Interaction of a Model Skin Surface Lipid With a Modified Triglyceride

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A study of the interaction between a model skin surface lipid (SSL) and an oil base skin softener (G2) was made by comparing the phase behavior of these substances in combination with the water/triethanolamine: oleic acid (1:1 wt ratio) system. A principle feature of the water/G2/triethanolamine:oleic acid (TEA:OL) system was the formation of a lamellar liquid crystal region that incorporated an average of 40% G2 over the 10-45% water range. The phase behavior of the water/SSL/TEA:OL system demonstrated only over a 4-9% water range. At greater than 5% SSL, there is the complete absence of single phase regions above 10% water.

From comparison of the phase regions and the small angle X-ray diffraction results, it is found that for G2/SSL mixtures the phase behavior of the lamellar liquid crystal is dominated by the SSL and the interlayer spacing of the lamellar liquid crystal is dominated by G2.

Xerosis, the term used to describe dry, rough skin, is a condition that is considered almost universal among the elderly. Despite the prompt response of the condition to the application of emollients, such skin softeners do not actually correct xerosis itself (1). This fact is evident from the return of the rough, dry appearance of the skin as soon as the emollient is worn away or removed by washing. Recently, a new type of skin softener has been developed. This product, 2-(alkoyloxy)-1-[(alkoyloxy)methyl]-ethyl-7-(4 heptyl-5,6-dicarboxy-2-cyclohexene-1-yl) heptanoate (G2), differs from otherskin softeners in its ability to change the lipid structure of the stratum corneum (2) even after washing.

G2 has a tryglyceride structure and is shown in Figure 1. The G2 interaction with the lipids of the skin, especially those of stratum corneum, has been demonstrated (2). Such an interaction could be a factor in the skin softening abilities of G2.

Skin surface lipids (SSL) originate from two sources, sebum from the sebaceous glands and epidermal lipids from the stratum corneum. They contain diglycerides, cholesterol, fatty acids, triglycerides, wax esters, cholesterol esters and squalene (3). Cholesterol is almost totaly of epidermal origin, while the wax esters and squalene are of sebaceous origin. With this in mind, the interactions and association structures in a system of G2, SSL, surfactants and water are a necessary and useful basis both for formulation efforts of skin care products and also in order to understand the structures formed on the skin and in the stratum corneum at application of G2 and at a subsequent washing process. It is obvious that the second problem is complex, involving the structure modifications of the interior lipids of stratum corneum.

In this publication we limit our efforts to the relations with skin surface lipid and the phase behavior of the systems water/triethanolamine:oleic acid (1:1 wt ratio) with G2 and SSL. The triethanolamine:oleic acid weight ratio was chosen as one in order to avoid the formation of a liquid crystal directly. The effect of these two substances on the lamellar liquid crystal found in the system was investigated using low angle X-ray diffraction.

EXPERIMENTAL

Model Skin Surface Lipid. A model skin surface lipid was formulated based upon chromatography results of various investigators (4-6). The components, weight percentage, source and purity are given in Table I. After mixing, a liquid which contained no crystalline material was obtained at room temperature. Care was taken to keep the model lipid mixture frozen when not being used for the preparation of samples.

Chemicals. G2 was purified as described previously (8), and the triethanolamine (Fisher Certified), oleic acid (Fisher Purified) and triolein (Sigma 99%) were used as received.

TABLE 1

Components, Weight Percentage, Source and Purity of Model Skin Surface Lipid

Component	Percentage	Source (purity)
Oleic acid	16.5	Fisher (purified)
Myristic acid	1.9	Fisher (reagent)
Triolein	41.8	Sigma (99%)
Oleic acid palmytic ester	20.3	Sigma (98%)
Cholesteryl oleate	3.0	Sigma (97%)
Pristane	2.8	Aldrich (96%)
Squalene	12.2	Aldrich (98%)
Lecithin	1.5	Purified according to (7)

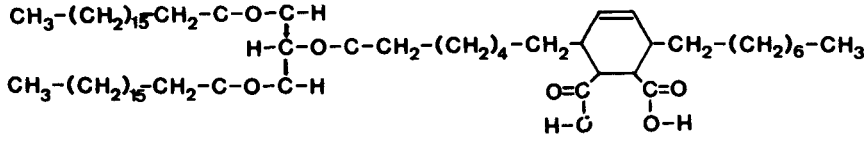

FIG. 1. The structure of G2.

Phase Determinations and X-ray Diffraction. Phase boundaries of the liquid isotropic phases were determined by mixing two of the components and titrating with the third, a method that also gave approximate informatin about the liquid crystalline regions. The borders of these regions, and especially those of the liquid crystalline regions, were obtained by thoroughly mixing selected compositions near phase boundaries and allowing them to equilibrate at 30 ± .1 C for a few days. Thorough mixing was achieved by centrifuging the matrix repeatedly through a constriction in a sealed 7 mm glass tube. The mixed sample was then checked by visual examination, optical microscopy and X-ray diffraction to distinguish the phase behavior.

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

RESULTS

The phase behavior of G2 in the four-component system water/G2/triethanolamine:oleic acid (TEA:OL) is shown in Figure 2 and is similar to more traditional three-component systems of water, surfactant and a hydrophobic amphiphile such as a long chain carboxylic acid (9). At high water content two isotropic phases exist. The isotropic region at highest water content exhibited a clear bluish appearance typical of larger particle size (∼ 1000 Å), while the isotropic phase between 60-85% water was clear and colorless. The large hexagonal liquid crystal region is virtually unaltered by the addition of G2 above 20% water. At lower water concentrations the destabilization of the hexagonal liquid crystal dictates the shape of the isotropic solubility region to accept water significantly decreases.

At higher G2 concentrations both an isotropic liquid phase and a lamellar liquid crystalline phase exist. The isotropic phase contained up to 38% water. The ratio of G2 to TEA:OL at which the maximum amount of water solubilization occurs is the same as the point where the maximum amount of TEA:OL is soluble in G2, i.e. G2/TEA:OL = 75/25. The lamellar liquid crystal region for the G2 system had a clear yellowish appearance, with the slight coloring being typical of systems containing the viscous, yellow G2. The interlayer spacings were determined for the lamellar and hexagonal liquid crystals for the compositions obtained by adding G2 to 50/50 and 75/25 TEA:OL/water mixtures (Fig. 3). The system in Figure 2 contains more than three components, and the tie-lines generally were not in the plane shown except in areas with low surfactant content. Approximate separations between two- and three-phase regions are indicated in the diagram.

The phase behavior for the water/SSL/TEA:OL in a 1:1 weight ratio (Fig. 4) demonstrates behavior vastly different from the previously described system with G2 as the third component. Immediately noticeable is the complete lack of single phase regions above 30% water and, with the addition of more than 5% SSL, the lack of single phase regions above 10% water. The hexagonal liquid crystal phase is incapable of solubilizing the SSL at water contents greater than 30%, and

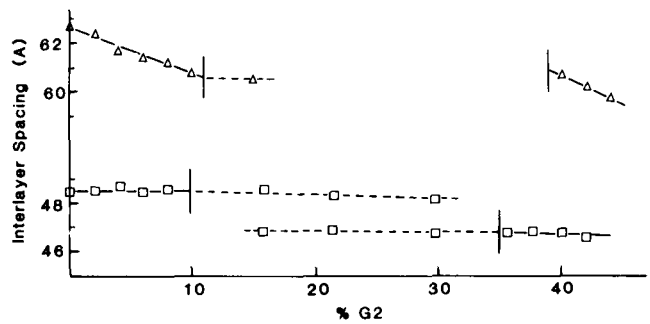

Fig. 3. Small angle X-ray diffraction results for the Water/G2/TEA:OL (1:1 wt ratio) system.

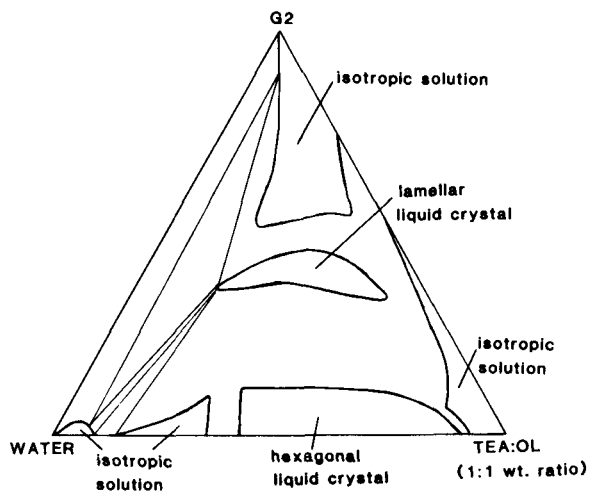

Fig. 2. Partial phase diagram for the system Water/G2/(TEA:OL) (1:1 wt ratio) at 30 C.

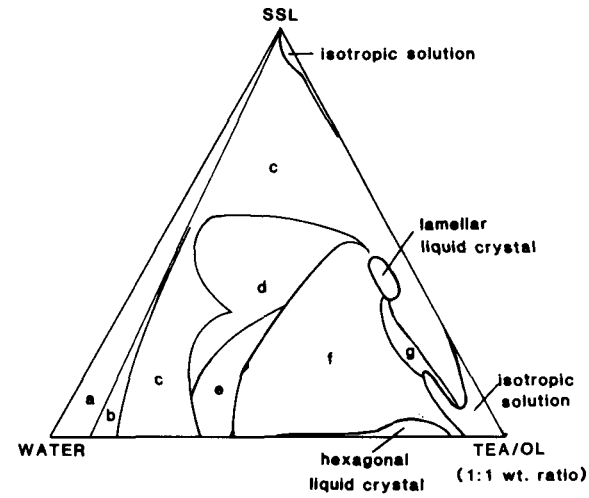

Fig. 4. Diagram showing the complex phase behavior for the multiple component Water/SSL/TEA:OL system. The multiple phase regions were observed to have the following appearance after centrifugation: a) cloudy white and clear gray isotropic layers; b) cloudy white, clear gray and anisotropic layers; c) cloudy white and clear colorless isotropic layers; d) cloudy white-stable to centrifuging; e) cloudy white, clear colorless isotropic and anisotropic layers; f) lamellar and hexagonal liquid crystal mixture; g) isotropic solution and lamellar liquid crystal mixture.

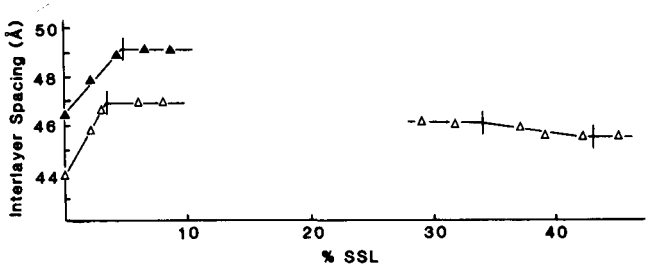

Fig. 5. Small angle X-ray diffraction results for the Water/SSL/TEA:OL (1:1 wt ratio) system. ▲, 20/80 wt ratio Water/TEA:OL; △, 13/87 wt ratio Water/TEA:OL.

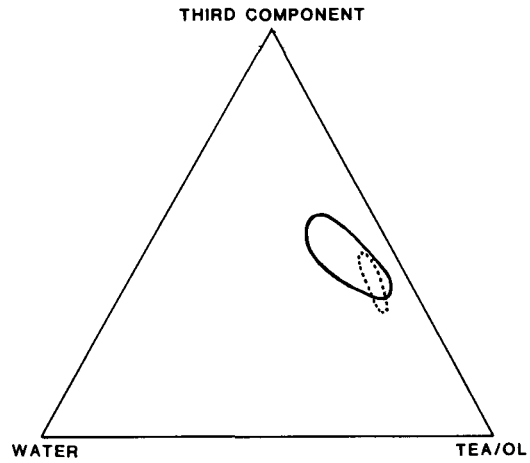

Fig. 6. Partial phase diagram showing the lamellar liquid crystal region at 30 C for the system Water/Third Component/TEA:OL (1:1 wt ratio) where the third component is ————, G2:SSL in 1:1 weight ratio; ----, Triolein.

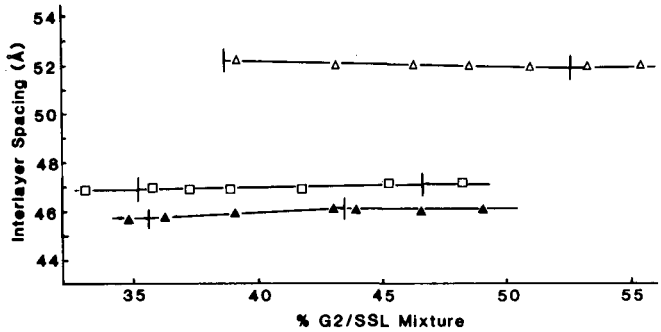

Fig. 7. Small angle X-ray diffraction results for the Water/G2:SSL (1:1 wt ratio)/TEA:OL (1:1 wt ratio) system. △, 25/75 wt ratio Water/TEA:OL; □, 13/87 wt ratio Water/TEA:OL; ▲, 10/90 wt ratio Water/TEA:OL.

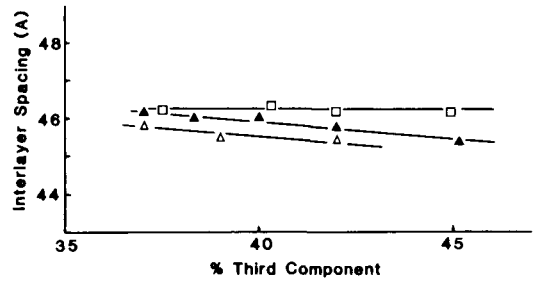

Fig. 8. Small angle X-ray diffraction results for the Water/Third Component/TEA:OL (1:1 wt ratio) system for the Water/TEA:OL wt ratio of 13/87. □, Triolein as the third component; ▲, Triolein/SSL as the third component; △, SSL as the third component.

can solubilize only 4% of the SSL at optimum water/TEA:OL ratio.

The solubility area at high TEA/OL content displayed a slightly different shape, while the lamellar liquid crystal region was significantly reduced in size compared to the G2 diagram. X-ray data for liquid crystalline phases are given in Figure 5. The isotropic liquid region at high SSL content reached 25% by weight of the TEA/OL mixture, but gave only limited solubilization (2-3%). At high water content various multiple phase behavior occurred in all parts of the diagram. Because more than three pure components are represented on the pseudo ternary phase diagram, the "tie-lines" between the different multi-phase regions are no longer necessarily straight.

The lamellar liquid crystal regions for a 1:1 by weight mixture of G2/SSL and for triolein as the third component also were determined. As seen in Figure 6, the mixture of the immiscible G2 and SSL mixture produced a significantly larger lamellar liquid crystal region that is located in the same concentration area of the diagram as the lamellar liquid crystal region in the water/SSL/TEA:OL system (Fig. 6). The triolein system exhibited phase behavior similar to the SSL system. Interlayer spacings for both systems are given in Figures 7 and 8.

DISCUSSION

The results clarified several aspects of the properties of G2 and its relations with sebum, surfactants and water. At first the phase diagram on Figure 2 shows that without sebum the behavior of G2 in contact with a surfactant and water is what may be expected from a carboxylic acid, not the behavior of a triblyceride.

The similarity of behavior with that of a carboxylic acid is exemplified by the pronounced solubility of the surfactant in G2 and the significant water solubilization into that solution (10). A formal calculation of carboxylic and triethanolamine groups for the composition of maximum solubility of the triethanolammonium oleate in G2 gives a ratio of the first two to the latter of 1.16. This is considerably lower than the corresponding value of 3 for the octanoic acid/sodium octanoate combination (10). An investigation into the bonding conditions in the present system appears to be of interest.

The difference from the phase behavior of sebum in the corresponding situation is distinct (Figs. 2 and 3). The sebum mixture behaves like a substance with an entirely hydrophobic character. This difference is well illustrated by the area of the lamellar liquid crystals in the two systems.

G2 gives a lamellar liquid crystal which accepts water to a level of 45% by weight; the corresponding structure with sebum accommodates a maximum of 9% water. On the other hand, a combination of G2 and SSL in a 1:1 ratio accepts only 16% water and the shape of the area similar to the one in the sebum system. In this situation the G2 behaves like a hydrophobic substance similar to triolein.

The packing of G2 into the lamellar phase is a different matter. The effect on the interlayer spacings is obtained by extrapolating the d-spacing vs percent third-component plot to 100% third component, as a reasonable point of comparison (Table 2). The triglyceride triolein gave an extrapolated value of 46 Å, which is dramatically larger than the value for sebum and significantly larger than the value of 44 Å observed when G2 is the third component (Table 2). From this we can conlcude that G2 strongly influences the packing within the lamellar liquid crystal, causing the chains of the bilayer to be more extended.

From this we would possibly expect the extrapolated interlayer spacing of the SSL/G2 mixture to be as large as that found for G2 alone, but this treatment cannot explain why the extrapolated interlayer spacing of the mixture is larger than that found for G2. The reason for this may be found after consideration of the components used in the model SSL. The model SSL contains not only lipids but also the hydrocarbons pristane (2.8%) and squalene (12.2%). The addition of G2 obviously caused an enhanced localization of these hydrocarbon compounds between the methyl group layers (11).

Taken as a whole, the results indicate that G2's ability to soften the skin may be linked to its interactions with the lipids of the skin. Especially so, the interaction between G2 and the lamellarly arranged lipids between the squames of the epidermis (12) may be an important factor. Awaiting further results, it is apparent that G2's skin softening properties, unlike other skin softeners that affect either the proteins or moisture content of the skin, are due to structural effects upon the lipids of the skin.

TABLE 2

Extrapolated Interlayer Distances for the Lamellar Liquid Crystal (Figs. 2 and 6)

Added Compound	W/(TEA:OL ratio	d_{100}	d_o
G2	25/75	44.4 ± 3.0	48.5 ± 2.0
SSL	13/87	39.8 ± 4.1	49.3 ± 2.8
SSL/G2	25/75	50.7 ± 1.2	53.1 ± 1.2
	13/87	48.1 ± 0.8	46.2 ± 1.0
Triolein	13/87	46.0 ± 1.8	46.4 ± 1.0
Triolein/SSL	13/87	39.9 ± 1.6	50.0 ± 1.2

Statistical ranges are for two standard deviations (∿ 95% confidence).

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[Received February 1, 1985]

ERRATUM

The Annual Index published in the December 1985 issue of the *Journal of the American Oil Chemists' Society* was for the *Journal's* 1985 issues. An incorrect year was given for the Index.