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Stig E. Friberg
Missouri University of Science and Technology, stic30kan@gmail.com

Lisa Goldsmith

Hamdan Suhaimi

Linda D. Rhein

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Surfactants and the Stratum Corneum Lipids

STIG E. FRIBERG and LISA GOLDSMITH
Chemistry Department, Clarkson University, Potsdam, NY 13676 (U.S.A.)
HAMDAN SUHAIMI
Chemistry Department, University of Missouri-Rolla, Rolla, MO 65401 (U.S.A.)
LINDA D. RHEIN
Colgate-Palmolive Research Center, 909 River Road, Piscataway, NJ 08854 (U.S.A.)
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ABSTRACT

A simplified mixture of model stratum corneum lipids was mixed with different surfactants to make a preliminary estimation of the influence of surfactants on the stratum corneum lipid structure. The results revealed differences between cationic and anionic surfactants and between anionic surfactants with different structures.

INTRODUCTION

The outer part of the skin, the stratum corneum, is an essential organ to sustain life. Its presence reduces the water evaporation rate by a factor of 25–50 [1], prevents the uptake of water into an animal's body, stabilizes the body temperature and also serves as a barrier to chemical and biological attack from the environment.

Attention has focused on the water transport through stratum corneum to a large degree [2–10] and available evidence indicates the lipids to be the main factor in the stratum corneum barrier to transdermal water transport. Hence, an intense interest has been directed towards the individual structure of the stratum corneum lipids [11–17] as well as towards their intermolecular organization. Certain attempts to assign the barrier to water transport to specific lipids have not been successful [9] and it appears probable that the responsible element is the structural organization of the lipids [6,8]. Such a view is in accordance with the clinical symptoms of the essential fatty acid deficiency syndrome [18] in which the dry and cracked skin also shows enhanced water transport rates. A model of stratum corneum with only saturated fatty acids showed no barrier to water transport, but addition of unsaturated fatty acids to the model reduced the water transport to the levels of stratum corneum

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[19]. It is interesting to note that the syndrome may be cured by topical application of linoleic acid [11,20].

Dry skin accompanied by enhanced transdermal water transport is also experienced after solvent extraction [10] or after treatment with surfactant solutions [16]. The latter compounds may also induce irritation of the skin to different extents [21]. In summary, the surfactants may be rated in the following order of irritancy effects: cationics ≥ anionics ≫ nonionics.

With regard to their potential influence on water transport and irritation, we considered a preliminary evaluation of the influence of surfactants on the structural organization of the stratum corneum lipids to be well justified. This publication describes the location and influence by surfactants on a simplified layer structural model of the stratum corneum lipids. The model was originally proposed by Elias [12] and has been developed further in our group [22].

EXPERIMENTAL

Model epidermal lipid

The components, source and purity for the model epidermal lipid are given in Table 1, according to Elias [12]. The materials were all of the highest purity and were used without further purification. Twice distilled water was used.

Surfactants

Anionic surfactants

Sodium dodecyl sulphate (SDS), $CH_3(CH_2)_{10}CH_2OSO_3Na$, obtained from BDH Chemical Limited was twice recrystallized using absolute ethanol.

Sodium-*N*-coconut acid-*N*-methyl taurate (Igepon TC-42), $RCON(CH_3)CH_2CH_2SO_3Na$, obtained from GAF Corporation was used as received.

Coconut acid ester of sodium isothionate (Igepon AC-78), $RCOOCH_2CH_2SO_3Na$, obtained from GAF Corporation was used as received.

Cationic surfactants

Cetyltrimethylammonium bromide (CTAB), $CH_3(CH_2)_{15}N(CH_3)_3Br$, obtained from Sigma Chemical Company was twice recrystallized using absolute ethanol.

Tetradecyltrimethylammonium bromide (TTAB), $CH_3(CH_2)_{13}N(CH_3)_3Br$, obtained from Sigma Chemical Company was twice recrystallized using absolute ethanol.

TABLE 1

Composition of model epidermal lipid

Component	Source	Purity	wt% in mixture
PE	Avanti Polar Lipids	99%	5
Cholesteryl sulfate	Research Plus	98%	2
Cholesterol	Fisher		14
Triolein	Sigma	99%	25
Free fatty acids	Sigma		19
Myristic		99%	3.8
Linoleic		99%	12.5
Oleic		99%	33.1
Palmitic		99%	36.8
Palmitoleic		99%	3.6
Stearic		99%	9.9
Oleic acid palmityl ester	Sigma	98%	6
Squalene	Aldrich	98%	7
Pristane	Aldrich	96%	4
Ceramides	Sigma	99%	18

Nonionic surfactants

Tergitol 15-S-9 obtained from Union Carbide Corporation was used as received.

Polysorbate 20 (Tween 20) obtained from ICI Americas Incorporation was used as received.

A compound $C_{12}H_{25}OT_{3.2}G_{4.0}$ from Pola Co., Japan, was used as received. ($OT = CH_2CH_2CH_2CH_2O$; $G = OCHCHOHCH_2OH$).

A compound $C_{12}H_{25}OT_{7.8}G_{7.9}$ from Pola Co., Japan, was used as received.

Preparation of samples for X-ray diffraction

Samples for the X-ray analysis were prepared as follows. First, all the six free fatty acids in their corresponding ratios (Table 1) were neutralized with sodium hydroxide to a degree of 41% at a water content of the sample varying from 30 to 40 wt%. The samples were mixed by centrifuging the mixture repeatedly through a constriction in a sealed 7 mm glass tube. The samples were then allowed to equilibrate at 30°C for 24 h. Next, the lipids from Table 1 were

added to the partially neutralized free fatty acids according to the sequence: (1) phosphatidylethanolamine (PE); (2) cholesterol; (3) ceramide; (4) oleic acid palmityl ester; (5) squalene.

For each lipid composition a series of samples was prepared with water content in the range 30 to 40%. The samples were mixed as described above. Finally, surfactant was added to a level of 15% of the lipid and the water content adjusted. Oxygen sensitive compounds, i.e., phosphatidylethanolamine and ceramide were handled in a nitrogen atmosphere. All glassware was rinsed with ether to eliminate the possibility of external lipid contamination. Care was taken to keep the model lipid mixture frozen when not in use.

Small angle X-ray diffraction measurements were obtained using a Kiessig low-angle camera from Richard Seifert. Nickel filtered copper radiation was used and the reflection determined by a Tennelec position sensitive detector system (Model PSD-1100).

Photomicrography

An Olympus-BH polarizing microscope, attached to an automatic exposure Olympus camera (Model C-35A) was used for photomicrography. Pre-cleaned microscope slides and covers were selected, and then buffed with lint-free tissue immediately before use. A small amount of the sample was transferred from the sample tube onto the glass slide and was immediately covered with a slide cover. The sample was then sheared between the slide and the cover to a thickness of about 5 to 10 μm and was left for a few minutes for equilibration. The appearance of the sample was then observed between crossed polarizers. A representative region was then selected and photographed at a magnification of 200 times.

RESULTS

The interlayer spacings calculated from the small angle X-ray diffraction patterns are given in Fig. 1 for the anionic surfactants used. Without surfactants present the acid/soap/water host liquid crystal showed interlayer spacings increasing from 49.7 to 51.4 Å with increasing water content. Addition of the five remaining stratum corneum lipid components increased the spacing to the range 63–65 Å with the same slope of interlayer spacing versus water content. Replacing 15% of the lipid mixture with sodium dodecyl sulphate gave interlayer spacings in between the original ones, i.e. in the range 57–61 Å. Addition of the Igepons also resulted in interlayer spacings in the range between the original lipid mixtures, but now with the spacing showing a marked dependence on the water content. The spacings were now found approximately in the 52–64 Å range.

The cationic surfactants, Fig. 2, gave an entirely different pattern. The in-

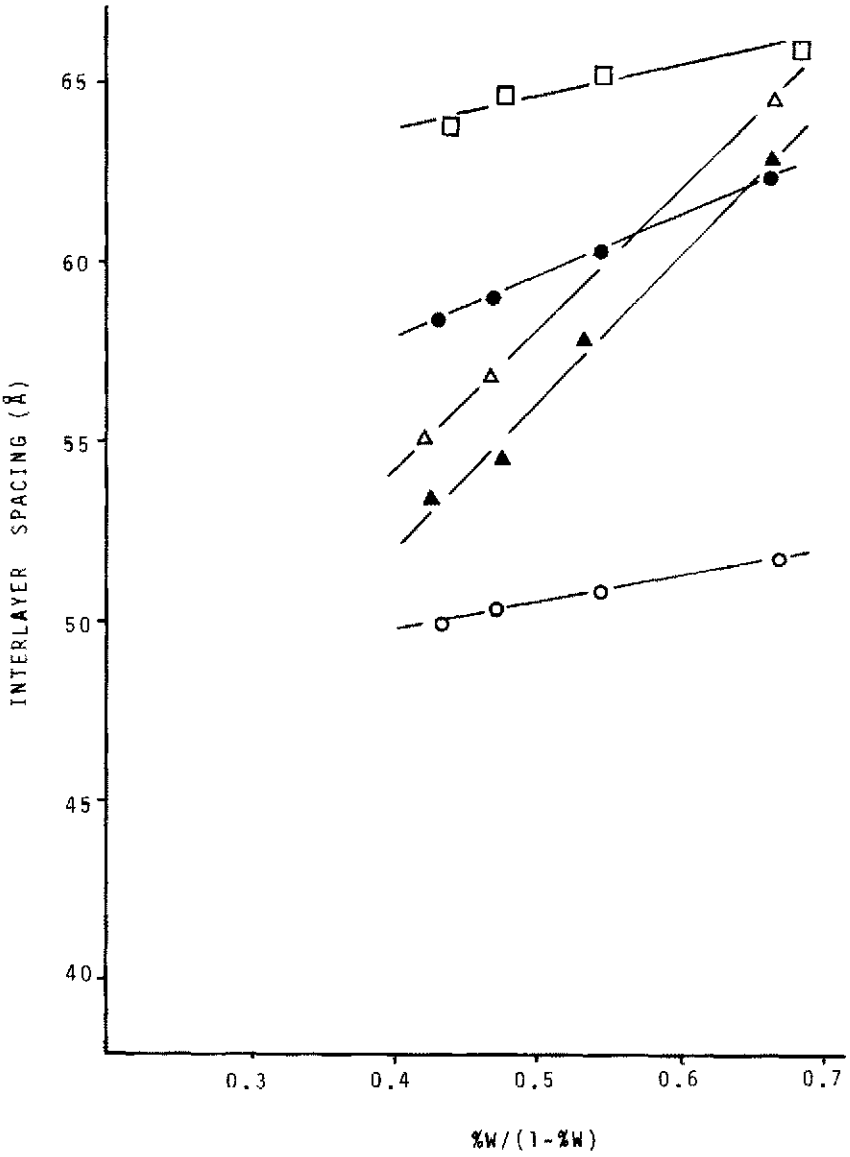

Fig. 1. Interlayer spacing as a function of water content for the anionic surfactants: (○), 41% neutralized fatty acids; (□), PE + cholesterol + ceramide + ester + squalene + (○); (▲), Igepon AC-78 + (□); (△), Igepon TC-42 + (□); (●), sodium dodecyl sulphate + (□).

terlayer distance now actually was reduced with enhanced water content so that the interlayer spacing was reduced to the level of the soap/acid/water host at the highest water content. The two curves for the cationic surfactants are parallel with approximately 1 Å difference between them.

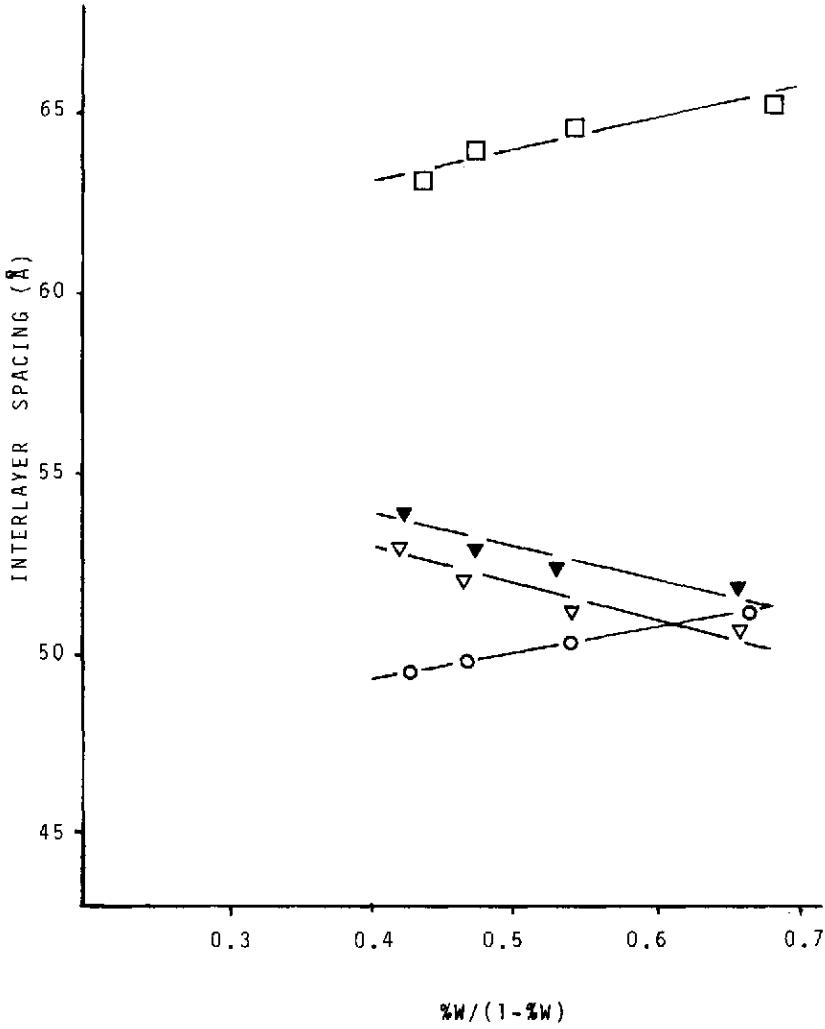

Fig. 2. Interlayer spacing as a function of water content for the cationic surfactants: (○), 41% neutralized fatty acids; (□), PE+cholesterol+ceramide+ester+squalene+(○); (▽), CTAB+(□); (▼) TTAB+(□).

The nonionic surfactants (Fig. 3) showed no comparable distinction; all of them gave interlayer spacings at the level of the total lipid composition, and combinations with Tween 20 and the Pola compound showed the maximum slope of interlayer spacing versus water content.

The microscopy photos in polarized light showed very little influence by the surfactants on the optical patterns. All the patterns are typical of the lamellar liquid crystal with a distorted dislocation pattern. By way of illustration the photos for the sodium dodecyl sulfate system are presented in Fig. 4.

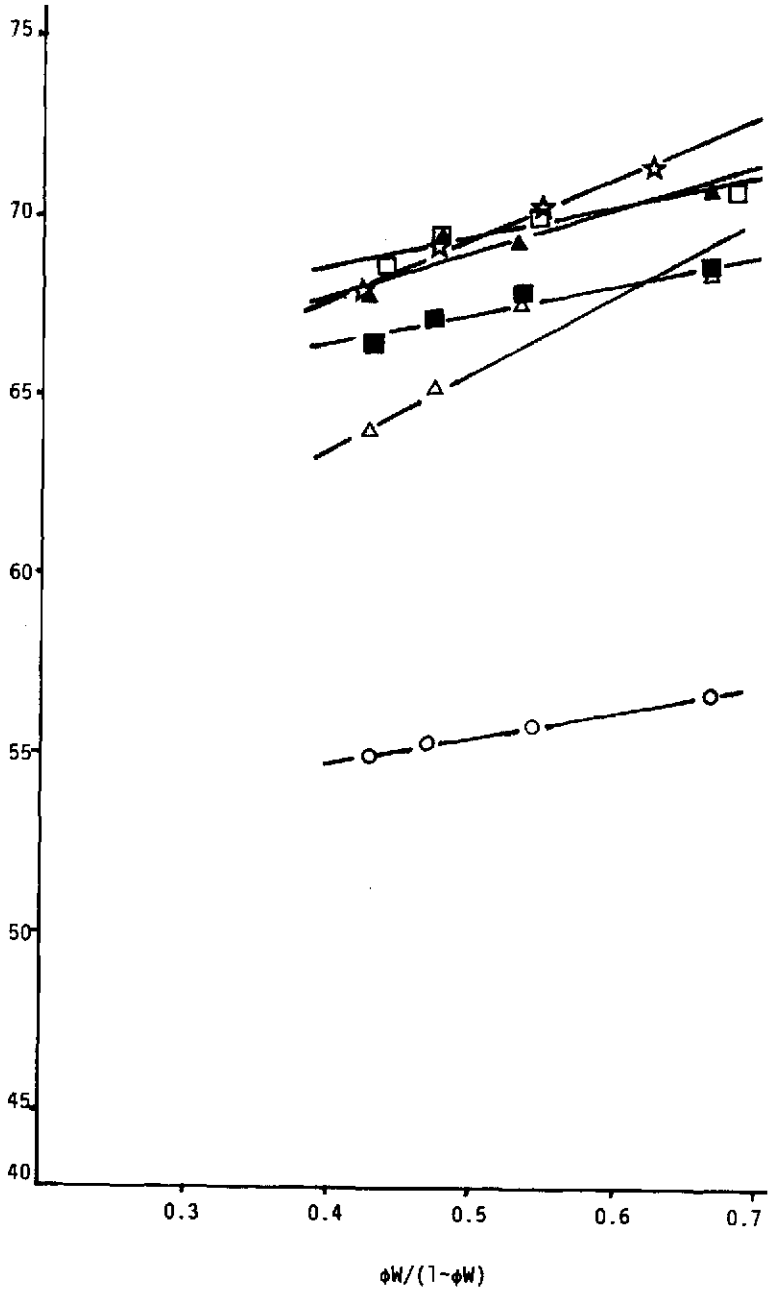

Fig. 3. Interlayer spacing as a function of water content for the nonionic surfactants: (○), 41% neutralized fatty acids; (□), PE+cholesterol+ceramide+ester+squalene+(○); (☆), Tween 20+(□); (■), Tergitol 15-S-9+(□); (△), $C_{12}H_{25}OT_{7.8}G_{7.9}$+(□), (▲), $C_{12}H_{25}OT_{3.2}G_4$+(□).

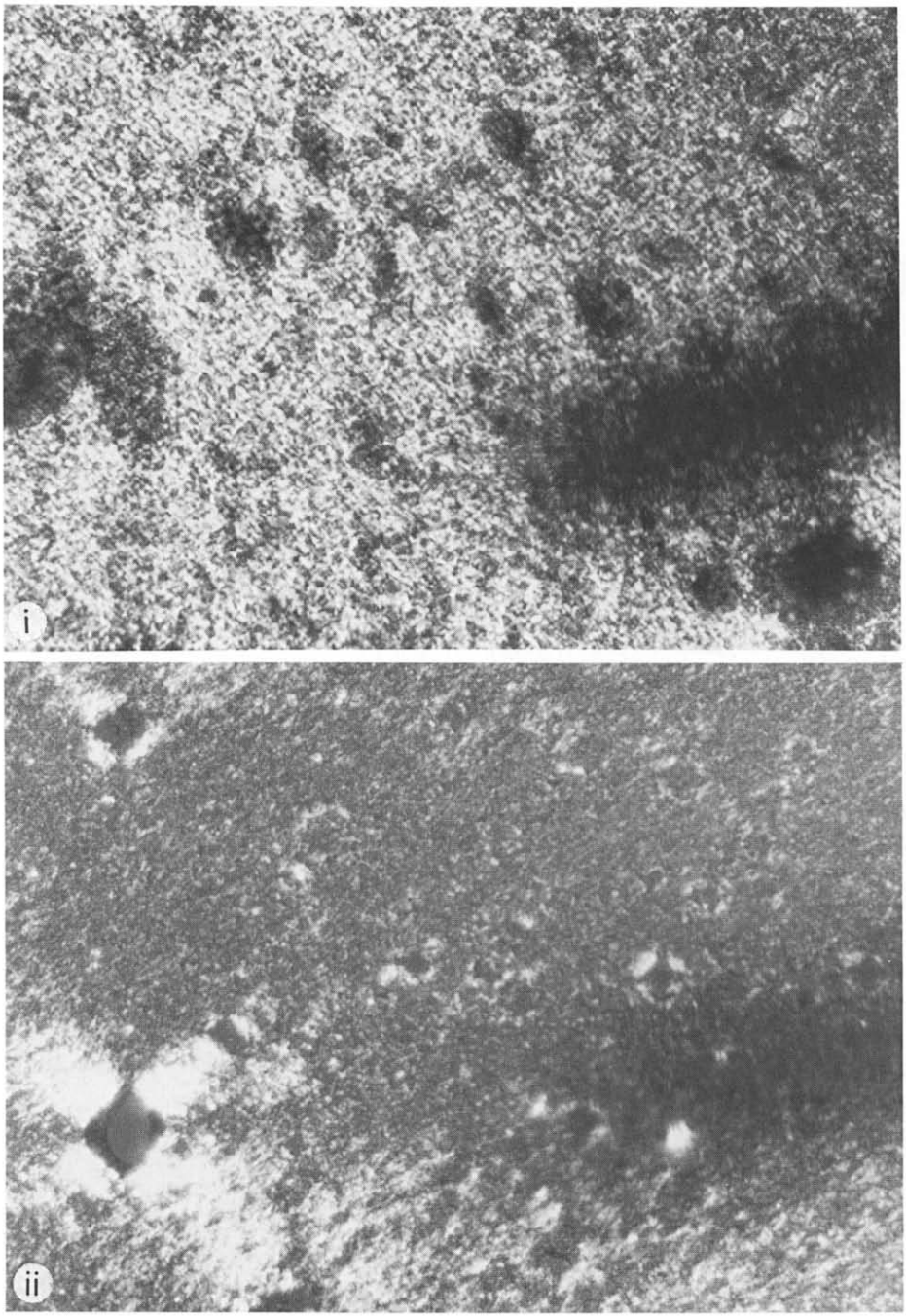

Fig. 4. Optical pattern after addition of sodium dodecyl sulphate to the model lipid at (i) 32% water and (ii) 40% water.

TABLE 2

Percent penetration of water when surfactants are introduced into the bilayer

Surfactants	d_0	d_{calc}	d_{exp}	% Penetration
Host	46.5	65.8	49.8	82.9
Host+lipids	60.5	85.6	65.0	86.1
SDS	51.2	72.8	58.4	66.7
Igepon AC-78	36.6	52.1	53.2	−7.4
Igepon TC-42	38.8	55.2	55.1	0.4
Tween 20	55.8	79.4	63.2	68.8
Tergitol 15-S-9	58.3	83.2	61.8	86.0
$C_{12}H_{25}OT_{7.8}G_{7.8}$	51.3	73.4	59.6	62.4
$C_{12}H_{25}OT_{3.2}G_4$	58.8	84.1	63.3	82.1
CTAB	57.2	81.4	53.2	116.4
TTAB	57.7	82.3	54.1	114.7

DISCUSSION

The interlayer spacings from the small angle X-ray diffraction patterns provide information about the conditions in the layered model structure after calculation of the interlayer spacings in the lipid and aqueous layer separately [23]. The thickness of the lipid layer is obtained by extrapolation of the interlayer spacings in Figs 1–3 to zero water content.

With that information available, Table 2, it becomes obvious that the behavior of the anionic surfactants (Fig. 1) are far from similar. They can now be separated into two groups. The first group is exemplified by sodium dodecyl sulphate; the second group by Igepons. The composition with sodium dodecyl sulphate revealed an increase of lipid bilayer thickness extrapolated to zero water content of only 4.7 Å to be compared to an increase of 14.0 Å when the non-fatty acid lipids were also added to the soap/fatty acid/water host. The increase of 14.0 Å may formally be interpreted as only 12% of the added five compounds to be located between the methyl group layer in the lamellar structure according to the following estimation. With all added components localized between the methyl groups the interlayer spacing extrapolated to zero water content becomes

$$d_0^{calc} = d_h^0(1 + \phi_a/\phi_h) \quad (1)$$

in which d_h is the extrapolated interlayer spacing in the soap/acid structure, ϕ_a is the volume of added lipids, and ϕ_h is the volume of the soap/acid combination.

A measure is obtained of the degree of penetration of the added lipids from the space between the methyl group layers into the host palisade according to

$$p = 100 \cdot \frac{d_{calc} - d_{exp}}{d_{calc} - d_0} \quad (2)$$

in which p is percentage penetration, d_{calc} is the interlayer spacing, if all the lipids were located beteen the methyl group layers, d_{exp} is the experimental value and d_0 is the value at zero added lipid. The obtained values for the lipids after addition of sodium dodecyl sulphate shows 88% of the lipids to have penetrated the palisade layer. Addition of SDS obviously caused a great number of the lipids to be moved into the space between the free fatty acids.

The second group, the Igepons, caused changes of a different nature. Now the addition of Igepon caused a reduction of the lipid interlayer spacing to even smaller numbers than the original value for the liquid crystal of the unsaturated fatty acid/soap mixture, 42.6 Å [24]. After addition of Igepon AC-78 the interlayer spacing extrapolated to zero water content was 36.6 Å, 6 Å *smaller* than the value of the soap/acid liquid crystal. The value of 42.6 Å for the soap/acid layered structure is identical to the value obtained by assuming a layered structure of fully extended hydrocarbon chains of the C_{18} acids. The 6 Å shorter distance would be equal to approximately three gauche bends of each of the hydrocarbon chains. It appears that the Igepons cause such a high degree of disorder that all the lipids penetrate into the space between the soap/acid chains. This resulting disorder may be due to the structure of the isothionate molecule which contains a carbonyl group in its internal structure which bends the isothionate molecule into a trigonal planar geometry.

The two groups of surfactants also showed differences as far as the degree of penetration of water molecules into the lipid space. This penetration may be semi-quantitatively estimated according to the following estimations. The relation between interlayer spacing and the amount of water in the structure is similar to the earlier relation used for the lipids.

$$d_{calc} = d_0 \ (1 + \phi_W / \phi_{lipid}) \quad (3)$$

d_{calc} is the calculated interlayer spacing assuming complete separation of the water and the lipids within the bilayer. d_0 represents the interlayer spacing of the lipids at zero water content, ϕ_W is the volume of water present and ϕ_{lipid} is obtained by using the density values of the lipids within the mixture. These values are given in Table 3. The density of each component in the bilayer was considered equal to its value in bulk. The penetration percentages according to Eqn (2), Table 2, reveal that the lipid mixture after addition of SDS and the two Igepons behaves entirely differently towards water. Not only did the Igepons attract all the lipids into the anchored layer but their presence obviously prevented any water penetration in between the lipids. It seems that the lipids extracted into the layers are efficient in preventing the water from penetrating the lipid part of the structure.

This behavior should be contrasted by that of the cationic surfactants. Ad-

TABLE 3

Lipid density values

Component	Density ($g\ cm^{-3}$)
Phosphatidylethanolamine	1.19[a]
Cholesterol sulphate	1.00[b]
Cholesterol	1.03[a]
Triolein	0.92[c]
Myristic	0.86[d]
Linoleic acid	0.90[c]
Oleic acid	0.88[c]
Palmitic acid	0.85[e]
Palmitoleic acid	0.90[b]
Stearic acid	0.85[c]
Oleic acid palmityl ester	0.85[b]
Squalene	0.86[c]
Pristane	0.78[c]
Ceramides	1.00[b]

[a]Crystal data, Ref. [25].
[b]Approximation.
[c]Merck Index, Ref. [26].
[d]For melt at 60°C, Ref. [25].
[e]For melt at 80°C, Ref. [25].

dition of this kind of surfactant left the d_0 values at a high level, i.e. their presence did not change the lipid organization to any significant degree. On the other hand, their presence gave a most enhanced water penetration into the lipid layer. The fact that the interlayer spacing decreased with increasing water content (Fig. 2) suggests that the fatty acid chains of the bilayer are opening up to accommodate the lipids from the methyl layer resulting in the observed decrease. We speculate that this occurs because water molecules solvate the positive and negative head groups of the corresponding cationic surfactant and the anionic lipid present in the bilayer. This weakens their attractive force and allows the chains to separate.

Hence the model presented gives a quantitative distinction between cationic and anionic surfactants. On the other hand, the model did not provide a clear difference between the anionic SDS and the nonionic Tween 20. This is surprising in that the SDS is a strongly irritating surfactant and Tween 20 is perhaps the mildest possible [21]. However, their relative irritancy is traditionally based on their ability to elicit an inflammatory response resulting in measurable erythema. If we consider that inflammation is a complex mechanism involving numerous factors the results are not surprising. Additionally, we do not as yet know anything about the comparative perceived skin drying

ects of these surfactants. This more immediate effect probably results from ect surfactant action on the stratum corneum components.

MMARY

A model for the lipid structure in stratum corneum showed a pronounced tinction between changes caused by cationic surfactants and anionic ones. ıe model failed to distinguished between anionic and nonionic surfactants.

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