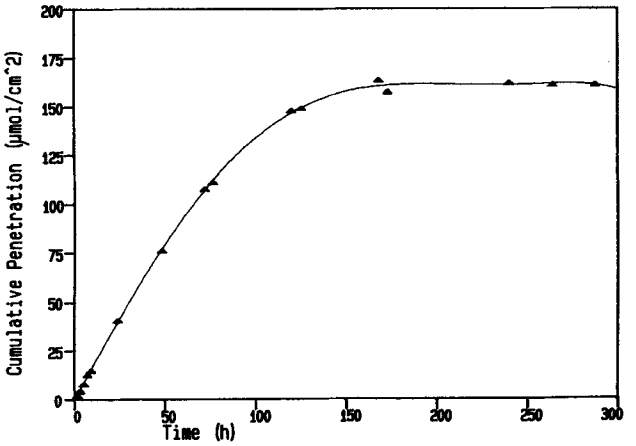

FIG. 3. SDS permeation curve.

by the membrane and causing the transport phenomenon would be to consider the total difference of surfactant concentrations between the two solutions. However, the experimental results obtained so far raise a series of obvious questions: What is the meaning of the stabilization in the amount of solute diffused in spite of increasing the initial surfactant concentration? Why is the equilibrium concentration for the SDS approximately 8 mmol/L and not 12.5 mmol/L as could be expected if the surfactant diffusion proceeded until the surfactant concentrations were the same in both vessels of the experimental device?

The simplest form of Fick's first law can be written (Equation 1) as

$$J = P \Delta C, \qquad [1]$$

where J is the molar flux, P is the permeability and Δ C is the concentration difference between the solutions separated by the membrane. Because in any normal situation the concentration in the applied phase has as its limiting value the solubility of the tested compound, the limiting value of the steady-state flux will also be determined by the donor phase solubility of the diffusant (9). What happens when the diffusant studied is a surfactant? The condition of maximum flux is not limited by the surfactant solubility, as normally has been observed for other compounds, because the surfactant is perfectly soluble at concentrations higher than the observed flux stabilization. The easiest explanation arises from considering the special properties of surfactants in aqueous media (10). For low surfactant concentrations, the only species present in solution is the surfactant monomer, and this species will thus be the cause of the diffusion. When the total surfactant concentration increases, the amount of surfactant monomer also increases and therefore the flux is expected to increase linearly in this zone. When the total surfactant concentration exceeds the surfactant CMC, a dynamic monomer/micelle aggregate equilibrium exists and the total amount of surfactant diffused should be the addition of two contributions: monomer diffusion and micelle diffusion. That can be expressed in Equation 2 as:

$$J = P \Delta C + n(P_M \Delta C_M) \qquad [2]$$

where n is the aggregation number, P the monomer permeability, P_M the micelle permeability, Δ C the monomer concentration difference and ΔC_M the micelle concentration difference.

Assuming the phase separation approach to the thermodynamic analysis of the micellization process, the monomer concentration in solution remains essentially constant after total surfactant concentration exceeds its CMC. On the other hand, the micelle concentration increases from this moment linearly against the total concentration. This means that the total flux, above the CMC value, can be considered as the result of a constant contribution of the monomeric species and a micelle contribution which is a function of the total concentration as given in the following Equation 3 expression:

$$J = P \cdot C_{CMC} + n(P_M \Delta C_M) = A + B(C_T - C_{CMC}) \qquad [3]$$

where C_{CMC} is the monomer concentration, C_M is the micelle concentration and C_T is the total surfactant concentration. Thus, the surfactant flux as a function of initial surfactant concentration might be expected to correspond to a graph as illustrated in Figure 4.

Accordingly, one might expect to observe an inflexion

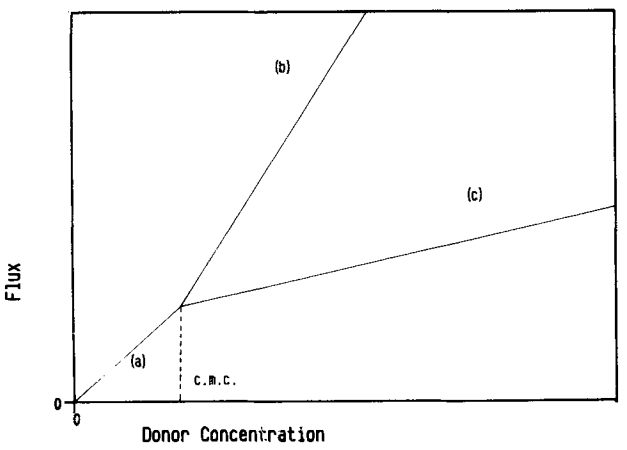

FIG. 4. Idealized flux curve *versus* donor concentration.

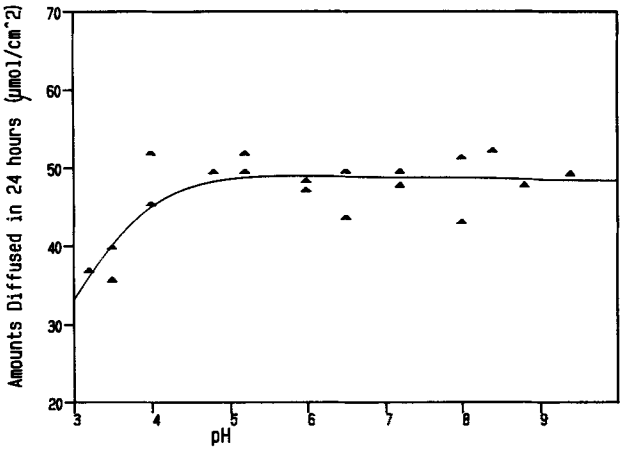

FIG. 5. SDS cumulative penetration *versus* pH.

at the CMC, causing a straight line with a higher (b) or lower (c) slope than that initially observed below the CMC (a), depending on the relative permeability of monomeric and micelle species. However, the experimental results show an initial linear region (which could be attributed to monomeric diffusion) and a second essentially flat region, where the flux hardly changes with concentration. This region with a slope near zero can only come about if the micelle aggregates are not able to penetrate the proteinaceous membrane. The monomers are the only effective species in the diffusion process. This means that once the CMC is reached, the flux remains essentially constant and independent of the total donor concentration.

SDS diffusion as a function of time shows stabilization in the amount diffused, which corresponds to the equilibrium state when the surfactant amount diffused reaches the value of 8000 µmol/L. This concentration is near the SDS CMC and supports the hypothesis of a diffusion process driven only by the monomeric concentration.

Influence of the pH value. In order to determine the effect of the pH on SDS diffusion, a series of essays was carried out. The duration of the essays and the initial SDS concentration were held constant at 24 hr and 25 mM, respectively. The influence of pH was studied over the range between 3.5 and 10. Figure 5 shows that SDS diffusion is not dependent on pH in the range between 4 and 10, which corresponds to the isoelectric pH zone of the collagen.

Permeability versus temperature. SDS diffusion was studied in a temperature range between 15 and 35°C. The experimental conditions for the essays were 24 hr duration and 25 mM initial SDS concentration. The amount of surfactant diffused as a function of time at the different temperatures is plotted in Figure 6. Linear relationships were observed for the temperature range studied. From the mean SDS flux values at different temperatures (which were obtained from the slopes of the curves plotted in Fig. 6) and the surfactant CMC values (experimentally determined), the permeabilities were calculated at each temperature. In Table 1, the SDS mean flux values and the permeabilities are given for the different temperatures studied. In order to verify that the permeabilities are related to temperature by an Arrhenius-type equation (Equation 4):

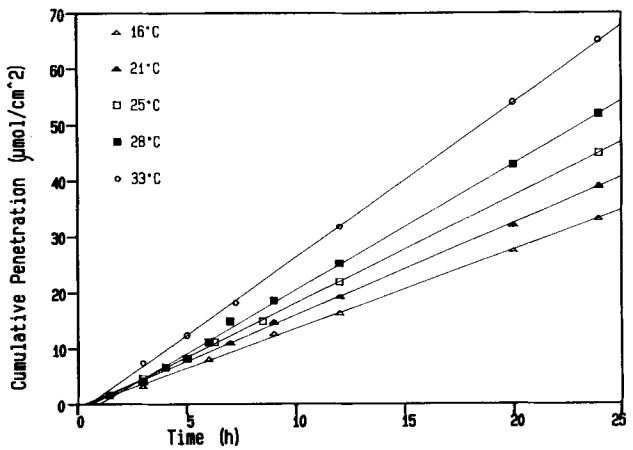

FIG. 6. SDS permeation curves for different temperatures.

$$P = P_o \cdot e^{-b/T} \quad [4]$$

which can also be expressed in a convenient logarithmic form as (Equation 5):

$$\log P = \log P_o - b/T \quad [5]$$

the logarithms of the permeabilities were plotted *versus* the reciprocal of absolute temperature (Fig. 7). A progressive increase in the permeation rate is observed with increasing temperature, and the permeabilities fit an Arrhenius-type equation well.

Influence of ionic strength. The SDS CMC values at different NaCl concentrations were determined by surface tension measurements. The results obtained are summarized in Table 2. When the logarithm of CMC values is plotted *versus* the logarithm of electrolyte concen-

TABLE 1

SDS Flux and Permeability Values at Different Temperatures (donor concentration 25 mM)

Temperature (C)	Mean flux (mmol/cm^2 • s)	Mean permeability (cm • 10^3/s)
16	0.39	5.23
21	0.47	6.24
25	0.55	7.31
28	0.61	8.17
33	0.81	10.81

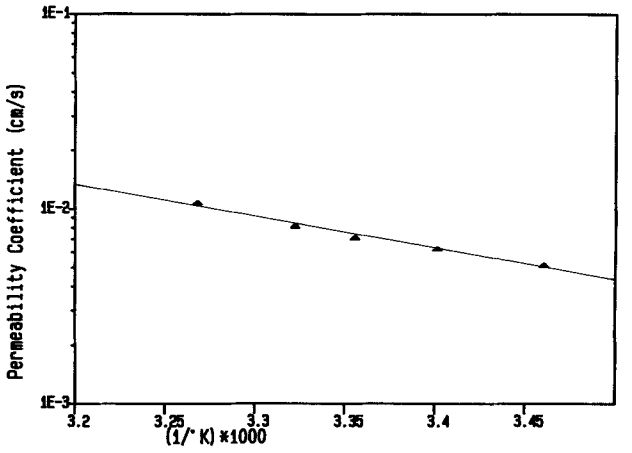

FIG. 7. Permeability *versus* temperature.

TABLE 2

SDS CMC Values for Different Electrolyte Concentrations

NaCl (mM)	CMC (mM)
1.0	4.8
12.5	2.3
75.0	1.0
150.0	0.7

tration, the equation of the graph corresponds to (Equation 6):

$$\log [CMC] = 0.69 - 0.38 \log [NaCl] \qquad [6]$$

The variation of SDS flux through the collagen as a function of ionic strength was determined by carrying out diffusion essays for several NaCl concentrations in both sections of the diffusion device. The results obtained are shown in Figure 8. Small amounts of electrolyte cause a remarkable decrease on the surfactant flux. The graph obtained seems to fit a negative exponential curve. When the logarithm of the surfactant flux is plotted *versus* ionic strength, a straight line is obtained (Fig. 9). The equation for this graph corresponds to (Equation 7):

$$\log J = 0.24 - 0.39 \log [NaCl] \qquad [7]$$

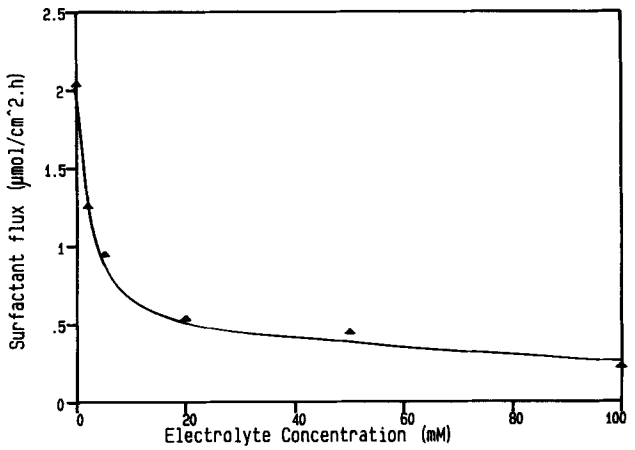

FIG. 8. Influence of ionic strength on SDS flux.

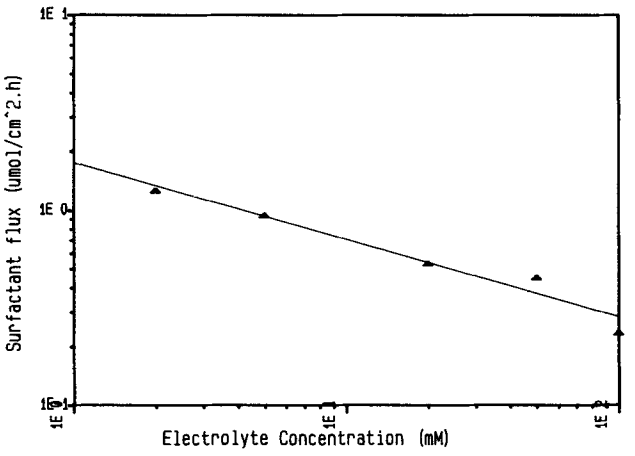

FIG. 9. Surfactant flux *versus* amount of electrolyte.

The decrease in SDS molar flux caused by the increase of ionic strength in aqueous medium could be explained by the hypothesis of monomeric diffusion. From the above experimental equations, which relate the flux and CMC values to the quantity of electrolyte added, it is easy to get the expression (Equation 8):

$$\log J = c + d \cdot \log [CMC] \qquad [8]$$

which relate the surfactant flux to the surfactant CMC. The values obtained for the constants c and d are − 0.34 and 1.03, respectively. Since the slope of this curve is near unity, this equation can be reduced to the following expression (Equation 9):

$$J = z' \cdot [CMC] \qquad [9]$$

Thus, the maximum surfactant flux will be limited by the surfactant's CMC, which is, in turn, related to the ionic strength of the aqueous medium.

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