Colloid Polym Sci 274:153–159 (1996)

ORIGINAL CONTRIBUTION

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Amphiphilic association structures in the system water, vitamin E, lecithin and phosal 75 SA

Received: 24 January 1995
Accepted: 27 July 1995

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Abstract The main features of the system water, vitamin E, lecithin and Phosal 75 SA was determined using optical microscopy and low angle x-ray diffraction.

The results showed the lecithin/water lamellar liquid crystal to be retained when the lecithin was gradually replaced by Phosal 75 SA. The vitamin E was solubilized in the lamellar liquid crystals to a maximum level in the range of 15–20% by weight.

The vitamin E intermingled with the amphiphile in the liquid crystal causing only minor structural changes.

Key words Microemulsions – surfactants detergents – liquid crystals – cosmetic compounds – fragrances

Introduction

The structure of lyotropic liquid crystals has been thoroughly investigated after Ekwall's pioneering research [1] in the area. Both the structure and the dynamics are known to a satisfactory degree for aqueous systems [2–10] as well as nonaqueous combinations, in which water is replaced by polar organic substances [11–18].

One structural feature, which has not attracted the attention it deserves is to use the lamellar liquid crystal to determine the location and conformation of a large and complex amphiphilic molecule at an interface [19–20]. This method has special appeal for biologically active molecules, because of the prevalence of lamellar structures in biological systems such as biomembranes, mitochondria, chloroplast and others.

One lamellar structure to attract significant interest in recent years is the stratum corneum lipid structure. Although complete agreement has not been reached [21, 22] as to the exact composition or the mobility of the structure [22–27] the fact that the stratum corneum lipids are in a lamellar arrangement is beyond dispute. The stratum corneum lipids encounter a great variety of amphiphilic structures during cleaning with aqueous solutions of surfactants and during application of cosmetic lotions and creams as well as different topical pharmaceutical formulations. These are in the form of solutions, microemulsions, emulsions or vesicular solutions; a fact that at first may indicate a multitude of interaction mechanisms. However, these different formulations rapidly lose water ($\simeq 0.5$ h) and the remaining vehicle is of a much more limited structural variety [28]. Hence, it is essential to understand the phase changes and structural modifications of each phase under reduced content of water and volatile solvents.

This information is obtained from phase diagrams and the present contribution describes the modification of the gross phase behavior of a system water, lecithin, vitamin E acetate, when lecithin is replaced by a commercial surfactant, a combination of lecithin, ethanol and fatty acids. It should be realized that the number of components is increased, but the phase maps presented are an exact description of the conditions in a plane through the total

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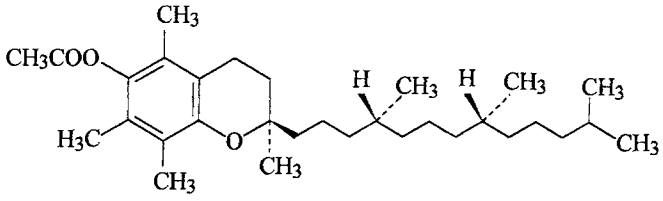


Fig. 1 The structure of vitamin E acetate

system. Such a representation cannot include tie-lines, but the special representation of one-phase areas is completely correct. Vitamin E acetate was chosen as the fourth component, because of the need for information about its location in a lamellar structure against its importance as an anti-oxidant for skin [29–31]. It is of utmost importance to realize that the anti-oxidant behavior of α-tocophecol depends on it being in a liquid crystalline structure (32).

All these phenomena depend on the location of the vitamin E acetate location in a lamellar structure, e.g., its potential localization to the space between the methyl group layers in the structure or the partition between this location and one interjected between the hydrocarbon chains of the liquid crystal. The complex structure of the vitamin E, Fig. 1, acetate with its weak polar components leaves no indication of the location. In addition, recent investigations (33) have demonstrated a surprising change in the dependence of the water content of the solubilization of the vitamin E acetate in a lamellar liquid crystal.

The present investigation answers this question and, in addition, provides information about the influence on these phenomena by the added components to lecithin in a typical commercial surfactant.

Experimental

Materials

Lecithin (LEC) extracted from egg (purified to be acceptable for intravenous injection) Kabi Chem. Co., Stockholm, Sweden. Vitamin E acetate (VE) (13601419) Sigma Chem. Co., St. Louis, Missouri. Phosal 75 Sa (PH) Rhone Poulenc Rorer, Köln, Germany (used as received, 75% by weight phospholipids, 15% glycerides, fatty acids, 10% ethanol) H_2O doubly distilled water.

Phase diagrams

The maximum solubility of PH in H_2O and boundaries for the various phases were established by direct titration using visual and microscopic observation. The liquid crystalline phase was identified from its pattern in an optical microscope between crossed polarizers and its phase limits confirmed by low-angle x-ray diffraction.

Low-angle X-ray diffraction

The samples were introduced into special thin glass capillary tubes of diameter 0.5 mm. A Ni-filtered Cu-radiation was used (1.542 Å) for the x-ray movement and the detector was a Tennelec gas ionization model (PSD-1100). The LAXD was used in the determination of the three phase regions. That is, any point taken within a three-phase region of a three-component system will have a constant interlayer spacing due to the contact with only one point of the liquid crystal region.

Results

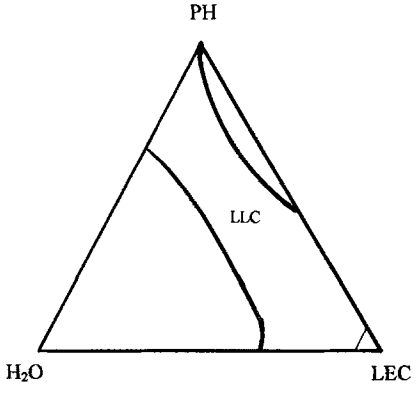
The results are described with phase diagrams first, followed by the low-angle x-ray results of the lamellar liquid crystal.

The four components water (W), lecithin (LEC), Phosal 75 SA (PH) and vitamin E (VE) give rise to four three-component diagrams. They will be described individually and subsequently a three-dimensional presentation will be made of the main features of the entire system.

W/LEC/PH, Fig. 2

Water added to PH gave a lamellar liquid crystal reaching from approximately 1% (by wt.) of water to 36%. With increased LEC/PH ratio the minimum water ratio to form

Fig. 2 The system water (H_2O)/lecithin (LEC)/Phosal 75 SA (PH) shows one large area of liquid crystal (LC)



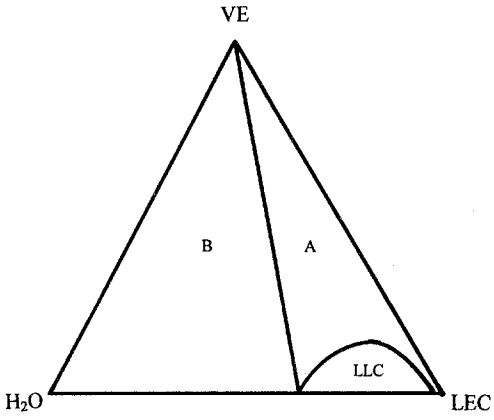


Fig. 3 The system water (H_2O)/lecithin (LEC)/vitamin E acetate (VE) shows a lamellar liquid crystal region (LLC) a three-phase region (B), H_2O/LLC/VE, and a two-phase region LLC/VE

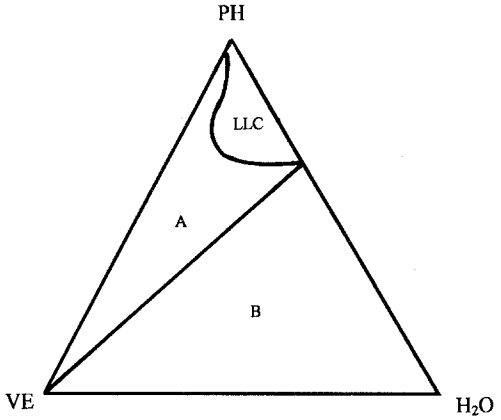


Fig. 4 The system water (H_2O)/lecithin (LEC)/Phosal 75 SA (PH) shows a lamellar liquid crystal region (LLC) a three-phase region (B), H_2O/LLC/PH and a two-phase region LLC/PH

the liquid crystal was increased to a maximum of 7% for a LEC/PH wt. ratio of 3/7. Increased LEC/PH ratio gave a reduction of the minimum water content reaching zero at an LEC/PH ratio of 1.56. The liquid crystal range for zero water content reached to LEC/PH equal to 92/8.

Greater LEC contents were not investigated. The maximum water content was reduced to 28% by wt. for an LEC/PH ratio of 87/13 and increased to 36% again for LEC. No significant solubility for the lecithin or the Phosal was found in the water for any ratio of the two. This statement should not be miscontrued to imply that no components of Phosal would be transferred to water at equilibration of the lamellar liquid crystal with water. A few percent ethanol would be present in the aqueous phase, and the indicated three-phase areas in Figs. 2 and 3 are approximate to a few percentage points.

W/LEC/VE, Fig. 3

This diagram is characterized by the lamellar liquid crystal of LEC +W in the water percentage range 5–35. With a maximum solubilization VE to 15% at a W/LEC weight ratio of 0.13. The three phases in equilibrium were 100% W, 100% VE and 64% LEC/36% W.

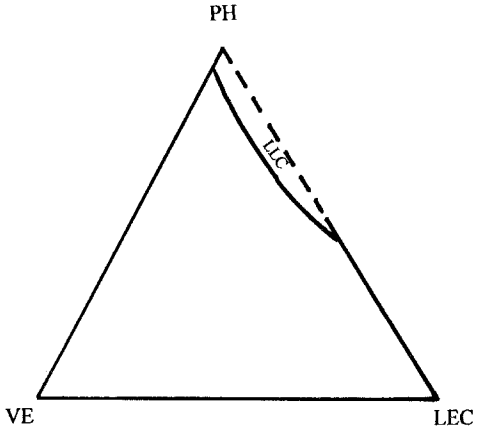
W/PH/VE, Fig. 4

This diagram is similar to the preceding one with a PH/W lamellar liquid crystal in water percentage range 1–35. The liquid crystal solubilized VE to a maximum of 20%. No significant solubility in water was detected by any of the two components with the exception of ethanol being extracted from the Phosal into water. Such a change cannot be depicted in the phase diagram because the tie-lines are not in the plane of the diagram. Again, and with this proviso, the three phases in equilibrium were 100% W, 100% VE and 64% LEC/36% W.

LEC/PH/VE, Fig. 5

PH is an isotropic liquid which accepted 55% LEC with less than 1% VE solubilized. Higher VE content gave a band of liquid crystal covering a region up to 5% of VE as a continuation of the lamellar liquid crystal on the LEC/PH axis between 8 and 44% PH, Fig. 2. In an overview of the total system, Fig. 6, the continuity of the lamellar liquid crystalline phase and the huge three-phase space W/VE/lamellar liquid crystal are illustrated.

Fig. 5 The system vitamin E acetate (VE)/lecithin (LEC)/Phosal 75 SA (PH) shows a small area of a lamellar liquid crystal



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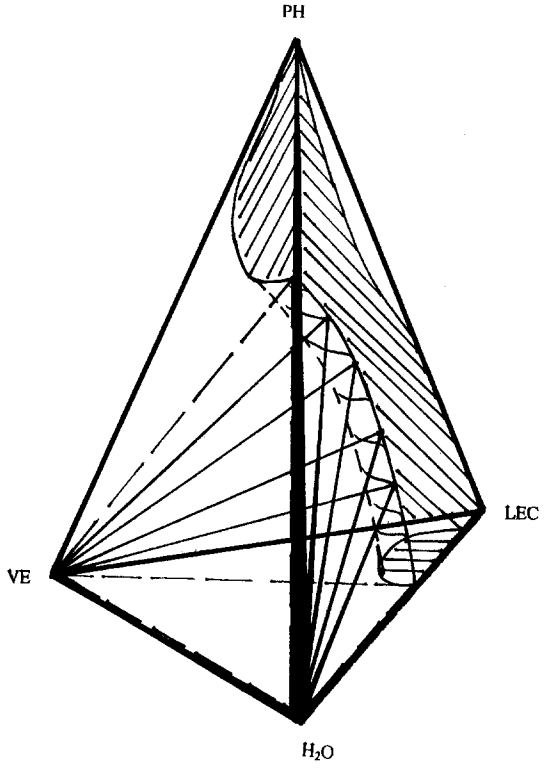

Fig. 6 The four-component system water (H_2O)/vitamin E acetate (VE), Phosal 75 SA (PH)/lecithin (LEC)

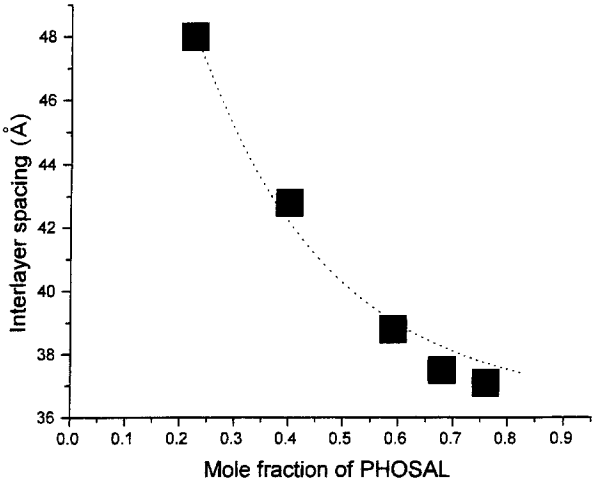

Fig. 7 Plot of interlayer spacing vs. mole fraction of Phosal 75 SA

Interlayer spacings were calculated from low-angle x-ray diffraction data. Figure 7 shows the interlayer spacing for the combination of LEC and PH with no additional compound present. The interlayer spacing is strongly reduced for increased Phosal content to a mol fraction of 0.6 and leveling off for higher contents of PH.

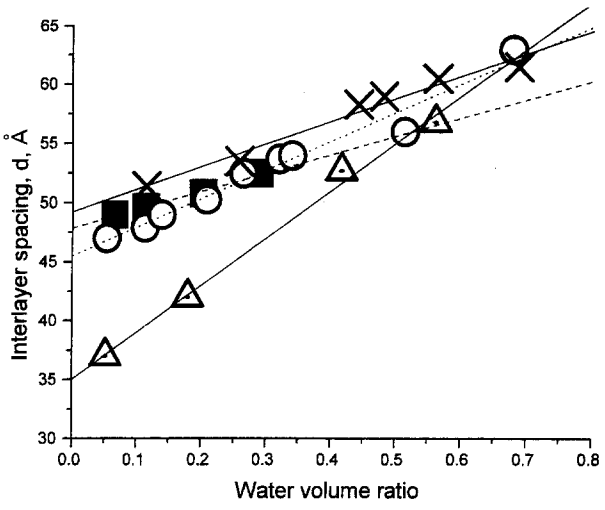

Fig. 8 Plot of interlayer spacing vs. volume ratio of added water for Phosal 75 SA/lecithin (LEC). ■ 100% lecithin (LEC), ○ 70% lecithin (LEC)/30% Phosal 75 SA, △ 100% Phosal 75 SA, x 10% Phosal 75 SA/90% lecithin (LEC)

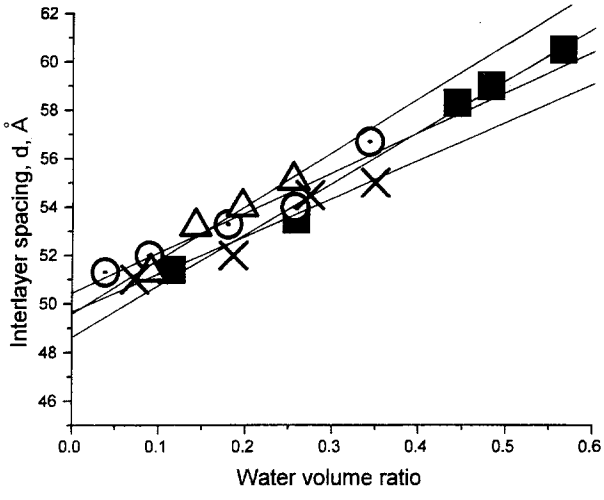

Fig. 9 Plot of interlayer spacing vs. volume ratio of added water for lecithin (LEC)/vitamin E (VE) system. ■ lecithin, ○ lecithin/vitamin E acetate (w/w) 95/5, x lecithin/vitamin E acetate (w/w) 90/10, △ lecithin/vitamin E acetate (w/w) 85/15

Figure 8 displays the interlayer spacings for LEC/PH combinations with added water. The lecithin pattern is retained for PH wt. fractions less than 0.3; higher content of PH resulted in a significant increase of the slope and reduction of the value at low water contents.

Addition of vitamin E to the lecithin up to 15% by weight gave no significant change of the interlayer spacings for the lecithin/water lamellar liquid crystal, Fig. 9.

The Phosal system, on the other hand, gave a significant response. Figure 10 reveals the increase in interlayer

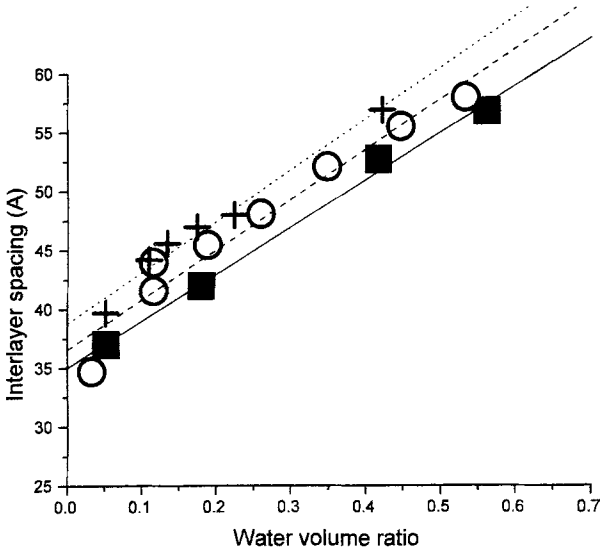

Fig. 10 Plot of interlayer spacing vs. volume ratio of added water for Phosal 75 SA/vitamin E (VE) system. ■ 100% Phosal, ○ 95% phosal 75 SA/5% vitamin E acetate (VE), + 80% Phosal 75 SA/10% vitamin E acetate (VE)

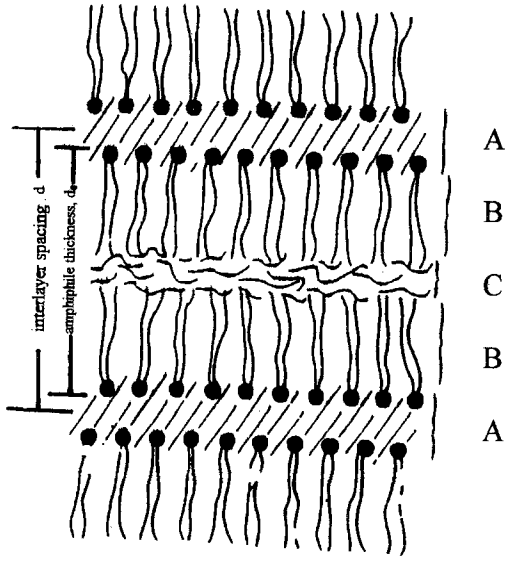

Fig. 11 The lamellar liquid crystalline structure

spacing after addition of vitamin E. The slopes of the lines did not change significantly.

Discussion

The results show a number of features, which deserve an analysis. At first, the Phosal 75 is a liquid, which is understood from the fact that, in addition to the phospholipid, it contains fatty acids, different glycerides and 15% by weight of ethanol. Secondly, the combination of Phosal and lecithin forms a lamellar liquid crystal without addition of a polar solvent. Obviously the added lecithin brought the phospholipid content to a sufficient level to change to a lamellar liquid crystal. It should be observed that a non-amphiphilic solvent is not needed to form a lamellar liquid crystal. An early investigation by Gan-Zuo [29] showed the addition of a polyoxyethylenealkylether to lecithin to result in the formation of a lamellar liquid crystal. It is instructive to note the similarity of the interlayer spacing in the present investigation and the one by Gan-Zuo [29]. In both cases the interlayer spacing is strongly reduced with addition of the compound causing a change from solid to liquid crystalline state. After this stage is reached, the interlayer spacing became fairly constant. The earlier explanation [29] for the change in interlayer spacing appears reasonable also in the present case. At low additions the amphiphile is localized in the space between the methyl group layer of the solid lecithin layer, C, Fig. 11, giving a large interlayer spacing. With increased addition the lecithin bilayer becomes sufficiently disordered to permit the added amphiphile to penetrate into the zone B, Fig. 11. This penetration causes a reduction of the interlayer spacing, which becomes approximately constant after all the added molecules are in zone B, Fig. 11.

The structural changes caused by addition of water to Phosal are also illustrative of the sensitivity of the liquid/liquid crystal transition. The isotropic liquid was changed to a lamellar liquid crystal for extremely small additions of water, $< 1\%$ by weight. A comparison of the properties and structure of this liquid crystal to the one with lecithin is interesting and will be made after a brief review of the relation between geometrical dimensions and x-ray diffraction.

The x-ray results provide direct information about the interlayer spacing d, Fig. 10, but also about the degree of water penetration into the amphiphilic layer, B, Fig. 10. Assuming no change in tilt of the molecules and accepting that changes in the degree of order have only a minor influence on interlayer spacing [30] one finds

$$d = d_0(1 + R)/(1 + \alpha R)\,, \tag{1}$$

in which d_0 is the interlayer spacing extrapolated to zero water content, R is the volume ratio of water and α the fraction of water penetrating into the zone B from zone A, Fig. 10.

Limiting the α value to small values of R, Eq. (1) is written

$$d = d_0(1 + R)(1 - \alpha R) \tag{2}$$

and neglecting the square term in R

$$d = d_0[1 + (1 - \alpha)\, R], \tag{3}$$

α is calculated directly,

$$\alpha = 1 - (\partial d/\partial R)/d_0\,. \tag{4}$$

With this background the geometrical characteristics of the entire system may be made. At first the interlayer spacing for the lamellar liquid crystal of Phosal 75 cannot be given, because it does not exist, Fig. 7. On the other hand, the straight line extrapolation to zero water content in Fig. 10 provides a value of 35 Å, which, in term, agrees with a non-linear extrapolation in Fig. 7 supporting the interpretation of the values in Fig. 7.

In contrast to the PH/W system, the LEC/W liquid crystal shows an extrapolated interlayer spacing to zero water content to 47 Å. This value is close to the maximum value in Fig. 7 for a mole fraction of LEC of 0.23 and a conclusion must be drawn that this value is the limiting distance for a lecithin double layer in a lamellar liquid crystal. This deduction is supported by an approximate calculation of an extended hydrocarbon chain with 18 carbon atoms. Counting the methyl group contribution as 1.5 Å and each of the methylene bond projections as 1.265 Å, the distance over a double layer would be 46.5 Å. Adding a reasonable length for the polar group, the value 47 Å is of a magnitude indicating fairly extended hydrocarbon chains of the lecithin. The slope in Fig. 8 gives a water penetration value of α, of 0.5, revealing a polar part permitting significant access of water into zone B, Fig. 11.

The Phosal amphiphile system is entirely different. The polar and nonpolar solvents are present in a sufficient amount to reduce the interlayer spacing by one third which is a reasonable value considering the phospholipid content of 75%. In this case, the penetration of water shows a negative value, Table 1, which means that the addition of water extracts polar solvents from zone B into A and possibly also causes a transfer of non-polar solvent into zone C, Fig. 11. It should be understood that these two transfers are dependent; extracting a polar solvent from B, Fig. 11 will separate a less polar component to be moved to zone C.

This kind of reasoning is also applicable to the location of vitamin E. The values of d_0 and the α values for the system water, lecithin, vitamin E, Fig. 9, Table 1 makes it obvious that the vitamin molecule is located in zone B, Fig. 11 in the water/lecithin system. Both the d_0 and the α values remain approximately constant after addition of vitamin E acetate. The result is not expected considering the molecular structure of vitamin E acetate, Fig. 1. The extremely weak polarity conferred by the ester group combined with the branched hydrocarbon would rather indicate a location in layer C, Fig. 11, but some steric reasons, which are not directly evident, may account for the results. The interaction between the ester group and the polar part of the lecithin favoring a location in layer B, may be assisted by the influence by the benzene ring in the vitamin. Christenson [34, 35] earlier demonstrated the preference for the polar parts in a colloidal association structure by benzene. As a matter of fact, the partition of benzene between the polar and non-polar part in a nonionic surfactant of the polyethyleneglycolalkylether type was 3/1 (36). The interaction is sufficiently strong also in ionic systems (37) to influence the onset of association. Hence, it may safely be assumed that the benzene ring of the vitamin E acetate contributes to its location in the lamellar liquid crystals of this investigation.

Table 1 Interlayer spacing and water penetration values for the three different systems

LEC/PH/H_2O	Interlayer spacing (Å)*	Water Penetration
100% PH	35	−0.11
30% PH/70% LEC	45.5	0.44
10% PH/90% LEC	46.5	0.43
100% LEC	47	0.47
LEC/VE/H_2O	Interlayer spacing (Å)	Water penetration
100% LEC	48.9	0.59
95% LEC/5% VE	50.2	0.64
90% LEC/10% VE	50.2	0.64
85% LEC/15% VE	50.2	0.64
PH/VE/H_2O	Interlayer spacing (Å)	Water penetration
100% PH	34.3	−0.16
95% PH/5% VE	36.9	−0.14
80% PH/20% VE	39.4	−0.06

* Interlayer spacing at zero water content

The results in the system water, Phosal, vitamin E, may, at first, be interpreted as demonstrating the vitamin molecule to be located in the C layer, Fig. 11. The interlayer spacing was increased after addition of vitamin E and the increase corresponds approximately to the amount of added vitamin E acetate. However, such an interpretation is premature. The increase in interlayer spacing may equally well be ascribed to a non-polar solvent component. In fact, considering the results for the water/Phosal lamellar liquid crystal and the chemical structure of vitamin E, a location in zone B appears most likely.

Acknowledgement This research was funded in part by PAYOT, France and by the New York State Science and Technology Foundation at the Center for Advanced Materials Processing at Clarkson University, Potsdam, New York.

References

1. Ekwall P (1975) In: Brown GH (ed) Advanced in Liquid Crystals Academic Press NY Vol I
2. Bleasdale TA, Tiddy G (1990) In: Bloor DM, Wyn-Jones E (eds) The Structure, Dynamics and Equilibrium Properties of Colloidal Systems Kluwer Academic Pub The Netherlands, p 397
3. Pacynko WF, Yarwood J, Tiddy G (1989) J Chem Soc Faraday Trans 85:1397
4. Kekicheff P, Tiddy G (1989) J Phys Chem 93:2520
5. Sadaghiani AS, Khan A, Lindman B (1989) J Colloid Interface Sci 132:352
6. Maciejewska D, Khan A, Lindman B (1986) Colloid Polym Sci 264:909
7. Ward AJI, Ku H, Phillippi MA, Marie C (1988) Mol Cryst Liq Cryst 154:55
8. Laughlin RG, Munyon RL, Fu Y-C, Fehl AJ (1990) J Phys Chem 94:2546
9. Laughlin RG (1990) JAOCS 67:11
10. Blokhus A, Sjöblom J (1991) J Colloid Interface Sci 141:2
11. Moucharafieh N, Friberg SE (1979) Molec Cryst 49:231
12. Larsen DW, Friberg SE, Christenson H (1980) J Am Chem Soc 102:6565
13. ElNokaly MA, Ford LD, Friberg SE, Larsen DW (1981) J Colloid Interface Sci 84:228
14. Ganzuo L, ElNokaly MA, Friberg SE (1982) Molec Cryst 72:183
15. Friberg SE, Liang P, Lockwood F, Tadros M (1984) J Phys Chem 88:1045
16. Auvray X, Petipas C, Perche T, Anthore R, Rico I, Lattes A (1989) J Phys Chem 93:7458
17. Auvray X, Petipas C, Perche T, Anthore R, Marti M, Rico I, Lattes, A (1990) J Phys Chem 94:23
18. Auvary X, Petipas C, Anthore R, Rico I, Lattes A (1989) J Phys Chem 93:7458
19. Flaim T, Friberg SE (1984) J Colloid Interface Sci 97:26
20. Friberg SE, Osborne D (1986) Colloid Polym Sci 264:182
21. Bartz JT, Wertz PW, Downing DT (1989) J Invest Dermatol 93:280
22. Elias PM (1988) Drug Development Research 13:97
23. Swartzendruber DC, Wertz PW, Kitko DJ, Madison KC, Downing DT (1989) J Invest Dermatol 92:251
24. Guy RH, Fleming R (1988) Chem Rev 88:455
25. Melnik BC, Hollman J, Erler E, Verhoeven B, Plewig G (1989) J Invest Dermatol 92:231
26. Lampe MA, Williams ML, Elias PM (1983) J Lipid Res 24:131
27. Wertz PW, Madison KC, Downing DT (1989) J Invest Dermatol 92:109
28. Friberg SE (1994) J Dispersion Sci Technol 15:359
29. Gan-Zuo L, El-Nokaly M, Friberg SE (1982) Mol Cryst Liq Cryst 72:183
30. Friberg SE, Moaddel T, Morris K, Abramowitz R, Amsberry KL (in press) J Pharm Sci
31. Mayer P, Hermann WP, Wollat S (1993) Cosmet Toiletries (1993) 108:99
32. Ruben C, Larsson K (1985) J Dispersion Sci Technol 6 213
33. Friberg SE, Moaddel T, Brin AJ, J Soc Cosmet Chem (submitted)
34. Christenson H, Friberg SE (1980) J Colloid Interface Sci 75:276
35. Christenson H, Friberg SE, Larsen DW (1980) J Phys Chem 84:3633
36. Friberg SE, Christenson H, Bertrand G, Larsen DW (1984) Rev Micelles 5:105
37. Sjöblom E, Friberg SE (1978) J Colloid Interface Sci 67:16